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Effect of Dexmedetomidine on Postoperative Delirium in Frail Elderly Patients Undergoing Surgery for Gastrointestinal Malignancies: A Randomized, Double-Blind, Controlled Study

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Abstract

Objective: To assess whether intraoperative dexmedetomidine infusion reduces the incidence of postoperative delirium (POD) in frail elderly patients undergoing resection for gastrointestinal malignancies.

Methods: A total of 302 patients were enrolled and randomized into receiving continuous intravenous infusion of dexmedetomidine or normal saline intraoperatively.

The primary outcome was the incidence of POD within 5 days after surgery. The secondary outcomes were the levels of IL-6, CRP, and Tau protein before surgery and on postoperative days 1 and 3, pain scores (at rest and on coughing) and sleep quality scores from postoperative days 1 to day 5.

Results: Compared with normal saline group, the incidence of POD within 5 days after surgery was significantly lower in dexmedetomidine group (13.8% vs. 22.9%, $P = 0.048$). The level of CRP on postoperative day 1 was lower in dexmedetomidine group ($P = 0.030$). The levels of Tau protein were lower on days 1 and 3 ($P = 0.013$ and $P = 0.032$, respectively). In addition, the dexmedetomidine group showed lower postoperative NRS pain scores at rest on day 3 ($P = 0.022$) and during cough on day 2 ($P = 0.031$), as well as better postoperative sleep quality on days 1, 2, and 4 ($P = 0.040$, $P = 0.005$, and $P = 0.018$, respectively).

Conclusion: In frail elderly patients undergoing surgery for gastrointestinal malignancies, intraoperative dexmedetomidine infusion might reduce the incidence of POD within 5 days after surgery.

Keywords: Elderly patients; Frailty; Gastrointestinal malignancy surgery; Dexmedetomidine; Postoperative delirium

Trail registration:http://www.chictr.org.cn/index.aspx, NO. ChiCTR2400092665

(Registration date: November 21, 2024, supplementary registration)

Introduction

Gastric cancer and colorectal cancer are among the most frequently encountered malignancies in clinical practice, and more than half of newly diagnosed cases occur in patients aged 65 years or older[1,2]. The prevalence of frailty is as high as 43.8% in patients with gastric cancer[3] and 60.5% in patients with colorectal cancer[4]. Frailty is defined as an age-related, non-specific clinical state that is mainly characterized by by diminished physiological reserve, leading to reduced capacity for self-repair and resistance to external stressors[5]. Accumulating evidence indicates that preoperative frailty is a significant predictor of adverse postoperative outcomes in elderly patients undergoing gastrointestinal surgery, manifesting as worse postoperative functional recovery, extended length of stay, elevated healthcare costs, and higher rates of both postoperative mortality and hospital readmission[6,7,8,9,10].

Postoperative delirium (POD) is an acute neuropsychiatric disorder characterized by an acute and fluctuating disturbance in attention, consciousness, and cognition[11,12]. POD is a common complication after anesthesia and surgery in elderly patients, with an incidence ranging from approximately 10% to 50% depending on the type of surgery[13,14,15]. POD leads to prolonged hospitalisation, increased hospital costs, higher postoperative mortality, and even an increased risk of dementia and long-term cognitive impairment[13,16]. Accumulating evidence has established preoperative frailty as a significant risk factor for POD, as shown in a meta-analysis of patients aged ≥65 years undergoing elective surgery[17] and in studies of older cancer patients undergoing

abdominal procedures[18]. The biological basis for this association may lie in shared inflammatory pathways, both frailty and POD are characterised by heightened inflammatory responses, with common biomarkers including TNF-α, IL-6, IL-10, and CRP[19,20,21]. Additionally, microtubule-associated protein tau (Tau protein) has recently emerged as a potential biomarker for POD[22].

Dexmedetomidine, a highly selective α_2-adrenergic receptor agonist, is commonly used during anaesthesia. The evidence regarding its role in preventing POD remains inconclusive. For instance, one study has shown that dexmedetomidine significantly reduced the incidence of POD[23], whereas another study has failed to confirm this benefit[24]. Although numerous studies have demonstrated that dexmedetomidine can reduce the incidence of POD, its effectiveness in specific high-risk populations, particularly frail adults, remains uncertain. Therefore, the present study aimed to evaluate whether intraoperative dexmedetomidine infusion would reduce the incidence of POD in frail elderly patients undergoing surgery for gastrointestinal malignancies.

Materials and methods

This randomized, double-blinded, prospective, controlled study was performed with adherence to the principles of the Declaration of Helsinki, approved by the Institutional Review Board (IRB) of the First Affiliated Hospital of Soochow University(approval number: 2024030), and the trial manuscript follows the CONSORT Checklist. Capacity of patients to give consent was determined by physician interview before enrollment in the study. All participants provided written informed consent, approved bythe local

institutional review boards .In addition, Human Ethics and Consent to Participate declarations: not applicable. All subjects provided written informed consent and the research was conducted from January 31, 2024 to June 30, 2025. The study was registered in the Chinese Clinical Trial Registry. (http://www.chictr.org.cn/index.aspx, NO. ChiCTR2400092665).

Study population

The patients were enrolled: age ≥ 65 years, body mass index (BMI) ≥ 18 or ≤ 30 $kg \cdot m^{-2}$, American Society of Anesthesiologists (ASA) physical status II~III, scheduled for elective surgery for gastrointestinal malignancies (preoperative biopsy-proven malignancy) under general anesthesia, surgical duration ≥ 2 hours, fried frailty score ≥3 points, and signed informed consent. The exclusion criteria: severe cardiac, hepatic, or renal insufficiency before surgery, pre-existing cognitive impairment, inability to communicate verbally, severe bradycardia (resting heart rate < 50 bpm), a pre-existing diagnosis of delirium, dementia, history of traumatic brain injury or neurosurgical treatment, and history of psychotropic medication use. The discontinuation criteria included: use of medications not specified in the protocol, missing monitoring records or incomplete case report forms, and voluntary withdrawal from the study.

Randomization and Blinding

Randomization was undertaken using a computer-generated table of codes (SPSS software, version 23.0) with a ratio of 1:1. The codes were sealed in sequentially numbered, opaque envelopes. Patients were randomly assigned to either

dexmedetomidine group or normal saline group.

Patients and the anesthesiologists in charge of data collection were kept blind to group assignment. Meanwhile, surgeons and postoperative assessors were also blinded to the patients' randomization.

Grouping Protocol

Eligible participants were randomly assigned to receive either dexmedetomidine or normal saline during surgery. In dexmedetomidine group, dexmedetomidine was intravenously infused at a loading dose of 0.5 $\mu g \cdot kg^{-1}$ over 15 min before anesthesia induction, followed by a continuous infusion at a maintenance dose of 0.4 $\mu g \cdot kg^{-1} \cdot h^{-1}$ [25]. The infusion was discontinued at abdominal closure. In normal saline group, an equal volume of normal saline was intravenously infused over 15 min before anesthesia induction and continuously infused at the same rate until abdominal closure phase.

Anesthetic management

Pulse oximetry, ECG, temperature, expiratory end tidal carbon dioxide ($EtCO_2$), arterial blood pressure (BP) and heart rate (HR) were monitored for all patients. General anesthesia was induced with propofol (1.0-2.0 $mg \cdot kg^{-1}$), sufentanil (0.4 $\mu g \cdot kg^{-1}$) intravenously. Muscle relaxation was achieved with 0.2 $mg \cdot kg^{-1}$ of cisatracurium intravenously to facilitate endotracheal intubation. Volume-controlled ventilation was used to achieve an $EtCO_2$ of 35-45 mmHg by adjusting respiratory rate and tidal volume. Anesthesia was maintained with 2.0-3.0 % of sevoflurane, remifentanil (0.1-0.3 $\mu g \cdot kg^{-1} \cdot min^{-1}$), and cisatracurium (1-2 $\mu g \cdot kg^{-1} \cdot min^{-1}$). Additional boluses of sufentanil (0.2

μg·kg^{-1}) were administered intermittently as needed. During surgery, dexmedetomidine or normal saline was infused according to the grouping protocol above. BP and HR variations were kept within 20% of the preoperative baseline values during surgery by adjusting the dosage of the anesthetics. And the bispectral index (BIS) value was maintained between 40 and 60 during surgery. Routine use of ondansetron (8 mg) during surgery aimed to prevent postoperative nausea and vomiting (PONV). After surgery, patients were transferred to the Post-Anesthesia Care Unit (PACU) or the Intensive Care Unit (ICU) according to their clinical condition. The tracheal tube was removed after the patient had fully recovered and was assessed to meet the extubation criteria. After surgery, all patients received patient-controlled intravenous analgesia (PCIA). The analgesic pump contained fentanyl 20 μg·kg^{-1} diluted with normal saline to a total volume of 100 ml, with a background infusion rate of 2 ml·h^{-1}. When the postoperative Numeric Rating Scale (NRS) pain score > 3, acetaminophen (oral or intravenous) for mild to moderate pain, and tramadol 50 mg intramuscularly for moderate to severe pain.

Outcomes

The primary outcome was the incidence of POD witnin 5 days after surgery. The secondary outcomes included levels of IL-6, CRP, and total Tau protein measured before surgery and on postoperative days 1 and day 3, pain scores (at rest and on coughing) and sleep quality scores from postoperative days 1 to day 5.

Data collection

The Fried Frailty Scale was used preoperatively to evaluate the frailty status of

patients. It includeded unintentional weight loss (defined as a loss of > 5% of body weight or > 4.54 kg in the past 12 months), reduced grip strength, self-reported exhaustion or fatigue, increased time to walk 4.57 m, and decreased weekly physical activity level. A point of 0 was classified as robust health, 1-2 as pre-frailty, and 3 or more as frailty. Mini-Mental State Examination (MMSE) was used to assess whether patients had pre-existing cognitive impairment. The total score ranges from 0 to 30, and a score < 27 was considered to indicate cognitive impairment.

The 3-Minute Diagnostic Interview for Confusion Assessment Method (3D-CAM) was used to assess preoperative delirium. The incidence of POD within 5 days after surgery was also evaluated using the 3D-CAM, twice daily (at 8:00 AM and 5:00 PM). For patients admitted to the ICU, the CAM for the Intensive Care Unit (CAM-ICU) was used to assess POD, still twice daily (at 8:00 AM and 5:00 PM).

The serum levels of IL-6, CRP, and Tau protein were tested by enzyme-linked immunosorbent assay (ELISA) before surgery, on postoperative day 1, and on postoperative day 3.

Postoperative pain intensity was evaluated with NRS. For the NRS, an 11-point scale was used, with “0” representing “no pain” and “10” representing the “worst pain”. The postoperative pain scores contained NRS at rest and NRS on coughing. NRS was also used to evaluate postoperative sleep quality. On this scale, a score of 0 denoted deep sleep, whereas a score of 10 denoted the most pronounced sleep disturbance.

The duration of postoperative hospital stay and 30-day all-cause mortality (via

telephone follow-up with patients or their family members) were recorded.

Statistical analysis

Based on previous research data, the incidence of POD in elderly patients undergoing gastrointestinal surgery ranges from 8.2% to 54.4%[26]. Another study reported that the incidence of POD in frail elderly patients undergoing non-cardiac surgery was 39.3%[27]. Therefore, we used a POD incidence of 39.3% as the basis for sample size calculation. Assuming that intraoperative administration of dexmedetomidine could reduce the incidence of POD by 40%, the sample size was calculated using PASS 15.0 software. With a power of 80%, a two-sided significance level of $\alpha = 0.05$, and a 1:1 allocation ratio, 137 patients were required per group. Considering a 10% dropout, 151 patients were required per group and the final total sample size was 302 patients.

The normality of continuous data was assessed using the Kolmogorov–Smirnov test. Continuous variables following a normal distribution were presented as mean ± standard deviation, and group comparisons were performed using the independent samples t-test. For continuous variables not following a normal distribution, data were expressed as median (M) and interquartile range (IQR), and intergroup differences were analyzed using the Mann-Whitney U test. Categorical data were described as frequencies and percentages (%) and analyzed using the chi-square test. For the primary outcome, univariate comparative analysis was first conducted, and factors showing significant differences were then entered into a binary logistic regression analysis, with 95% confidence intervals calculated using the Wald method. All statistical analyses were performed using SPSS

23.0 software, and a two-sided *P* value < 0.05 was considered to be statistically significant.

Results

Participants

A total of 282 patients were finally completed the study. A flow chart was shown in(**Figure 1**). The results showed that the baseline characteristics of the two groups were comparable, and the differences between the groups were not statistically significant (*P* > 0.05) (**Table 1**). There were no statistically significant differences in duration of surgery, duration of anesthesia, propofol consumption, intraoperative blood loss, total fluid infusion, and urine output between groups (*P* > 0.05). Regarding anesthetic consumption, patients in the dexmedetomidine group required significantly less sufentanil (52.8 ± 9.2 μg vs. 57.4 ± 7.3 μg, *P* < 0.001) and remifentanil (949.7 ± 343.3 μg vs. 1096.2 ± 281.6 μg, *P* < 0.001) than those in the normal saline group. By contrast, the dexmedetomidine group had a significantly prolonged time to tracheal extubation (30.9 ± 11.7 min vs. 24.9 ± 10.3 min, *P* < 0.001) (**Table 2**). None of the patients exhibited severe bradycardia and hypertension or hypotension (more than or less than 20% of normal blood pressure) intraoperatively.

Primary outcomes

The incidence of POD within 5 days postoperatively in dexmedetomidine group was 13.8% (19/138), while that in normal saline group was 22.9% (33/144). The incidence of POD differed significantly between the groups (13.8% vs. 22.9%, *P* = 0.048). Patients were divided into three groups based on their Fried scores: score = 3, score = 4, and score

= 5. Comparative analysis showed that the incidence of POD was 13.7% in patients with a Fried score of 3, increased to 26.9% in those with a score of 4, and reached 28.6% in those with a score of 5. Further statistical analysis revealed a significant difference in POD incidence among the three groups, which was statistically significant (P = 0.023) (**Table 3**).

Secondary outcomes

On postoperative day 1, the levels of CRP in dexmedetomidine group were significantly lower than those in normal saline group (16.2 [4.9, 41.2] pg/ml vs. 32.3 [15.1, 53.3] pg/ml, P = 0.030). For IL-6 levels, there were no statistical significances between the two groups (P = 0.451). In addition, the levels of serum Tau protein were lower in dexmedetomidine group than in normal saline group (10.0 [2.9, 20.6] pg/ml vs. 18.2 [8.4, 304] pg/ml, P = 0.013). On postoperative day 3, Tau protein levels showed a statistically significant difference (7.2 [2.9, 14.0] pg/ml vs. 12.6 [6.6, 30.2] pg/ml, P = 0.032) between the two groups. However, for CRP and IL-6 levels, no statistically significant differences (P > 0.05) (**Table 4**).

On postoperative day 3, the NRS pain score at rest was lower in dexmedetomidine group than in normal saline group (1.0 [1.0, 2.0] vs. 2.0 [1.0, 2.0], P = 0.022). On postoperative day 2, the NRS pain score on coughing was lower in dexmedetomidine group than in normal saline group (3.0 [2.0, 4.0] vs. 3.0 [3.0, 4.8], P = 0.031). Compared with normal saline group, the NRS sleep quality scores showed statistically lower on postoperative day 1, day 2, and day 4 (3.0 [2.0, 4.0] vs. 3.0 [2.3, 4.8], P = 0.040; 3.0 [2.0,

3.0] vs. 3.0 [2.0, 4.0], $P = 0.005$; 2.0 [1.0, 3.0] vs. 3.0 [2.0, 3.0], $P = 0.018$) (**Table 5**).

Regarding length of hospital stay, there was no significant difference between the two groups (12.2 ± 6.5 d vs. 12.6 ± 7.0 d, $P = 0.658$). The number of deaths within 30 days after surgery was 2 in dexmedetomidine group and 3 in normal saline group. The 30-day all-cause mortality had no statistically significant difference (1.4% vs. 2.1%, $P > 0.999$) (**Table 6**).

Discussion

The present study demonstrated that dexmedetomidine significantly reduced the incidence of POD within 5 days after surgery in frail elderly patients undergoing gastrointestinal malignancy surgery, and also decreased the levels of CRP and Tau protein. Furthermore, dexmedetomidine reduced intraoperative opioid consumption, lowered postoperative pain scores, and ameliorated postoperative sleep.

Although the pathogenesis of POD remains unclear, numerous studies have demonstrated that POD is associated with risk factors such as pre-existing cognitive impairment, postoperative pain, opioids and sedatives consumption, and surgical inflammatory responses[28,29]. Moreover, the prevailing pathogenic mechanism of POD is the neuroinflammatory response mechanism, which posits that surgery-related stimuli lead to increased release of cytokines in the body, thereby triggering inflammatory responses in the nervous system and even systemically[30]. In addition, other studies suggest that surgical stimulation promotes the release of pro-inflammatory cytokines, which in turn cause vascular endothelial injury, further impairing circulatory function and

disrupting the blood-brain barrier. This induces an inflammatory response in the nervous system, ultimately leading to neuronal apoptosis and necrosis, and consequently resulting in POD[31,32,33]. In the present study, dexmedetomidine reduced the incidence of POD within 5 days after surgery, which was consistent with the findings of a meta-analysis[34]. The reduction in POD incidence by dexmedetomidine might be associated with its unique pharmacological property-namely, its highly selective action on α_2-adrenergic receptors.This property enabled it to significantly reduce intraoperative opioid consumption, and alleviated postoperative pain and discomfort[35,36]. Studies have shown that dexmedetomidine possesses the capacity to modulate systemic inflammatory responses[37,38], thereby attenuating the systemic inflammatory response induced by surgical stress and consequently reducing POD incidence. In the present study, dexmedetomidine lowered CRP levels, implying an attenuation of the postsurgical inflammatory response. Furthermore, dexmedetomidine reduced serum tau protein levels, which were closely correlated with POD. These results together suggested that dexmedetomidine might contribute to a decreased POD incidence. In addition, intraoperative dexmedetomidine infusion reduced sufentanil and remifentanil consumption, and postoperative pain scores were also lower, thereby corroborating the pharmacological profile of dexmedetomidine. Owing to its analgesic and sedative properties, dexmedetomidine improved patient tolerance of the tracheal tube, which consequently prolonged the time to extubation.

Our results also suggested that dexmedetomidine had play a positive role in mitigating postoperative sleep disturbance and improving sleep quality. Elderly patients, a population prone to sleep disorders[39], are at greater risk owing to postoperative pain, prolonged surgery, and major surgical trauma. Prior studies have shown that sleep deprivation activates microglia aberrantly and promotes synaptic pruning via phagocytosis, resulting in cognitive dysfunction and increased POD risk. Dexmedetomidine, by stimulating α_2A-adrenergic receptors on astrocytes, inhibits complement C3 release from hippocampal astrocytes and C3aR expression on microglia, thereby restoring synaptic connections and reversing sleep deprivation-induced cognitive deficits[40]. This further corroborated the effectiveness of dexmedetomidine in lowering POD incidence.

However, some other studies have reported findings that contradict our results[24,41,42]. For example, Deiner et al.[24] conducted a clinical trial involving 390 patients and found no difference in POD incidence between the dexmedetomidine group and the placebo group. This discrepancy may be related to differences in study design, as our study excluded patients with ASA classification > III during preoperative screening. Given that such patients often have more severe underlying conditions, their inclusion might have interfered with an accurate assessment of dexmedetomidine's effects. In subgroup analysis, POD incidence increased incrementally with higher Fried frailty scores. Patients with a score of 5 had a higher incidence than those with a score of 4, who in turn had a significantly higher incidence than those with a score of 3. This graded association

suggested that frailty severity was positively correlated with POD risk. Clinically, these findings highlighted the need for enhanced perioperative vigilance and tailored preventive interventions in patients with more advanced frailty.

There were some limitations in our study. Firstly, this study was a single-centered study, and the evidence supporting dexmedetomidine -induced POD reduction wass relatively weak. Thus, large-sample multicenter studies will be needed to strengthen this conclusion. Secondly, as the current study only included gastrointestinal surgery patients, further studies should expand to wider populations, such as non-gastrointestinal surgery and other high-risk patients, to explore whether dexmedetomidine exerts the same POD-lowering effect in these patients.

Conclusions

Intraoperative continuous intravenous pump infusion of dexmedetomidine can decrease the incidence of delirium within 5 days after surgery in frail elderly patients undergoing gastrointestinal malignancy surgery. And dexmedetomidine also alleviated postoperative pain scores and improved postoperative sleep quality.

Declarations

1.Abbreviations

Abbreviations

Abbreviations	English name in full
ASA	American society of Aneshesiologists
ECG	electrocardiogram
BMI	body mass index
MAP	mean arterial pressure
HR	heart rate
SPO2	pulse blood oxygen saturation
BIS	bispectral index
ETCO2	end-tidal carbon dioxide
MMSE	mini-mental state examination
CRP	C-reactive protein
IL6	Interleukin-6
TNF-α	Tumor Necrosis Factor-alpha
Tau proteins	Microtubule-associated protein tau
PONV	Postoperative nausea and vomiting
COPD	Chronic obstructive pulmonary disease
NRS	Numeric Rating Scale
CAM	confusion assessment method
ICU	Intensive Care Unit

PCIA	Patient Controlled Intravenous Analgesia
PACU	Post-Anesthesia Care Unit

2. Ethics approval and consent to participate

This randomized, double-blinded, prospective, controlled study was performed with adherence to the principles of the Declaration of Helsinki, approved by the Institutional Review Board (IRB) of the First Affiliated Hospital of Soochow University(approval number: 2024030).Capacity of patients to give consent was determined by physician interview before enrollment in the study.

3. Consent for publication

This article has obtained written informed consent from the patient and their family members for publication

4. Availability of data and materials

All data generated or analyzed during this study are included in this published article and its supplementary information files.

5. Competing Interests

The authors declare that they have no competing interests.

6. Funding

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7. Authors' contributions

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Tables

Table 1 Comparison of baseline characteristics

	dexmedetomidine (n = 138)	normal saline (n = 144)	*P* value
Sex [n (%)]			0.794
Male	89(64.5)	95(66.0)	
Female	49(35.5)	49(34.0)	
Age, year ($\bar{x}$±s)	73.8±5.4	74.5±5.9	0.349
BMI, kg/m^2($\bar{x}$±s)	22.7±3.1	22.5±3.2	0.635
ASA [n (%)]			0.185
II	105(76.1)	99(68.8)	
III	33(23.9)	45(31.2)	
Educational level [n (%)]			0.359
Illiterate	41(29.7)	47(32.6)	
Primary school	68(49.3)	78(54.2)	
Middle school	15(10.9)	11(7.6)	
High school and above	14(10.1)	8(5.6)	
Frailty score [n (%)]			0.311
3	95(68.8)	87(60.4)	
4	40(29.0)	53(36.8)	
5	3(2.2)	4(2.8)	
Hypertension [n (%)]	81(58.7)	89(61.8)	0.594
Diabetes mellitus [n (%)]	30(21.7)	25(17.4)	0.354

	dexmedetomidine (n = 138)	normal saline (n = 144)	*P* value
Cerebral infarction [n (%)]	17(12.3)	15(10.4)	0.615
COPD [n (%)]	2(1.4)	5(3.5)	0.275
Coronary heart disease [n (%)]	19(13.8)	14(9.7)	0.291
Type of surgery [n (%)]			0.530
Open	44(31.9)	51(35.4)	
Laparoscopic	94(68.1)	93(64.6)	
Surgical site [n (%)]			0.805
Gastric	51(37.0)	58(40.3)	
Intestinal	67(48.5)	68(47.2)	
Other	20(14.5)	18(12.5)	
Transfer to ICU [n (%)]	25(18.1)	24(16.7)	0.748

Data were reported as mean±standard deviation or proportion. BMI, body mass index; ASA, American Society of Anesthesiologists; COPD, Chronic Obstructive Pulmonary Disease; ICU, Intensive Care Unit.

Table 2 Intraoperative characteristics

	dexmedetomidine (n = 138)	normal saline (n = 144)	*P* value
Duration of surgery (min)	198.7±76.0	187.5±50.3	0.145
Duration of anesthesia (min)	221.4±77.9	210.0±52.0	0.147
Sufentanil used during surgery (μg)	52.8±9.2	57.4±7.3***	<0.001
Remifentanil used during surgery (μg)	949.7±343.3	1096.2±281.6***	<0.001
Propofol used during surgery	103.3±17.5	105.4±17.3	0.322
Extubation time (min)	30.9±11.7	24.9±10.3***	<0.001
Blood loss (ml)	108.0±38.1	103.5±30.5	0.273
Total fluid infusion (ml)	1488.2±522.1	1402.1±426.7	0.130
Urine output (ml)	313.8±133.2	318.2±111.9	0.764

Data were reported as mean±standard deviation. ***different from dexmedetomidine group, significant at $P < 0.05$.

Table 3 Comparison of POD incidence across different frailty scores

	patients with POD n (%)	patients without POD n (%)	*P* value
Frailty score =3 (n = 182)	25(13.7)	157(86.3)	
Frailty score =4 (n = 93)	25(26.9)	68(73.1)	0.023
Frailty score =5 (n = 7)	2(28.6)	5(71.4)	

Data were reported as proportion. significant at $P < 0.05$

Table 4 Comparison of serum CRP, IL-6, and Tau protein levels

	Before surgery	Postoperative days 1	Postoperative days 3
CPR(pg/ml)			
dexmedetomidine	2.1(1.0, 5.0)	16.2(4.9, 41.2)	41.9(24.2, 58.3)
normal saline	3.0(1.7, 7.8)	32.3(15.1, 53.3)*	45.0(26.0, 78.1)
P value	0.194	0.030	0.309
IL6(pg/ml)			
dexmedetomidine	2.8(2.1, 5.9)	26.5(15.3, 42.4)	8.8(4.8, 22.9)
normal saline	2.9(2.4, 5.3)	30.9(12.6, 60.6)	16.9(7.4, 33.1)
P value	0.843	0.451	0.077
Tau protein (pg/ml)			
dexmedetomidine	9.2(3.4, 17.0)	10.0(2.9, 20.6)	7.2(2.9, 14.0)
normal saline	13.2(5.2, 23.0)	18.2(8.4, 30.4)*	12.6(6.6, 30.2)*
P value	0.327	0.013	0.032

Data were present as median (IQR). *different from dexmedetomidine group, significant at $P < 0.05$.

Table 5 Postoperative NRS pain scores and sleep quality scores

	Day 1	Day 2	Day 3	Day 4	Day 5
NRS pain score at rest					
dexmedetomidine	2.0(2.0, 3.0)	2.0(1.0, 3.0)	1.0(1.0, 2.0)	0.0(0.0, 1.0)	0.0(0.0, 1.0)
normal saline	2.0(2.0, 3.8)	2.0(1.0, 3.0)	2.0(1.0,2.0)*	1.0(0.0, 2.0)	0.0(0.0, 1.0)
P value	0.374	0.531	0.022	0.084	0.201
NRS pain score on coughing					
dexmedetomidine	4.0(4.0, 5.0)	3.0(2.0, 4.0)	2.0(2.0, 3.0)	2.0(1.0, 3.0)	1.0(0.0,2.0)
normal saline	4.0(3.0, 5.0)	3.0(3.0,4.8)*	2.0(2.0, 3.0)	2.0(1.0, 3.0)	1.0(0.0,2.0)
P value	0.783	0.031	0.181	0.085	0.692
NRS sleep quality score					
dexmedetomidine	3.0(2.0, 4.0)	3.0(2.0, 3.0)	3.0(2.0, 3.0)	2.0(1.0, 3.0)	2.0(1.0,3.0)
normal saline	3.0(2.3,4.8)*	3.0(2.0,4.0)**	3.0(2.0, 3.0)	3.0(2.0,3.0)*	2.0(1.0,3.0)
P value	0.040	0.005	0.084	0.018	0.070

Data were present as median (IQR). *different from dexmedetomidine group, **different from dexmedetomidine group, significant at $P < 0.05$.

Table 6 Follow-up Outcomes at Postoperative Days 30

	dexmedetomidine (n = 138)	normal saline (n = 144)	*P* value
Qor-15 score on the first postoperative day(score)	109.9±10.4	105.4±11.6**	<0.001
Time to first flatus(day)	2.9±0.6	3.1±0.7*	0.026
Length of stay(day)	12.2±6.5	12.6±7.0	0.658
pulmonary infection[n(%)]	6(4.3)	7(4.9)	0.837
second surgery[n(%)]	3(2.2)	2(1.4)	0.679
incisional infection[n(%)]	1(0.7)	0(0.0)	0.489
Death[n(%)]	2(1.4)	3(2.1)	>0.999

Data were reported as mean±standard deviation or proportion.*different from dexmedetomidine group, **different from dexmedetomidine group, significant at $P < 0.05$.

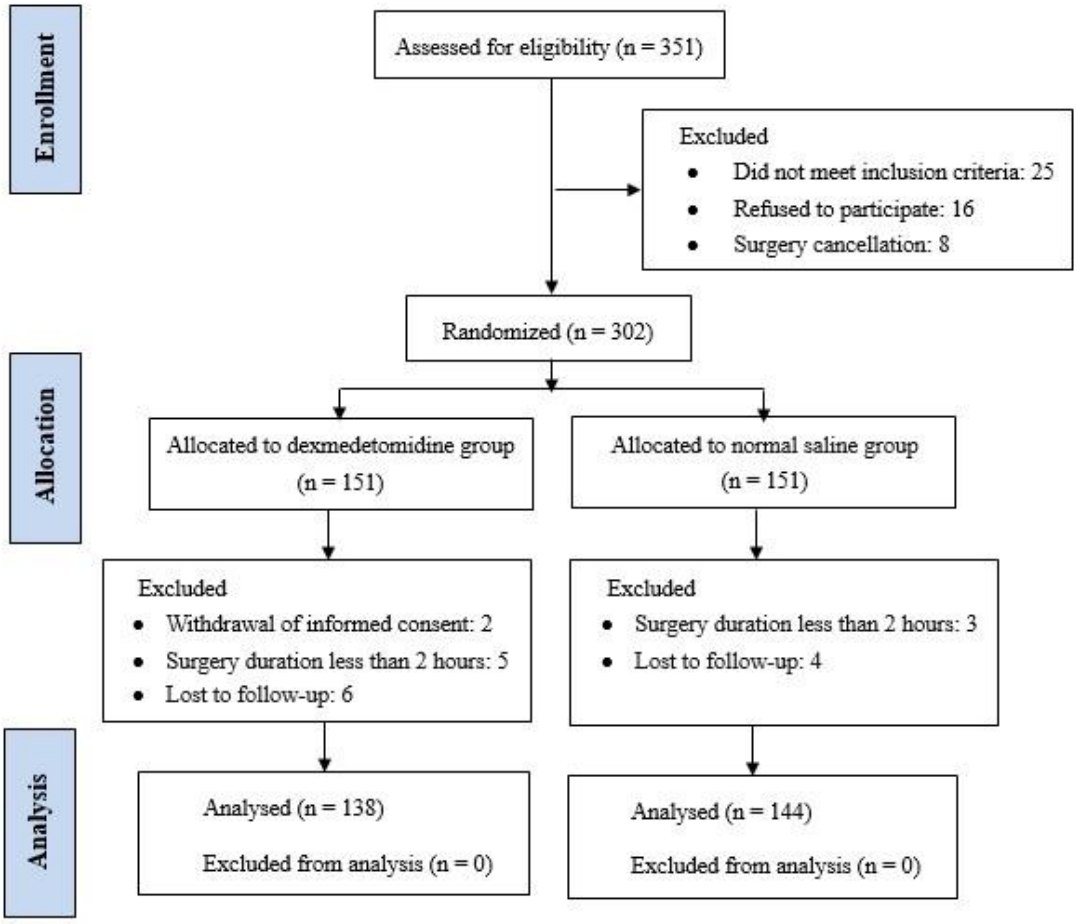


Figure 1 Study flow diagram of patient enrollment and exclusion

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