

Comparison of the synergistic effects of sevoflurane and desflurane on muscle relaxant vecuronium in laparoscopic colon cancer surgery

Qianqian Song, MM, Xiujie Zhao, MM, Yewen Wang, MM, Quanyi Zhang, MD^{a,*} 

Abstract

Sevoflurane and desflurane are commonly used inhalation anesthetics in clinical practice. This study compared the synergistic effects of sevoflurane and desflurane on the muscarinic agent vecuronium in laparoscopic colon cancer surgery. The aim of this study was to compare sevoflurane and desflurane in a synergistic effect on the muscle relaxant vecuronium in laparoscopic colon cancer surgery. Sixty patients undergoing elective laparoscopic radical resection of colon cancer were randomly divided into sevoflurane ($n = 30$) and desflurane ($n = 30$) groups. After anesthesia and successful tracheal intubation, patients in both groups were maintained with combined remifentanyl. Muscle relaxant effects were monitored in both groups using a muscle relaxant monitor (train of stimuli-Watch), the onset time, T1 and T2 recovery time, and muscle relaxant dosage of vecuronium were observed. Hemodynamic changes were observed in both groups, and the dosage of vasoactive drugs was recorded. The quality of recovery of the patients was evaluated using the Mini-Mental State Examination (MMSE) and the discharge from the Aldrete score criteria. There was no significant difference in the onset time of vecuronium between the two groups ($P > .05$). The desflurane group's T1 and T2 recovery times were later than that of the sevoflurane group. The dosage of vecuronium was statistically significantly less than that in the sevoflurane group ($P < .05$); the extubation time in the desflurane group was statistically significantly longer than that in the sevoflurane group ($P < .05$). There were no significant differences in preoperative and intraoperative mean arterial pressure, heart rate, ephedrine and atropine dosage, MMSE score, and Aldrete score between the 2 groups ($P > .05$). Compared with sevoflurane, desflurane has a stronger synergistic effect on the muscle relaxant of vecuronium without increasing the incidence of cardiovascular adverse reactions and affecting patient recovery.

Abbreviations: BIS = bispectral index, HR = heart rate, MAP = mean arterial pressure, MMSE = Mini-Mental State Examination, $P_{et}CO_2$ = pressure of end-tidal carbon dioxide, TOF = train of stimuli.

Keywords: desflurane, radical resection of colon cancer, sevoflurane, synergistic effect of muscle relaxant, vecuronium

1. Introduction

Colon cancer is a common digestive system disease in clinical practice,^[1] closely related to smoking, intestinal inflammation, poor dietary habits, genetic factors and age.^[2] Based on the advantages of laparoscopic surgery, such as less trauma and rapid postoperative recovery, laparoscopic tumor resection has become the first choice for the treatment of colon cancer.^[3] Endotracheal intubation combined with general anesthesia is a commonly used anesthesia method in clinical practice. Laparoscopic surgery requires a good muscle relaxant, and muscle relaxants are essential adjuvant drugs in general anesthesia, facilitating endotracheal intubation during general anesthesia and maintaining good muscle relaxants during surgery.^[4] Vecuronium has no histamine-releasing effect and less

adverse reactions, and is a commonly used non-depolarizing neuromuscular blocker in general anesthesia. Excessive use of intraoperative inotropes can lead to delayed postoperative recovery of patients. Inhaled anesthetics also have muscle relaxant effects up to a certain depth and can enhance the effect of muscle relaxants. Their synergistic effect on muscle relaxants also gradually increases with increasing inhalation concentration and time. Sevoflurane and desflurane are commonly used inhalation anesthetics in clinical practice. Both have low blood/gas partition coefficient^[5] and are easy to operate.^[6] At present, there is no relevant study on the comparison of the synergistic effect of sevoflurane and desflurane on muscle relaxant vecuronium, so we selected 60 patients undergoing elective laparoscopic radical resection of colon cancer in our hospital as the study subjects to observe the difference in the synergistic effect

This work was supported by the Provincial construction fund for key clinical specialty in Shandong Province (SLCZDZK-20 Department of Anesthesiology).

The authors declare that they have no competing interests.

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

This study has been approved by the medical ethics committee of the Binzhou Medical University Hospital ([2021] Ethical Review No. KT-017), and all patients signed an informed consent form.

^a Department of Anesthesiology, Binzhou Medical University Hospital, Shandong, China.

* Correspondence: Quanyi Zhang, Department of Anesthesiology, Binzhou Medical University Hospital, No. 661 Huanghe 2nd Road, Binzhou 256603, Shandong, China (e-mail: zhang_quan_yi@126.com).

Copyright © 2022 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and build up the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

How to cite this article: Song Q, Zhao X, Wang Y, Zhang Q. Comparison of the synergistic effects of sevoflurane and desflurane on muscle relaxant vecuronium in laparoscopic colon cancer surgery. *Medicine* 2022;101:45(e31569).

Received: 6 August 2022 / Received in final form: 6 October 2022 / Accepted: 6 October 2022

<http://dx.doi.org/10.1097/MD.00000000000031569>

of 1.3 MAC sevoflurane and desflurane on vecuronium muscle relaxant.

2. Materials and methods

2.1. General information

This study has been approved by the medical ethics committee of the hospital ([2021] Ethical Review No. KT-017), and all patients signed an informed consent form. The study was conducted on sixty patients who underwent elective laparoscopic radical resection of colon cancer in the Affiliated Hospital of Binzhou Medical College from June 2021 to April 2022. Inclusion criteria aged ≥ 18 years, ASA I-II, normal liver and kidney function, normal cardiopulmonary function. Exclusion criteria: malnutrition, suffering from neuromuscular system diseases, recent use of anti-sympathetic and sedatives, allergy to the selected anesthetic drugs. Methods: 60 patients were randomly divided into sevoflurane group and desflurane group, with 30 people in each group.

2.2. Methods

After the patients were admitted to the operating room, venous access was routinely established, electrocardiogram (ECG) was monitored, mean arterial pressure (MAP), heart rate (HR), saturation (SpO₂), bispectral index (BIS) were measured by radial artery puncture, and muscle relaxant monitoring was performed. Anesthesia induction: intravenous injection of midazolam 2 mg, fentanyl 4 μ g/kg, vecuronium 0.1 mg/kg, etomidate 20 mg, after the patient's consciousness completely disappeared, when the four train of stimuli (TOF) count was 0, tracheal intubation was performed, after successful intubation, continuous inhalation of 100% O₂ 2L/min. Maintenance of anesthesia: The concentration of inhalation anesthetics was adjusted to maintain the end-tidal concentration of sevoflurane and desflurane at 1.3 MAC. Remifentanyl was continuously pumped in both groups, and the pumping rate was adjusted according to hemodynamic changes. When the muscle relaxant monitor showed T2 recovery, additional muscle relaxants were added in time, and each additional dose was 1/3 to 1/5 of the induction dose. BIS 40 to 60 and partial pressure of end-tidal carbon dioxide (P_{et}CO₂) 35 mm Hg to 45 mm Hg were maintained. If HR < 45 beats/min, atropine was given to increase HR, MAP < 60 mm Hg, and ephedrine to increase blood pressure. HR and MAP were recorded at four-time points: t1 (before induction), t2 (before intubation), t3 (before skin incision), and t4 (at the end of surgery) in both groups. After the surgery, inhalation of sevoflurane or desflurane was stopped and pump infusion of remifentanyl was stopped. Muscle relaxant monitoring was stopped after TOF $\geq 90\%$. When the patient opened his eyes on call, looked up for more than 5 seconds, and clenched his fist for more than 5 seconds, the endotracheal tube was removed and sent to the PACU for further observation.

2.3. Outcome measures

2.3.1. Muscle relaxant effect. The muscle relaxant of the patients was monitored using a muscle relaxant monitor, and the skin on the running surface of the ulnar nerve at the wrist was defatted with alcohol. Two electrodes were placed on the surface of the ulnar nerve at an interval of 3 cm to 5 cm at the wrist, respectively, fix the transducer on the thumb pulp, keep the temperature of monitoring arm not less than 32 °C, adopt TOF stimulation form, electrical stimulation frequency 2 Hz, stimulation current 30 mA, each train of stimulation interval 15 seconds, record onset time: the time from the first injection of vecuronium bromide to the TOF count of 0, muscle relaxant recovery time: the recovery time of T1 (equivalent to 95% of

the neuromuscular block) and T2 (equivalent to 90% of the neuromuscular block) after the first injection of vecuronium bromide,^[7] total dose of vecuronium.

2.3.2. Quality of recovery. Thirty minutes after admission to the PACU, the patients were assessed using the Mini-Mental State Examination (MMSE) and the Out of Recovery Room Scoring Criteria (Aldrete), in which the MMSE total score was 30 points, the score ≥ 27 was normal,^[8] the Aldrete total score was 10 points. The patients could leave the PACU and return to the ward if the score was ≥ 9 points.^[9]

2.4. Statistical methods

SPSS 24.0 statistical software was used for data analysis. Quantitative data were expressed as mean \pm standard deviation ($\bar{x} \pm s$) or median (25%, 75%). Paired sample *t*-test was used for within-group comparison. An independent sample *t*-test or independent sample non-parametric test was used for comparison. One-way analysis of variance was used for repeated measurement data. Qualitative data were expressed in number of cases. Chi-square test (X^2) was used for comparison. $P < .05$ was considered statistically significant.

3. Results

3.1. General information

Eighty-eight patients undergoing elective laparoscopic radical resection of colon cancer were initially screened. Twenty-three patients with ASA physical status III and above and 23 patients who refused to participate in this study were excluded. Sixty-five patients were randomly divided into the sevoflurane group ($n = 32$) and the desflurane group ($n = 33$). Patients who underwent partial hepatectomy due to intraoperative liver metastases in the groups sevoflurane ($n = 2$) and desflurane ($n = 3$) were excluded. Finally, 30 patients in each group participated in this study (Fig. 1). There was no significant difference in gender composition, age, BMI, ASA grade composition, operation time, anesthesia time, atropine and ephedrine dosage, blood loss, urine volume, infusion volume and hospital stay between the two groups ($P > .05$); the extubation time in the sevoflurane group and remifentanyl dosage in the sevoflurane group were less than that in the sevoflurane group, and the differences had statistical significance ($P < .05$) (Table 1).

3.2. Comparison of HR and MAP between the two groups

The HR and MAP at t2, t3 and t4 in the two groups were statistically significantly lower than those at t1 ($P < .05$), but there was no significant difference between the two groups at the same time point ($P > .05$). More details are shown in Figure 2A and B.

3.3. Muscle relaxant comparison

T1 and T2 recovery times in desflurane group were later than that in sevoflurane group, and the difference had statistical significance ($P < .05$) (Fig. 3). There was no significant difference in the onset time of muscle relaxant between the two groups ($P > .05$) (Fig. 4A). The dosage of muscle relaxant in the desflurane group was statistically significantly less than that in the sevoflurane group ($P < .05$) (Fig. 4B).

4. Discussion

Vecuronium bromide is a medium-acting non-depolarizing muscle relaxant with a rapid onset of action, good muscle relaxant effect, and no significant effect on the body's circulatory function. Its pharmacological effects are mainly through competing

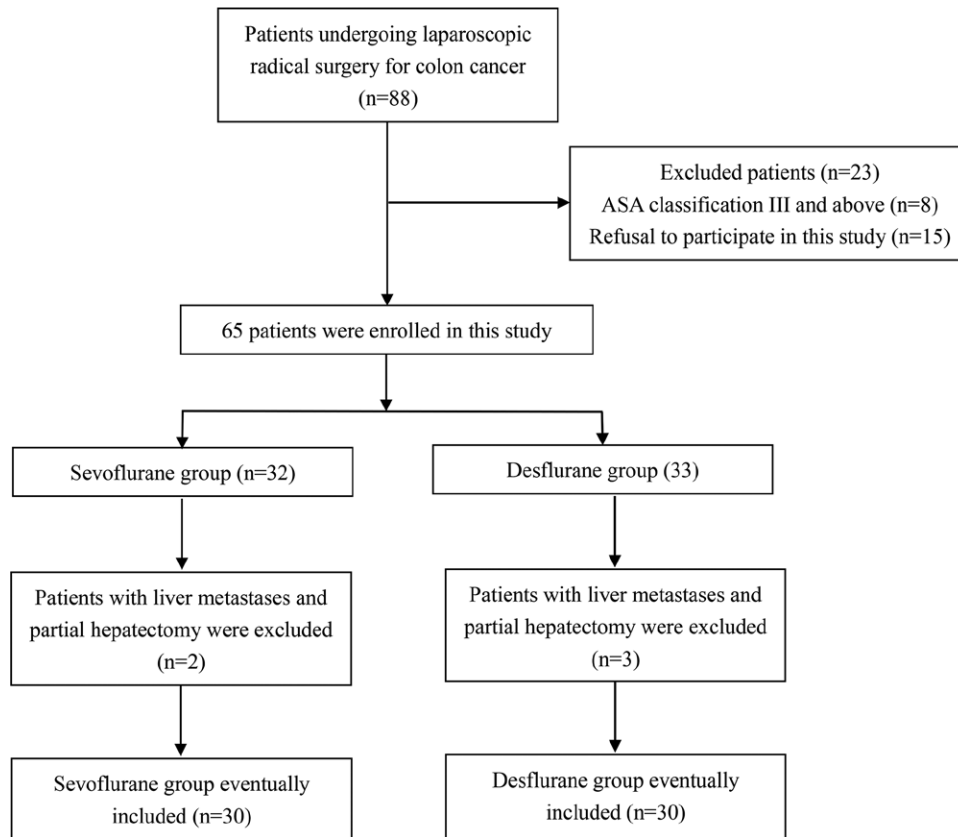


Figure 1. Flow chart of patient's recruitment.

Table 1
Comparison of general and surgery information between the two groups of patients.

Factor	Sevoflurane group (n = 30)	Desflurane group (n = 30)	P
Age (years)	64.43 ± 9.89	67.03 ± 7.55	.257
Gender (male/female)	22/8	21/9	.774
BMI (kg/m ²)	23.22 ± 2.73	24.37 ± 2.16	.076
ASA (I/II)	20/10	15/15	.190
Operation time (min)	174.40 ± 5.08	175.63 ± 4.75	.336
Anesthesia time (min)	208.73 ± 4.32	210.07 ± 5.71	.312
Extubation time (min)	13.47 ± 2.11	11.13 ± 1.98*	<.001
Atropine (mg)	0.33 ± 0.14	0.37 ± 0.12	.610
Ephedrine (mg)	4.33 ± 1.37	4.00 ± 1.26	.670
Remifentanil (ug)	761.00 ± 105.42	667.33 ± 113.41*	.002
Blood loss (mL)	20 (20, 30)	30 (20, 40)	.152
Urine volume (mL)	200 (200, 300)	200 (200, 300)	.500
Infusion (mL)	1600 (1600, 2100)	1600 (1600, 2100)	.934
Hospitalization time (d)	16 (15, 17)	16 (14.75, 17)	.651
MMSE score	28 (27, 29)	28 (27, 29)	.994
Aldrete score	9 (9, 9.25)	9 (9, 10)	.813

ASA = American Society of Anesthesiologists, BMI = Body Mass Index, MMSE = Mini-Mental State Examination; *P < .05.

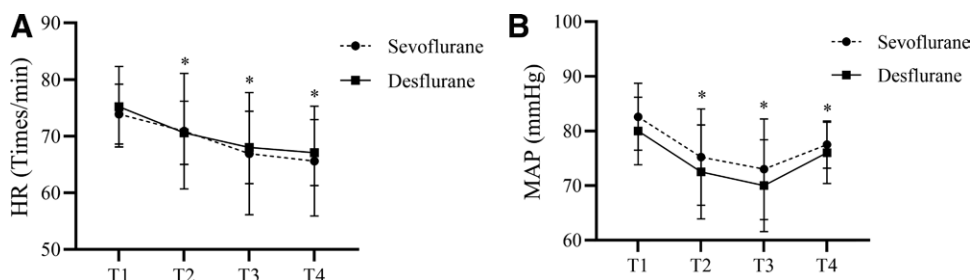


Figure 2. Changes in heart rate (HR) and mean arterial pressure (MAP) at different time points. (A) HR and (B) MAP.

with acetylcholine for nicotinic receptors located on the motor endplate of striated muscle, thereby blocking the conduction between striated muscle and nerve endings. The difference from depolarizing muscle relaxants is that this drug will not cause fasciculation of muscle fibers, and has no histamine release effect^[10] and less adverse reactions. Intraoperative use of vecuronium can reduce abdominal muscle tension and relax abdominal wall muscles,^[11] It is conducive to a smooth operation.

Inhalation anesthetics can also produce muscle relaxants with increasing concentration, time, and synergistic effects on muscle relaxants. Its mechanisms of action may be: inhibition of presynaptic voltage-gated sodium channels and reduction of acetylcholine release; increased sensitivity of skeletal muscle to non-depolarizing myosinoids; and decreased sensitivity of post-synaptic acetylcholine receptors to acetylcholine;^[12] indirectly promote muscle relaxant through central inhibitory effects; increase muscle and transport more myotonics to act at the nerve-muscle junction; increase the threshold of endplate potentials to produce action potentials and weaken the conduction of nerve excitation, thereby inhibiting muscle fiber contraction.^[13]

Sevoflurane and desflurane are commonly used inhalation anesthetics in clinical practice.^[14] Both are characterized by low blood/gas partition coefficient, good controllability, and rapid recovery,^[15] Combined use of remifentanyl with rapid metabolism can prolong intraoperative analgesic effect.^[16] Xu et al^[17] showed that 1.3 MAC sevoflurane could significantly shorten the onset time of rocuronium. At the same time, 1.0 MAC had no significant effect. The concentration of inhalation anesthetics was usually above 1.3 MAC to inhibit the noxious stimulation of large and medium surgery, so the concentration of inhalation anesthetics selected in this study was 1.3 MAC.

Our study found that the T1 and T2 recovery time in the desflurane group was significantly longer than that in the sevoflurane group, and the amount of muscle relaxant was

significantly less than that in the sevoflurane group, indicating that desflurane has a better muscle relaxant synergy effect on vecuronium than sevoflurane. Hemmerling et al^[18] found that the requirement of cisatracurium was reduced by 41% and 60% at 1.3 MAC with sevoflurane and desflurane, respectively, compared with sevoflurane, which significantly reduced the amount of cisatracurium compared with sevoflurane, which is consistent with the conclusions of our study. However, a study by Kang et al^[19] on elderly patients found that. There was no significant difference in the myorelaxant enhancement effect between 1.3 MAC sevoflurane and desflurane p-rocuronium. In this study, the mode of administration of rocuronium was continuous pumping rather than divided administration, which may be why the study's conclusions differed from ours. Chen et al^[20] demonstrated that continuous intravenous infusion of vecuronium was superior to divided administration in maintaining muscle relaxant. The neuromuscular block time was prolonged by nearly 1 time at the same dose, which may be because continuous intravenous infusion would keep the plasma concentration in the body at a steady-state level and the drug concentration at the site of action was also relatively dynamic and stable, so in this case, the synergistic effect of inhalation anesthetics on vecuronium may not be so significant.

In our study, patients in the desflurane group were extubated earlier than those in the sevoflurane group, which is consistent with the conclusions of the study by Wu et al^[21] The possible reasons for this may be that the blood/gas partition coefficient of desflurane is 0.45, which is significantly lower than the blood/gas partition coefficient of sevoflurane (0.65),^[22] so that desflurane elutes more rapidly.^[23] The catabolic rate and biotransformation rate of desflurane in the body are very low,^[24] with no significant accumulation after long-term use, conducive to patient recovery.

Our study showed that remifentanyl consumption was significantly less in the desflurane group than in the sevoflurane group, which is consistent with the view of Ryu et al^[25] The reason for this difference may be that desflurane has more vasodilatory properties than sevoflurane, so maintaining the same SPI during desflurane anesthesia (surgical stress index, a value between 20 and 50 under general anesthesia represents an appropriate level of analgesia, >50 indicates inadequate analgesia, and <20 indicates excessive analgesia),^[26] and requiring less opioids.

This study has some limitations. First, our sample size is small and may require a larger sample size to validate our conclusions; second, it is well-known that desflurane is somewhat irritating to the airways. The study did not address the incidence of respiratory complications.

5. Conclusion

Compared with sevoflurane, desflurane has stronger synergistic effect on the muscle relaxant vecuronium without increasing the

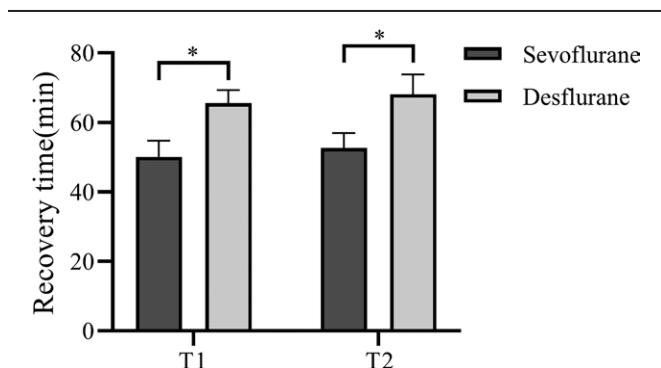


Figure 3. T1 and T2 recovery time between in groups of sevoflurane and desflurane.

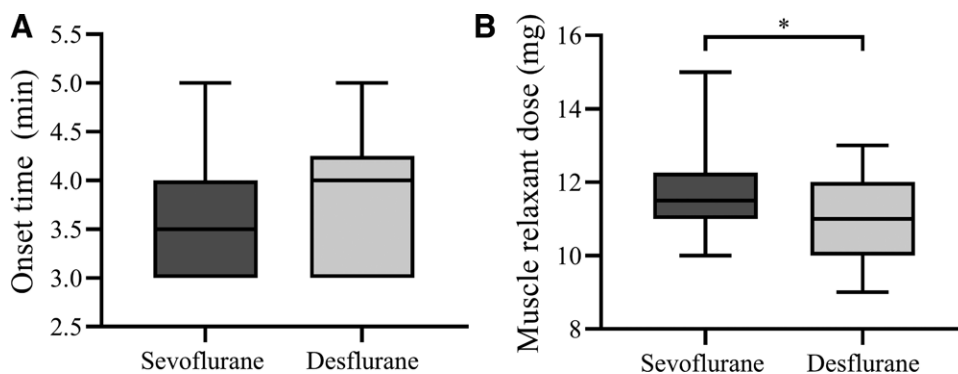


Figure 4. The onset of muscle relaxant and dose of muscle relaxant in the two groups.

incidence of cardiovascular adverse reactions and affecting the quality of recovery of patients.

Acknowledgments

None.

Author contributions

Conceptualization: Qianqian Song.

Data curation: Qianqian Song.

Formal analysis: Qianqian Song.

Funding acquisition: Quanyi Zhang.

Investigation: Xiujie Zhao.

Methodology: Xiujie Zhao.

Resources: Xiujie Zhao, Yewen Wang.

Software: Yewen Wang.

Supervision: Quanyi Zhang.

Project administration: Quanyi Zhang.

Validation: Quanyi Zhang, Yewen Wang.

Visualization: Quanyi Zhang.

Writing – original draft: Qianqian Song.

Writing – review & editing: Qianqian Song, Quanyi Zhang.

References

- [1] Zhang L. Comparison of the clinical effect of laparoscopic radical resection of colorectal cancer and laparotomy in the treatment of patients with colorectal cancer. *Med Equip.* 2022;35:42–3.
- [2] Rezapour S, Hosseinzadeh E, Marofi F, et al. Epigenetic-based therapy for colorectal cancer: prospect and involved mechanisms. *J Cell Physiol.* 2019;234:19366–83.
- [3] Wang CM, Cai CH, Zhang J, et al. Comparison of the effect of different anesthesia methods in the recovery period of laparoscopic colorectal cancer surgery. *J Pract Med.* 2018;34:3454–7.
- [4] Goodner JA, Likar EJ, Hoff AL, et al. Clinical impact of sugammadex in the reversal of neuromuscular blockade. *Cureus.* 2021;13:e15413.
- [5] Wu Z-W, Wang H, Huang Y, et al. Comparison of the effects of sevoflurane and desflurane on regional cerebral oxygen saturation and caspase-3 protein levels in neurosurgical patients. *Pharm Biotechnol.* 2021;28:275–9.
- [6] Wu X, Shan C, Peng B, et al. Comparison of desflurane and sevoflurane on postoperative recovery quality after tonsillectomy and adenoidectomy in children. *Exp Ther Med.* 2019;17:4561–7.
- [7] Čaušević S, Rizvanović N, Pojskić B. Comparison of intubation condition and the quality of muscle relaxation between rocuronium and vecuronium using “timing principle”. *Med Glas (Zenica).* 2020;17:7–14.
- [8] Ren Y, Wang T, Zhou Q, et al. Comparison of MoCA and MMSE scales in cognitive assessment of presbycusis. *Chin Sci J Hear Speech Rehabil.* 2022;20:107–11.
- [9] Zhao N, Zhou BZ, Liu LY, et al. Effect of systematic nursing on physiological function and respiratory and circulatory function in elderly patients undergoing surgical anesthesia under the background of modified Aldrete score. *Lab Med Clin.* 2022;19:796–9.
- [10] Wang B, Liu JB, Zhao RX, et al. Analysis of the anesthetic effect of vecuronium bromide complex in laparoscopic cholecystectomy. *Mod Diagn Treat.* 2019;30:205–1207.
- [11] Jiang WF, Luo JY, Wang XY, et al. Study on the effect of vecuronium bromide on transpulmonary pressure in patients with acute respiratory distress syndrome and abdominal hypertension. *Chongqing Med.* 2019;48:1216–8.
- [12] Zhou L, Xiang SL, Yang J, et al. Effect of anesthesia maintenance methods on residual muscle relaxant after short surgery. *Med J Chin People's Liberat Army.* 2021;46:935–9.
- [13] Wang YH, Cui XG, Ran H, et al. Effect of aminophylline on residual muscle relaxant of rocuronium under sevoflurane anesthesia in laparoscopic surgery. *Chin Remed Clin.* 2019;19:742–4.
- [14] Lei XH, Li M, Huang GZ. Comparison of recovery time and quality of recovery between desflurane and sevoflurane after anesthesia in obese surgical patients. *Contemp Med.* 2019;25:42–4.
- [15] Wang YP, Wang J, Zhang LX, et al. Comparison of desflurane and sevoflurane in the recovery of children after laparoscopic surgery. *China Health Stand Manag.* 2020;11:111–3.
- [16] Niu XY, Pan H, Wang HL. Comparison of the efficacy and safety of sevoflurane and desflurane in patients with femoral neck fracture. *Mod Diagn Treat.* 2021;32:1038–9.
- [17] Xu GH, Zhang J. Effect of inhalation of different concentrations of sevoflurane on the myorelaxant effect of rocuronium. *Acta Univer Med Anhui.* 2007;42:104–5.
- [18] Hemmerling TM, Schuettler J, Schwilden H. Desflurane reduces the effective therapeutic infusion rate (ETI) of cisatracurium more than isoflurane, sevoflurane, or propofol. *Can J Anaesth.* 2001;48:532–7.
- [19] Kang DX, Rao YQ, Shangguan WN, et al. Comparison of the effects of sevoflurane and desflurane on the continuous infusion rate of rocuronium in elderly patients. *Chin J Clin Pharm.* 2017;26:23–7.
- [20] Chen XZ, Cheng H, Wang BG, et al. Comparison of the time-effect of continuous intravenous infusion of vecuronium. *J Capital Med Univer.* 2001;22:162–4.
- [21] Wu YM, Su YH, Huang SY, et al. Recovery profiles of sevoflurane and desflurane with or without M-entropy guidance in obese patients: a randomized controlled trial. *J Clin Med.* 2021;11:162.
- [22] Gangakhedkar GR, Monteiro JN. A prospective randomized double-blind study to compare the early recovery profiles of desflurane and sevoflurane in patients undergoing laparoscopic cholecystectomy. *J Anaesthesiol Clin Pharmacol.* 2019;35:53–7.
- [23] Lin XY. A clinical comparative study of sevoflurane and desflurane in the quality of recovery after maintenance of pediatric anesthesia. *Chin Foreign Medi Res.* 2020;18:5–7.
- [24] Chen XF, Wei Y, Wang J, et al. Study on the effect of target-controlled infusion combined with desflurane inhalation anesthesia on elderly patients undergoing gynecological laparoscopic surgery. *Med Forum.* 2019;23:1363–5.
- [25] Ryu KH, Kim JA, Ko DC, et al. Desflurane reduces intraoperative remifentanyl requirements more than sevoflurane: comparison using surgical pleth index-guided analgesia. *Br J Anaesth.* 2018;121:1115–22.
- [26] Yang L, Wang YY. Effects of desflurane and sevoflurane on bispectral index and surgical volume tracing index during shoulder arthroscopy. *J China Med Univ.* 2022;51:238–42.