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ORIGINAL ARTICLE

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Application value of dexmedetomidine in anesthesia for elderly patients undergoing radical colon cancer surgery

Hui-Min Bu, Min Zhao, Hong-Mei Ma, Xiao-Peng Tian

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Abstract

BACKGROUND

Colon cancer presents a substantial risk to the well-being of elderly people worldwide. With advancements in medical technology, surgical treatment has become the primary approach for managing colon cancer patients. However, due to age-related physiological changes, especially a decline in cognitive function, older patients are more susceptible to the effects of surgery and anesthesia, increasing the relative risk of postoperative cognitive dysfunction (POCD). Therefore, in the surgical treatment of elderly patients with colon cancer, it is of paramount importance to select an appropriate anesthetic approach to reduce the occurrence of POCD, protect brain function, and improve surgical success rates.

AIM

To explore the value of dexmedetomidine (Dex) in anesthesia for elderly patients undergoing radical colon cancer surgery.

METHODS

One hundred and seventeen patients with colon cancer who underwent elective surgery under general anesthesia were selected and divided into two groups: A and B. Group A received Dex before anesthesia induction, and B group received an equivalent amount of normal saline. Changes in the mini-mental state examination, regional cerebral oxygen saturation (rSO2), bispectral index, glucose uptake rate (GluER), lactate production rate (LacPR), serum S100β and neuron-specific enolase (NSE), POCD, and adverse anesthesia reactions were compared between the two groups.

RESULTS

Surgical duration, duration of anesthesia, and intraoperative blood loss were comparable between the two groups ($P > 0.05$). The overall dosage of anesthetic drugs used in group A, including propofol and remifentanil, was significantly lower than that used in group B (P < 0.05). Group A exhibited higher rSO2 values at the time of endotracheal intubation, 30 min after the start of surgery, and immediately after extubation, higher GluER values and lower LacPR values at the time of endotracheal intubation, 30 min after the start of surgery, immediately after extubation, and 5 min after extubation (P < 0.05). Group A exhibited lower levels of serum S100β and NSE 24 h postoperatively and a lower incidence of cognitive dysfunction on the 1st and 5th postoperative days (P < 0.05).

CONCLUSION

The use of Dex in elderly patients undergoing radical colon cancer surgery helps maintain rSO2 Levels and reduce cerebral metabolic levels and the incidence of anesthesia- and surgery-induced cognitive dysfunction.

Key Words: Colon cancer; Dexmedetomidine; General anesthesia; Elderly; Radical colon cancer surgery; Bispectral index; Cognitive function; Regional cerebral oxygen saturation

Core Tip: This study aimed to explore the impact of dexmedetomidine (Dex) as an adjunct to general anesthesia on bispectral index, cognitive function, and local brain oxygen saturation in elderly patients undergoing radical colon cancer surgery. The use of Dex as an adjunct to general anesthesia in elderly patients undergoing radical colon cancer surgery helps maintain regional cerebral oxygen saturation levels and reduce cerebral metabolic levels, thereby lowering the incidence of anesthesia- and surgery-induced cognitive dysfunction and reducing the dosage of related anesthetic drugs.

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INTRODUCTION

Colon cancer, a common malignant tumor, presents a substantial risk to the well-being of elderly people worldwide. With advancements in medical technology, surgical treatment has become the primary approach for managing colon cancer patients[1]. However, due to age-related physiological changes, especially a decline in cognitive function, older patients are more susceptible to the effects of surgery and anesthesia, increasing the relative risk of postoperative cognitive dysfunction (POCD)[2]. Therefore, in the surgical treatment of elderly patients with colon cancer, it is of paramount importance to select an appropriate anesthetic approach to reduce the occurrence of POCD, protect brain function, and improve surgical success rates. Dexmedetomidine (Dex) belongs to the class of α2-adrenergic receptor agonists and is widely used in anesthetic practice owing to its sedative and analgesic effects[3]. Research indicates that Dex has the potential to protect the nervous system, particularly by reducing perioperative neurocognitive disorders[4]. However, its specific effects and mechanisms of action in certain surgical procedures, such as radical colon cancer surgery in elderly patients, require further research and clarification. Therefore, this study explored the application of Dex as an adjunct to general anesthesia in elderly patients undergoing radical colon cancer surgery and its impact on the bispectral index (BIS), cognitive function, and regional cerebral oxygen saturation (rSO2), with an aim to provide an optimized and safe anesthetic management approach for elderly patients with colon cancer.

MATERIALS AND METHODS

Patients selection

This randomized clinical trial involved 117 patients with colon cancer who underwent elective surgery under general anesthesia between January 2021 and June 2023. Among them, 59 received Dex before anesthesia induction (group A), whereas the remaining 58 received an equivalent amount of normal saline before anesthesia induction (group B). Sample size was calculated as follows: According to our previous research, the incidence of postoperative pain in patients undergoing colon cancer surgery is almost 100%. When the test power (1-β) is 0.9 and the test level (α) is 0.05, the sample size (n) for each group was calculated to be 60. Based on the actual clinical case collection and extrapolation, 59 eligible patients and 58 controls were included in the final study. The study protocol was approved by the local Medical Ethics Committee, and informed consent was obtained from the patients before surgery.

Inclusion criteria: (1) Patients diagnosed with colon cancer according to the diagnostic criteria outlined in the 'Chinese Society of Clinical Oncology (CSCO) Colorectal Cancer Diagnosis and Treatment Guidelines 2020 Edition'[5]; (2) Age between 65 and 79 years old; (3) Patients who underwent preoperative colonoscopy, with tissue specimens obtained for pathological examination to confirm the diagnosis; (4) American Society of Anesthesiologists grades I–III; (5) Preoperative New York Heart Association class ≤ II; and (6) Patients who underwent elective surgery, with the operation performed by the same group of medical staff.

Exclusion criteria: (1) Metastatic colorectal cancer; (2) Intestinal obstruction, perforation and abdominal infection; (3) Immune diseases; (4) HIV infection; (5) Abnormal coagulation function; (6) History of epilepsy or senile dementia; and (7) Arrhythmia.

Anesthesia methods

Group A received Dex (Jiangsu Enhua Pharmaceutical, H20110086) *via* intravenous infusion before anesthesia induction. A loading dose was administered at 1.0 μg/kg, followed by a maintenance dose of 0.3 μg/kg/h until the completion of the surgery.

Group B group received an equivalent volume of normal saline *via* intravenous infusion before anesthesia induction. The treatment duration and dosage were the same as those used in group A.

Both groups received sevoflurane inhalation (maintaining the minimum alveolar concentration value between 1.0-2.0) with a continuous infusion of remifentanil (Jiangsu Enhua Pharmaceutical; approved under the national drug standard H20143314) at a rate of 0.1-0.2 μg/kg/min post-anesthesia induction. Additional fentanyl (Yichang Renfu Pharmaceutical; approved under the national drug standard H20003688) was administered during surgery as needed, at a dosage of 1-3 μg/kg. When the total fentanyl dose reached or exceeded 0.4 mg, the remifentanil dosage was adjusted to 0.04-0.4 μg/kg/min. During surgery, one-fifth of the induction dose of cisatracurium [Dongying (Jiangsu) Pharmaceutical; approved under the national drug standard H20060926] was administered every hour as a supplement. In case of blood pressure increases exceeding 20% above baseline persisting for 5 min without improvement, prompt adjustments were made to anesthesia depth, including sedation and analgesia. If the blood pressure dropped below 20% of the baseline value and did not improve within 5 min, 6 mg of ephedrine (Tonghua Baishan Pharmaceutical; approved under the national drug standard H22020730) was administered intravenously. If the patient's heart rate remained below 50 beats per minute and did not improve for 1 min, atropine (0.5 mg) (Tianjin Jinyao Pharmaceutical; approved under the national drug standard H12020384) was administered intravenously. Additionally, the sedation depth was adjusted as needed to ensure that the BIS value remained between 40-60. Detailed records of the duration of surgery, duration of anesthesia, intraoperative blood loss, consumption of propofol, and remifentanil dosage were maintained during surgery.

Observation indicators and evaluation methods

The study monitored variations in the mini-mental state examination (MMSE), rSO2, BIS, glucose extraction rate (GluER), cerebral lactate production rate (LacPR), and serum S100β and neuron-specific enolase (NSE) in both patient groups. Additionally, the incidence of POCD and adverse anesthetic reactions was recorded in the two groups.

The MMSE scale[6] primarily comprises the following categories: Orientation (10 points), attention and calculation (5 points), memory (3 points), recall (3 points), and language ability (9 points). The total score was 30 points, with a score of ≥ 27 points considered normal and a score < 27 points indicating cognitive dysfunction.

The rSO2 parameters were measured using a non-invasive near-infrared spectroscopy device (Tocor 8, Nihon Kohden).

BIS and rSO2 values were recorded at the following time points: Before anesthesia induction, immediately after endotracheal intubation, 30 min after the start of surgery, immediately after extubation, and 5 min after extubation. Arterial blood from the radial artery and venous blood from the internal jugular vein bulb were collected at these time points. The glucose and lactate levels were measured using an AU5800 biochemical autoanalyzer (Beckman Coulter).

The formulas used for the calculations are as follows:

GluER = [(arterial glucose - venous glucose at the internal jugular vein bulb)/arterial glucose] × 100.

LacPR = [(arterial lactate - venous lactate at the internal jugular vein bulb)/arterial lactate] × 100.

Preoperatively and 24 h postoperatively, 5 mL of venous blood was collected from patients, and the serum was separated after centrifugation. Enzyme-linked immunosorbent assay was then employed to quantify serum S100β and NSE levels.

Statistical analysis

Statistical software SPSS21.0 was used for all analyses. Serum S100β, NSE, BIS, rSO2, and other indicators as measurement data are presented as the mean ± SD. Measurement data collected at multiple time points were analyzed utilizing repeated measures analysis of variance, while non-repetitive measurement data were assessed using the *t*-test. Enumeration data, expressed as rates (%), were compared using the χ^2 test.

RESULTS

Comparative of general demographic information between the two groups

General demographic information, including age and sex, was comparable between the two groups ($P > 0.05$; Tables 1 and 2).

Table 1 Comparison of demographic information between the two groups, *n* (%)

Group	*n*	Age (years)	BMI (kg/m²)	Sex		Years of education	ASA grade		
				Male	Female		I	II	III
A	59	71.4 ± 4.3	21.99 ± 1.90	39 (66.10)	20 (33.90)	4.88 ± 1.25	15 (25.42)	28 (47.46)	16 (27.12)
B	58	70.8 ± 4.5	22.20 ± 2.14	32 (54.24)	26 (44.07)	5.04 ± 1.64	20 (34.48)	25 (43.1)	13 (22.41)
t/χ^2		0.737	-0.562	1.464		-0.594	1.186		
P value		0.462	0.576	0.264		0.554	0.553		

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

Table 2 Comparison of disease information between the two groups, *n* (%)

Group	*n*	Systolic pressure (mmHg)	Diastolic pressure (mmHg)	Fasting blood glucose (mmol/L)	Heart rate (times/min)	Lesion diameter (cm)	TNM stage		
							I	II	III
A group	59	124.0 ± 6.8	76.5 ± 7.2	6.15 ± 0.64	78.8 ± 7.2	4.48 ± 1.40	17 (28.81)	32 (54.24)	9 (15.25)
B group	58	122.6 ± 6.2	78.5 ± 8.0	6.28 ± 0.71	80.4 ± 8.1	4.81 ± 1.67	11 (18.97)	34 (58.62)	14 (24.14)
t/χ^2		1.163	-1.422	-1.041	-1.130	-1.159	2.425		
P value		0.247	0.158	0.300	0.261	0.249	0.297		

TNM: Tumor-node-metastasis.

Table 3 Comparison of operation and anesthetic dosage between the two groups (mean ± SD)

Group	*n*	Operation time (min)	Anesthesia time (min)	Bleeding volume (mL)	Dosage of propofol (mg)	Remifentanil dosage (μg)
A	59	167.9 ± 16.8	183.4 ± 15.0	277.5 ± 43.8	654.7 ± 67.0	866.4 ± 55.8
B	58	170.5 ± 17.2	189.1 ± 17.4	273.8 ± 47.2	695.8 ± 74.1	913.0 ± 68.6
t		-0.827	-1.899	0.440	-3.148	-4.034
P value		0.410	0.060	0.661	0.002	0.000

Comparative analysis of surgical procedures and anesthetic dosages between the two groups

Surgical duration, duration of anesthesia, and intraoperative blood loss were comparable between the two groups (P > 0.05). However, the total anesthesia drug usage in group A, including the doses of propofol and remifentanil, was markedly lower than that of group B (P < 0.05; Table 3).

Comparison of BIS and rSO2 values between the two groups

Before anesthesia induction, the BIS and rSO2 values were comparable between the two groups (P > 0.05). However, at the time of endotracheal intubation, 30 min after the start of surgery, and immediately after extubation, the rSO2 values in group A were higher than those of group B (P < 0.05; Table 4).

Comparison of GluER and LacPR values between the two groups

Before the induction of anesthesia, the baseline values of GluER and LacPR in the two groups were comparable (P > 0.05). The GluER values in group A were significantly higher than those of group B immediately after tracheal intubation, 30 min during after the start of operation, immediately after extubation, and 5 min after extubation, while the LacPR values were significantly lower than those of group B (P < 0.05; Table 5).

Comparison of serum S100β and NSE levels between the two groups of patients

Preoperative serum S100β and NSE levels were comparable between the two groups (P > 0.05). However, serum S100β and NSE in group A were significantly lower than those of group B at 24 h after operation (P < 0.05; Table 6).

Table 4 Comparison of bispectral index and regional cerebral oxygen saturation values between the two groups (mean ± SD)

Index	Group	Before anesthesia induction	Immediately after tracheal intubation	30 min after start of surgery	Immediately after extubation	5 min after extubation
rSO2 (%)	A (*n* = 59)	73.40 ± 4.40	66.18 ± 2.94	67.40 ± 2.86	69.04 ± 3.10	72.26 ± 3.35
	B (*n* = 58)	74.53 ± 3.78	64.07 ± 3.11	64.67 ± 3.15	66.12 ± 3.76	71.54 ± 3.43
	t	-1.489	3.772	4.910	4.587	1.149
	P value	0.139	0.000	0.000	0.000	0.253
BIS	A (*n* = 59)	93.78 ± 1.65	48.40 ± 2.44	51.73 ± 2.73	56.20 ± 3.45	89.76 ± 2.80
	B (*n* = 58)	93.16 ± 1.73	49.23 ± 2.61	52.50 ± 2.87	57.43 ± 3.61	88.72 ± 3.41
	t	1.984	-1.777	-1.487	-1.884	1.804
	P value	0.050	0.078	0.140	0.062	0.074

rSO2: Regional cerebral oxygen saturation; BIS: Bispectral index.

Table 5 Comparison of glucose uptake rate and lactate production rate between the two groups (mean ± SD)

Index	Group	Before anesthesia induction	Immediately after tracheal intubation	30 min after start of surgery	Immediately after extubation	5 min after extubation
GluER (μg/L)	A (*n* = 59)	6.83 ± 0.21	6.77 ± 0.19	6.73 ± 0.21	6.75 ± 0.19	6.70 ± 0.20
	B (*n* = 58)	6.89 ± 0.25	6.43 ± 0.42	6.28 ± 0.48	6.29 ± 0.34	6.31 ± 0.33
	t	-1.407	5.657	6.589	9.054	7.746
	P value	0.162	0.000	0.000	0.000	0.000
LacPR (μg/L)	A (*n* = 59)	4.41 ± 0.27	4.89 ± 0.30	5.10 ± 0.37	5.19 ± 0.35	4.94 ± 0.30
	B (*n* = 58)	4.35 ± 0.31	5.28 ± 0.41	5.43 ± 0.40	5.49 ± 0.38	5.21 ± 0.47
	t	1.117	-5.879	-4.634	-4.443	-3.710
	P value	0.266	0.000	0.000	0.000	0.000

GluER: Glucose uptake rate; LacPR: Lactate production rate.

Comparison of incidence of cognitive dysfunction between the two groups

On postoperative days 1 and 5, the incidence of cognitive dysfunction in group A was 11.86% and 5.08%, respectively, while those in group B were 27.59% and 18.97%, respectively; there were significant differences between the two groups ($P < 0.05$; Table 7).

Comparison of incidence of adverse reactions caused by anesthesia between the two groups

The incidence of adverse reactions was 8.47% and 24.14% in groups A and B, respectively, with a significant difference between the two groups ($P < 0.05$; Table 8).

DISCUSSION

Radical colorectal cancer surgery serves as the primary treatment method for elderly patients, aiming to achieve a curative effect by removing the tumor and its surrounding lymph nodes[7,8]. However, in the elderly population, physiological function decline, heightened sensitivity to anesthetic drugs, and organ function impairment can lead to reduced drug metabolism and excretion abilities. Consequently, greater caution is necessary in the selection of anesthetic agents and their dosages[9]. Notably, parameters such as BIS and rSO2 play crucial roles in assessing anesthesia depth

Table 6 Comparison of serum S100β and neuron-specific enolase levels between the two groups (mean ± SD)

Group	*n*	S100β (ng/L)		NSE (ng/L)	
		Before operation	24 h after operation	Before operation	24 h after operation
A	59	0.58 ± 0.15	0.96 ± 0.25	3.96 ± 0.88	5.27 ± 1.03
B	58	0.53 ± 0.17	1.21 ± 0.29	3.84 ± 0.90	6.91 ± 1.27
t		1.688	-4.997	0.729	-7.678
P value		0.094	0.000	0.467	0.000

NSE: Neuron-specific enolase.

Table 7 Comparison of incidence of cognitive dysfunction between the two groups, *n* (%)

Group	*n*	1 d after operation	3 d after operation	5 d after operation	7 d after operation
A	59	7 (11.86)	7 (11.86)	3 (5.08)	1 (1.69)
B	58	16 (27.59)	14 (24.14)	11 (18.97)	3 (5.17)
χ^2		4.577	2.992	5.350	1.071
P value		0.032	0.084	0.021	0.301

Table 8 Comparison of incidence of adverse reactions caused by anesthesia between the two groups

Group	*n*	Nausea	Vomiting	Bradycardia	Respiratory depression	Overall adverse reactions (%)
A	59	3	1	1	0	5 (8.47)
B	58	8	3	2	1	14 (24.14)
χ^2						5.275
P value						0.022

and preserving brain function. BIS, an indicator that estimates anesthesia depth by analyzing electroencephalogram signals, is crucial for adjusting the dosage of anesthetic drugs and ensuring an appropriate level of anesthesia in patients [10]. Meanwhile, rSO2, an indicator of cerebral oxygenation levels, allows for the timely detection of cerebral hypoxia during surgery. Additionally, anesthetic drugs and surgical stress can have short- or long-term adverse effects on cognitive function in elderly patients. Cognitive protection during anesthesia management can help predict and identify POCD[11]. Therefore, optimizing the anesthesia plan is of paramount importance to enhance surgical safety, reduce postoperative complications, and expedite patient recovery.

This research revealed that group A required significantly lower doses of propofol and remifentanil compared to group B, indicating that the use of Dex could reduce the need for anesthetic drugs and decrease the intraoperative sedative and analgesic use ($P < 0.05$). Dex achieves sedative and analgesic effects by activating α2-adrenergic receptors in the central nervous system, decreasing the activity of the sympathetic nervous system, thus reducing dependence on other anesthetic drugs[12]. Additionally, at the time of endotracheal intubation, 30 min after the start of surgery, and immediately after extubation, group A showed significantly higher rSO2 and GluER values and significantly lower LacPR values than group B, illustrating that the use of Dex can improve the intraoperative cerebral oxygen supply and significantly enhance the metabolic state of the brain. Hemodynamic stability is crucial for ensuring a stable blood supply to vital organs, particularly the brain. Dex, through the activation of α2 receptors on presynaptic membranes, can inhibit the release of norepinephrine, thereby reducing the excitability of the sympathetic nervous system. This inhibitory effect helps maintain hemodynamic stability during surgery and reduces fluctuations in the heart rate and blood pressure caused by excessive activation of the sympathetic nervous system[13]. Furthermore, when Dex is used in combination with intravenous anesthetics, it can further enhance the anesthetic effect in patients, especially by suppressing the transmission of pain signals to the brain. This helps reduce intraoperative patient stress responses and decreases the need for other anesthetic drugs, thereby better maintaining hemodynamic stability during surgery[14]. Through these mechanisms, Dex contributes to ensuring a stable blood supply to the brain, which is crucial for maintaining normal oxygenation and metabolism. Adequate cerebral blood flow promotes the efficient utilization of glucose and reduces the accumulation of metabolic waste products such as lactate, thus protecting the brain tissue from potential damage during surgery[15].

S100β, mainly produced by astrocytes, is considered related to brain injury and repair processes. Elevated levels of S100β are usually associated with brain cell damage[16]. NSE, a neuron-specific enzyme, is used to evaluate neuronal damage, with increased levels typically indicating neuronal damage or death[17]. In this study, brain injury was compared between the two groups, and the results demonstrated that serum S100β and NSE levels in group A were significantly lower than those of group B 24 h following surgery, indicating that Dex usage could reduce the degree of brain injury postoperatively.

The study results also indicated that group A exhibited a significantly lower incidence of cognitive dysfunction compared to group B on the 1st and 5th days after surgery, suggesting that the application of Dex is beneficial in reducing the risk of cognitive dysfunction after surgery. The rationale for this lies in Dex's effective reduction of norepinephrine secretion by activating the α2 receptor on the medulla oblongata and pons[18]. This action diminishes the patient's body stress response, lowers the release of inflammatory mediators, and mitigates damage to hippocampal neurons in the hippocampus, consequently preserving brain tissue. Additionally, Dex's high expression in cerebral cortex neurons directly contributes to the growth, proliferation, and differentiation of neurons. This involvement not only sustains the stability of brain nerve function, but it is also essential for preventing postoperative delirium, cognitive dysfunction, and other complications. Furthermore, the application of Dex can reduce the dosage of propofol and remifentanil, minimizing the cognitive function damage caused by these anesthetics[19].

We found that the rate of adverse reactions in group A was 8.47%, significantly lower than that of group B (24.14%; $P < 0.05$). This underscores that the use of Dex in surgical anesthesia can markedly reduce the occurrence of adverse reactions. Primarily, this reduction stems from the group A's adjustment of propofol and remifentanil dosages after incorporating Dex. Although these anesthetics are commonly used in anesthesia, they also have potential side effects, such as nausea, vomiting, bradycardia, and respiratory depression. Reducing the use of these drugs can reduce the risk of adverse effects[20].

This study found that Dex assisted general anesthesia significantly reduced the incidence of postoperative cognitive impairment in elderly patients with colon cancer radical surgery, and improved local cerebral oxygen saturation and brain metabolic indicators. These results indicate that Dex has important clinical significance in reducing postoperative cognitive impairment, helping to optimize anesthesia management and improve the quality of postoperative recovery in elderly patients. However, this study also has some limitations, such as small sample size, single center study, and short follow-up duration. Future multicenter randomized controlled trials with larger sample size and extended follow-up duration are needed to further validate the effectiveness and safety of Dex in different surgical types and patient populations.

CONCLUSION

The use of Dex as an adjunct to general anesthesia in elderly patients undergoing radical colon cancer surgery helps maintain rSO2 Levels and reduce cerebral metabolic levels, thereby lowering the incidence of anesthesia- and surgery-induced cognitive dysfunction and reducing the dosage of related anesthetic drugs.

FOOTNOTES

Author contributions: Bu HM and Tian XP designed the research; Bu HM and Zhao M performed the research; Bu HM and Ma HM analyzed the data; Bu HM and Tian XP wrote the manuscript.

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