

Application of sevoflurane inhalation combined with epidural anesthesia in patients with colorectal cancer and its effect on postoperative perceptual function

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Received October 12, 2018; Accepted February 19, 2019

DOI: 10.3892/ol.2019.10074

Abstract. Effect of sevoflurane inhalation combined with epidural anesthesia on postoperative perceptual function in patients with colorectal cancer (CRC) was investigated. The clinical data of 78 patients undergoing laparoscopic CRC radical surgery in The Second Cancer Hospital of Heilongjiang Province from June 2016 to June 2017 were retrospectively analyzed and divided into 2 groups: Sevoflurane inhalation combined with epidural anesthesia (observation group, n=40); propofol intravenous general anesthesia (control group, n=38). The mean arterial pressure and heart rate before anesthesia (T0), immediate intubation (T1), 30 min after surgery started (T2), end of surgery (T3), 10 min after extubation (T4) were compared between the two groups. The recovery conditions were also compared between the two groups. The cognitive functions were evaluated by mini-mental state scale (MMSE). The mean arterial pressure and heart rate in the observation group were significantly lower than those in the control group at T2, T3 and T4 ($P<0.05$). The recovery time, extubation time, anal exhaust time, eating time, urinary catheter removal time and hospital stay in the observation group were significantly lower than those in the control group ($P<0.05$). There was a significant difference in cognitive function between the two groups at different time points ($P<0.001$). Postoperative cognitive function showed a trend of decreasing first and then increasing; the scores of cognitive function in both groups 1 day after surgery were at trough level, and recovered gradually from 3 days after surgery. The mean arterial pressure and heart rate during the perioperative period are more stable in the elderly patients with sevoflurane inhalation combined

with epidural anesthesia; the recovery time is shorter and more rapid, and the recovery time of postoperative cognitive function is also faster. Therefore, it provides a reference for patients undergoing CRC radical surgery to select high-quality and appropriate anesthetic protocols.

Introduction

Colorectal cancer (CRC) is the third most common malignant tumor in the world and the fourth leading cause of cancer death, with approximately 1.4 million new cases and nearly 700,000 deaths in 2012 (1). Resection is one of the most important methods for the treatment of early CRC in clinical practice. Laparoscopic CRC radical surgery is widely used in clinic because of its clear vision, less trauma, less immune system interference, rapid postoperative recovery, and low overall operating costs (2). General anesthesia is required during laparoscopic radical surgery to avoid the effect of artificial pneumoperitoneum on respiratory and circulatory function of patients (3), and postoperative cognitive impairment may be caused after surgery and anesthesia in the elderly, which can affect the postoperative recovery and quality of life (4). Therefore, in order to reduce the incidence of postoperative cognitive impairment, appropriate anesthesia methods should be selected.

There are two main techniques for anesthesia: i) General anesthesia, where gas or intravenous drugs achieve central nervous system depression and ii) local anesthesia, where the drug is directly administered to the spinal cord or nerve to locally block the input of afferent and efferent nerve (5). Propofol for total intravenous injection and sevoflurane for inhalation anesthesia are mainly used in general anesthesia because their pharmacological properties facilitate rapid recovery after anesthesia (6-8). Propofol is superior in recovering features and reducing postoperative adverse reactions (9). Sevoflurane is volatile, nonflammable and aromatic, non-irritating to the respiratory tract, and has low blood gas partition coefficient, which is conducive to the regulation of anesthesia depth, smooth induction and rapid recovery (10). However, sevoflurane is superior to propofol in anesthetic applications requiring rapid induction and recovery of cognitive function (11,12).

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Key words: sevoflurane, epidural, anesthesia, colorectal cancer, cognitive functions

Epidural anesthesia and analgesia are commonly used to manage postoperative pain after abdominal surgery. Afferent block induced by epidural anesthesia can reduce neuroendocrine stress during and after surgery (13,14). Epidural anesthesia can reduce neuroendocrine stress and prevent immune suppression caused by surgery and general anesthesia, thus protecting patients from complications after infection or postoperative development of tumor metastasis (15,16).

This study analyzed the application of sevoflurane inhalation combined with epidural anesthesia in CRC radical surgery and its effect on cognitive function of elderly patients, and to provide references for the selection of clinical anesthetic methods in elderly patients.

Patients and methods

Patient information. The clinical data of 78 patients undergoing laparoscopic CRC radical surgery in The Second Cancer Hospital of Heilongjiang Province (Harbin, China) from June 2016 to June 2017 were retrospectively analyzed, including 44 males and 34 females, and with an age range of 60-75 years. Among them, 40 patients received sevoflurane inhalation combined with epidural anesthesia as observation group; 38 patients received propofol general anesthesia as control group. There was no significant difference between the two groups in general data ($P>0.05$). All patients were diagnosed with colon cancer or rectal cancer by Pathology Department of The Second Cancer Hospital of Heilongjiang Province. Patients with other malignant tumors, heart, liver and kidney dysfunction, coagulation dysfunction, mental illness and incomplete clinical data were excluded.

The study was approved by the Ethics Committee of The Second Cancer Hospital of Heilongjiang Province. Patients who participated in this research, signed an informed consent and had complete clinical data. Patient information is provided in Table I.

Anesthetic methods. All patients were prohibited from eating 8 h before surgery and using drugs before surgery. 0.1g of luminal (Tianjin Kingyork Pharmaceutical Co., Ltd., Tianjin, China, SFDA approval no. H12020381), and 0.3 mg of scopolamine (Shanghai Harvest Pharmaceutical Co., Ltd., Shanghai, China, SFDA approval no. H31021519) were intramuscularly injected 30 min before surgery. Invasive arterial pressure, central venous pressure, electrocardiogram, blood pressure, heart rate, pulse and oxygen protection monitoring were established, and intravenous channel was established to infuse 500 ml of succinyl gelatin (Shenyang Beilang Pharmaceutical Co., Ltd., Shenyang, China, SFDA approval no. H20040609). Midazolam (0.04 mg/kg; Jiangsu Enhua Pharmaceutical Group Co., Ltd., Jiangsu, China, SFDA approval no. H20031037), 2-4 $\mu\text{g}/\text{kg}$ fentanyl (Yichang Humanwell Pharmaceutical Co., Ltd., Yichang, China, SFDA approval no. H42022076), 0.1 mg/kg vecuronium bromide (Zhejiang Xianju Pharmaceutical Co., Ltd., Zhejiang, China, SFDA approval no. H19991172), and 1 mg/kg propofol (Xi'an Libang Pharmaceutical Co., Ltd., Xi'an, China, SFDA approval no. H20010368) were used for anesthesia induction in both groups. Anesthesia apparatus was connected to control breathing after intubation. In the control group, propofol was pumped 4-6 mg/kg per hour; fentanyl and vecuronium was

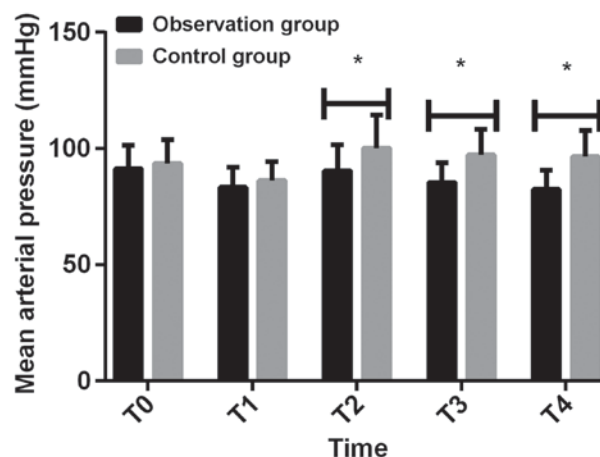


Figure 1. Comparison of mean arterial pressure at different time points between the two groups. The results showed that there was no significant difference in mean arterial pressure between the observation group and the control group at T0 and T1 ($P>0.05$); the mean arterial pressure in the observation group was significantly lower than that in the control group at T2, T3 and T4, and the difference was statistically significant ($P<0.05$).

injected intermittently to maintain anesthesia. In the observation group, epidural puncture was performed before anesthesia induction; 3 ml of the mixture of 1% lidocaine (Shanghai Chaohui Pharmaceutical Co., Ltd., Shanghai, China, SFDA approval no. H31021071) and 0.25% ropivacaine (Guangdong Resources Shunfeng Pharmaceutical Co., Ltd., Guangdong, China, SFDA approval no. H20050325) were injected for the first time. After 10 min of observation, additional dose was injected after confirmation of no signs of spinal esthesia. Anesthesia maintenance: In the observation group, an additional dose was injected into the epidural every 45-60 min. Intermittent intravenous injection of vecuronium bromide was conducted and 2-3% sevoflurane (Fujian Gutian Pharmaceutical Co., Ltd., Fujian, China, SFDA approval no. H35020148) was inhaled to maintain anesthesia, and sevoflurane was discontinued during skin suture.

Observation index. The mean arterial pressure and heart rate before anesthesia (T0), immediate intubation (T1), 30 min after surgery started (T2), end of surgery (T3), 10 min after extubation (T4) were compared between the two groups.

The recovery conditions including recovery time, extubation time, anal exhaust time, eating time, urinary catheter removal time and hospital stay were compared between the two groups.

The cognitive functions, including orientation, attention, calculation, reading, comprehension, memory, were evaluated by mini-mental state scale (MMSE) at 1 day, 3 days and 5 days after surgery, respectively. The total score was 30, and the smaller the score, the worse the cognitive function.

Statistical analysis. SPSS 20.0 statistical software (IBM Corp., Armonk, NY, USA) was used for analysis. Chi-square test was used for enumeration data, and t-test was used for measurement data. One-way ANOVA with Dunnett's test was used for multi-group comparison, and repeated measures ANOVA was used for comparisons at different times within the group. $P<0.05$ was considered to indicate a statistically significant difference.

Table I. Patient information [n (%)].

Factor	Observation group (n=40)	Control group (n=38)	t/ χ^2 value	P-value
Age (years)	67.63±6.22	66.07±7.14	1.030	0.306
Sex			0.430	0.648
Male	24 (60.00)	20 (52.63)		
Female	16 (40.00)	18 (47.37)		
BMI (kg/m ²)	23.46±1.92	23.83±2.14	0.805	0.424
Surgical duration (min)	218.82±45.19	212.53±49.37	0.587	0.559
Intraoperative bleeding volume (ml)	207.56±36.24	216.22±34.53	1.079	0.284
Rehydration (ml)	2587.27±14.05	2613.54±166.77	0.993	0.324
ASA classification [(n%)]			0.781	0.469
I	29 (72.50)	24 (63.16)		
II	11 (27.50)	14 (36.84)		
Education degree [(n%)]			2.000	0.204
Primary and below	32 (80.00)	25 (65.79)		
Above primary	8 (20.00)	13 (34.21)		

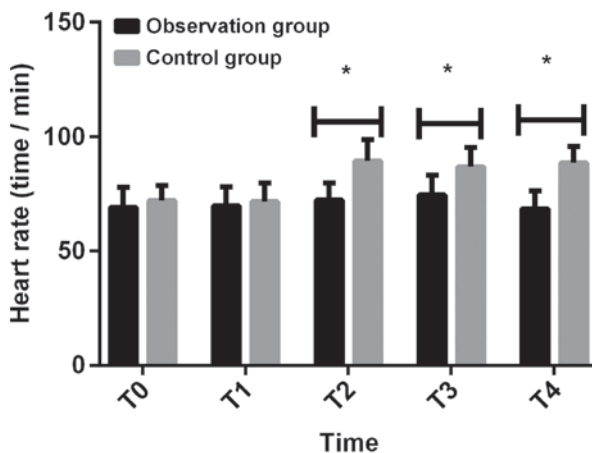


Figure 2. Comparison of heart rate at different time points between the two groups. The results showed that there was no significant difference in heart rate between the observation group and the control group at T0 and T1 (P>0.05). Heart rate in observation group was significantly lower than that in control group at T2, T3 and T4, and the difference was statistically significant (P<0.05). *P<0.05.

Results

Comparison of mean arterial pressure and heart rate at different time points between the two groups. There was no significant difference in mean arterial pressure and heart rate between the observation group and the control group at T0 and T1 (P>0.05), while the mean arterial pressure and heart rate in the observation group were significantly lower than those in the control group at T2, T3 and T4, and the difference was statistically significant (P<0.05) (Figs. 1 and 2, and Tables II and III.

Comparison of the recovery conditions between the two groups. The recovery time, extubation time, anal exhaust time, eating time, urinary catheter removal time and hospital stay in

Table II. Mean arterial pressure at different time points in the two groups (mmHg).

Time	Observation group (n=40)	Control group (n=38)	t value	P-value
T0	91.26±10.14	93.56±10.32	0.993	0.324
T1	83.37±8.53	86.14±8.25	1.457	0.149
T2	90.42±11.29	100.21±14.25	3.372	0.001
T3	85.38±8.51	97.26±10.91	5.377	<0.001
T4	82.43±8.27	96.57±11.28	6.336	<0.001

Table III. Heart rate at different time points in the two groups (times/min).

Time	Observation group (n=40)	Control group (n=38)	t value	P-value
T0	69.24±8.63	72.16±6.51	1.680	0.097
T1	69.86±8.25	71.56±8.11	0.917	0.362
T2	72.37±7.38	89.42±9.26	9.016	<0.001
T3	74.53±8.62	86.79±8.51	6.318	<0.001
T4	68.62±7.64	88.58±7.25	11.820	<0.001

the observation group were significantly lower than those in the control group, and the difference was statistically significant (P<0.05) (Fig. 3 and Table IV).

Comparison of postoperative cognitive functions between the two groups. There was no significant difference in cognitive

Table IV. Comparison of the recovery conditions between the two groups.

Time	Observation group (n=40)	Control group (n=38)	t value	P-value
Recovery time (min)	7.38±2.64	14.62±4.37	8.908	<0.001
Extubation time (min)	8.13±2.98	19.57±5.38	11.690	<0.001
Anal exhaust time (days)	2.37±0.87	3.14±0.97	3.695	<0.001
Eating time (days)	2.51±0.95	3.21±1.02	3.138	0.002
Urinary catheter removal time (days)	1.29±0.43	1.77±0.32	5.570	<0.001
Hospital stay (days)	9.26±2.45	12.07±2.14	5.383	<0.001

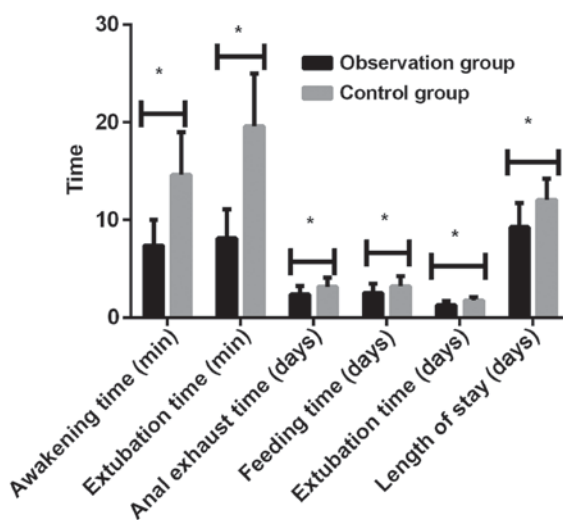


Figure 3. Comparison of the recovery conditions between the two groups. The results showed that the recovery time, extubation time, anal exhaust time, eating time, urinary catheter removal time and hospital stay in the observation group were significantly lower than those in the control group, and the difference was statistically significant ($P < 0.05$).

functions between the two groups before anesthesia ($P > 0.05$), but there was a significant difference in cognitive functions between the two groups at different time points ($P < 0.001$). There was no significant difference in cognitive functions between the two groups before anesthesia and 5 days after anesthesia ($P > 0.05$); the cognitive functions at 1 and 3 days after surgery was significantly lower than that before anesthesia; 3 days and 5 days after surgery was significantly higher than 1 day after surgery, and 5 days after surgery was significantly higher than 3 days after surgery, and the differences were statistically significant ($P < 0.05$) (Fig. 4 and Table V).

Discussion

Life and death are the normal state of life, and the function of the organ is irreversibly degraded with age, and the morbidity and mortality of elderly patients are also affected by this physiological phenomenon (17). With the development of aging society, the number of elderly patients with CRC have increased gradually (18). According to literature, carbon dioxide pneumoperitoneum may threaten the life of patients undergoing laparoscopic surgery (19,20). In particular, the postoperative recovery of elderly patients is often affected

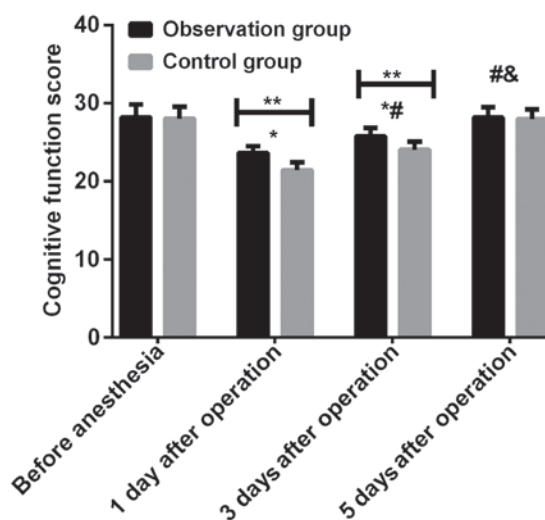


Figure 4. Comparison of postoperative cognitive functions between the two groups. The results showed that there was no significant difference in cognitive functions between the two groups before anesthesia ($P > 0.05$), but there was a significant difference in cognitive functions between the two groups at different time points ($P < 0.001$). There was no significant difference in cognitive functions between the two groups before anesthesia and 5 days after anesthesia ($P > 0.05$); the cognitive functions at 1 day and 3 days after surgery was significantly lower than that before anesthesia; 3 days and 5 days after surgery was significantly higher than 1 day after surgery, and 5 days after surgery was significantly higher than 3 days after surgery, and the differences were statistically significant ($P < 0.05$). ** $P < 0.05$; * $P < 0.05$ compared with before anesthesia; # $P < 0.05$ compared with 1 day after surgery; & $P < 0.05$ compared with 3 days after surgery.

by anesthesia and other factors (21), and it can also directly affect the cost of treatment, length of stay, and morbidity (22). According to reports in the literature, the proportion of elderly patients who have experienced unconsciousness after major surgery has reached 20% (23,24). At present, the pathogenesis of postoperative cognitive dysfunction has not been clarified, but a large number of comprehensive studies have shown that it may be related to anesthesia, patient age, type of surgery, education degree and other factors (25-27). In elderly patients, the immune function is reduced due to the gradual degradation of organ function in the body, and the body's ability to metabolize anesthetic drugs is also slower, resulting in a longer recovery time (28). Therefore, in order to make the elderly patients recover as soon as possible after anesthesia, safe, fast metabolized volatile anesthetics should be chosen to avoid the occurrence of postoperative cognitive dysfunction.

Table V. Comparison of postoperative cognitive functions between the two groups.

Time	Observation group (n=40)	Control group (n=38)	t value	P-value
Before anesthesia	28.19±1.64	28.01±1.52	0.502	0.617
1 day after surgery	23.64±0.87 ^a	21.41±1.05 ^a	10.230	<0.001
3 days after surgery	25.76±1.07 ^{a,b}	24.01±1.03 ^{a,b}	7.352	<0.001
5 days after surgery	28.15±1.32 ^{b,c}	27.96±1.24 ^{b,c}	0.654	0.515
F value	120.300	263.000		
P-value	<0.001	<0.001		

^aP<0.05 compared with before anesthesia; ^bP<0.05 compared with 1 day after surgery; ^cP<0.05 compared with 3 days after surgery.

The results showed that there was no significant difference in mean arterial pressure and heart rate between the observation and the control group at T0 and T1 (P>0.05). Although the mean arterial pressure and heart rate in the observation group were significantly lower than those in the control group at T2, T3 and T4, the hemodynamic parameters in the two groups were stable and normal. The recovery time, extubation time, anal exhaust time, eating time, urinary catheter removal time and hospital stay in the observation group were significantly lower than those in the control group, and the difference was statistically significant (P<0.05). The findings of Zhang *et al* (29) were basically consistent with ours, which indicated that sevoflurane inhalation general anesthesia combined with epidural block resulted in more stable hemodynamics and shorter recovery time. At the end of surgery, due to reducing the amount of general anesthesia and relying on epidural anesthesia to complete the final abdominal closure, suture skin, the postoperative pain was alleviated; extubation time was brought forward, and the recovery time was accelerated. Study of Akarsu Ayazoğlu *et al* (30) also showed that general anesthesia combined with epidural block could make hemodynamics more stable and recovery time shorter. In the study of Nishikawa *et al* (31), it was once again demonstrated that sevoflurane might be superior to propofol for general anesthesia and epidural analgesia in elderly patients undergoing long-term laparoscopic surgery, with less impact on patients' mental function. Murata *et al* (32) found that long-term high dose intravenous infusion of propofol changed pharmacokinetics and enhanced analgesic effect, thus prolonging the time of recovery and tracheal intubation extubation.

MMSE can effectively evaluate the cognitive function of the patient's brain, has high effectiveness and credibility, and the operation is relatively simple (33). Therefore, MMSE was used to evaluate the postoperative cognitive functions of the two groups in this study, and the results showed that, there was no significant difference in cognitive function between the two groups before anesthesia (P>0.05), but there was a significant difference in cognitive function between the two groups at different time points (P<0.001). Postoperative cognitive function showed a trend of decreasing first and then increasing; the scores of cognitive function in both groups 1 day after surgery were at trough level, and recovered gradually from 3 days after surgery. It speculated that sevoflurane inhalation anesthesia combined with epidural block can accelerate the metabolism

of anesthetics and reduce the damage of residual anesthetics to the central nervous system. The study of Fu and Li (34), showed that general anesthesia combined with epidural anesthesia had a faster recovery of postoperative cognitive function than that of general anesthesia alone in dystocia women, which is basically consistent with our research results.

However, there are some shortcomings in this study, such as the small number of cases, so the results and conclusions of this study still need to be verified by more research and larger clinical data. We also hope that this study will promote the participation of more scholars in the study of anesthesia in patients undergoing CRC radical surgery.

In conclusion, the mean arterial pressure and heart rate during the perioperative period are more stable in the elderly patients with sevoflurane inhalation combined with epidural anesthesia; the recovery time is shorter and more rapid, and the recovery time of postoperative cognitive function is also faster. Therefore, it provides a reference for patients undergoing CRC radical surgery to select high-quality and appropriate anesthetic protocols.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Authors' contributions

XZ helped with anesthetic methods and wrote the manuscript. XZ and HJ collected and interpreted the observation index. Both authors read and approved the final manuscript.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of The Second Cancer Hospital of Heilongjiang Province (Harbin,

China). Patients who participated in this research had complete clinical data. Signed written informed consents were obtained from the patients and/or guardians.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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