Reducing Remifentanil Usage in Laparoscopic Rectal Cancer Surgery for Elderly Patients by Optimizing Dosing

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ABSTRACT

Background • Colorectal cancer is a prevalent and serious health concern globally, particularly among the elderly population. Laparoscopic surgery is a commonly used approach for colorectal cancer treatment. However, the use of appropriate anesthesia and muscle relaxants is essential to ensure optimal surgical outcomes. Elderly patients undergoing surgery often have unique physiological characteristics and comorbidities, such as hypertension, diabetes, and coronary heart disease. These factors can affect treatment efficiency and patient outcomes.

Objective • This study aimed to investigate the impact of different target-controlled infusion concentrations of rocuronium bromide on elderly patients undergoing laparoscopic colorectal cancer surgery.

Methods • This is a prospective randomized controlled study. Ninety senior adults who underwent laparoscopic colorectal cancer surgery at our hospital between September 2018 and May 2020 were selected as the eligible participants. They were randomly divided into three groups: the low-dose group (0.6 mg/L of rocuronium bromide), the middle-dose group (0.9 mg/L of rocuronium bromide), and the high-dose group (1.2 mg/L of rocuronium bromide). The purpose of this division was to administer target-controlled infusions of rocuronium bromide to maintain skeletal muscle relaxation during the surgical procedure. Data on various outcome measures, including skeletal muscle relaxation effectiveness, patient satisfaction, skeletal muscle relaxation recovery times and indices, extubation duration, and remifentanil dosage, were collected and analyzed.

Results • The middle-dose group and the high-dose group exhibited notably higher levels of satisfaction with skeletal muscle relaxation compared to the low-dose group. As the rocuronium bromide dosage increased, the patients experienced prolonged recovery times and had higher skeletal muscle indices ($P < .05$). Additionally, the middle-dose group demonstrated significantly reduced extubation times and lower remifentanil dosages compared to the other groups ($P < .05$). The enhanced satisfaction levels in the middle-dose and high-dose groups, indicating that higher concentrations of rocuronium bromide may be more effective in achieving optimal skeletal muscle relaxation during laparoscopic colorectal cancer surgery. The prolonged recovery times and higher skeletal muscle indices associated with increased dosage suggest a dose-dependent effect on muscle relaxation.

Conclusion • For elderly patients undergoing laparoscopic rectal cancer surgery, the use of a target-controlled infusion of 0.9 mg/L of rocuronium bromide appears to be a viable option. It maintains adequate skeletal muscle relaxation, shortens postoperative recovery time, and reduces the demand for remifentanil, demonstrating excellent potential for clinical application. These findings provide valuable insights for anesthesiologists and healthcare professionals involved in the perioperative management of elderly patients undergoing laparoscopic rectal cancer surgery. Implementing the optimized dosage of rocuronium bromide can contribute to enhanced surgical outcomes, improved patient satisfaction, and more efficient resource utilization in the clinical setting. (*Altern Ther Health Med.* [E-pub ahead of print.])

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INTRODUCTION

Colorectal cancer is a prevalent and escalating clinical malignancy, characterized by a rising morbidity and mortality rate over the years. Global cancer data from 2019 revealed that colorectal cancer ranks third in terms of incidence and second in terms of mortality among all malignancies.[1] This disease presents a substantial challenge in the field of healthcare worldwide, as its high prevalence and associated healthcare expenses exert significant pressure on healthcare systems. Moreover, the impact of colorectal cancer extends beyond the medical realm, profoundly affecting the well-being and daily lives of patients and their families.[1] It is worth noting that the escalating trend of population aging significantly raises the risk of colorectal cancer among the elderly population, thereby further intensifying the burden on healthcare systems. The increasingly high prevalence in the elderly population in China and comorbid diseases, including hypertension, diabetes, and coronary heart disease, result in compromised treatment efficiency.[2,3] Moreover, the recovery process in elderly patients is often slower compared to younger individuals. Postoperative complications, such as infections, delirium, and functional decline, are more common in the elderly population. Tailoring anesthesia protocols, including the use of muscle relaxants like rocuronium bromide, to optimize recovery and minimize complications becomes crucial. At present, the most radical clinical management for colorectal cancer is surgery, but traditional open surgery is associated with large trauma, slow postoperative recovery, and multiple complications. The

advancement of minimally invasive techniques enhances the treatment efficiency of colorectal cancer, among which laparoscopy and colonoscopy are commonly used in the diagnosis and treatment of multiple diseases.[4] Laparoscopic combined with colonoscopic surgery improves the accuracy and success of the procedure through colonoscopy to reduce the residual lesion.[5]

Currently, laparoscopic surgery is commonly performed for colorectal cancer under general anesthesia. Rocuronium bromide is a new intermediate-acting non-depolarizing muscle relaxant drug with characteristics of rapid onset, long duration, short half-life, and no biologically active metabolites.[6] The decreased plasma clearance rate of the medication in older persons lowers the muscle relaxing effect, which underlines the safety and controllability of muscular relaxation.[7] Adequate skeletal muscle relaxation is essential because it allows the surgeon to access and visualize the surgical site more effectively. It creates a relaxed and immobile surgical field, enabling precise manipulation of instruments, improved exposure, and accurate suturing. Insufficient muscle relaxation can hinder the surgeon's ability to maneuver, leading to difficulties in performing delicate surgical tasks and potentially compromising the procedure's success. The pharmacokinetic properties of rocuronium bromide conform to the three-compartment model, which allows and provides rapid delivery of the set target concentration and maintenance of the patient's skeletal muscle relaxation level.[8] Despite survival benefits after surgical management, postoperative complications are associated with compromised recovery and physiological status of patients. Research has shown that traditional Chinese medicine (TCM) treatment of colorectal cancer regulates the immune microenvironment of patients through multiple pathways.[9]

TCM approaches cancer treatment from a holistic perspective, focusing on restoring the body's balance and promoting overall health and well-being. And the potential benefits of TCM in cancer treatment include symptom management, immune system support, adjunctive therapy and holistic approach. According to TCM, colorectal cancer is related to "diarrhea" and "blood in the stool," which are mainly caused by deficiency of vital energy due to congenital deficiency, dietary disorders or invasion of external evil, and the accumulation of damp-heat and toxic evil in the intestine. Damp-heat is a common type of evidence in colorectal cancer patients, and damp-heat is a pathological product as well as a causative factor that merits clinical attention.[10] Gegen Qinlian Decoction is a classic formula for the treatment of damp-heat evidence, which synergistically enhances immunotherapy with programmed cell death protein-1.[11] Thus, Gegen Qinlian Decoction is adopted for postoperative treatment.

Limited knowledge exists regarding the optimal target concentration and pharmacodynamics of rocuronium bromide specifically in the context of laparoscopic surgery, particularly in the elderly population.[12] To this end, the present study explores the impact of different target-controlled infusion concentrations of rocuronium bromide on elderly patients with laparoscopic colorectal cancer surgery.

MATERIALS AND METHODS
Baseline information

A total of 90 senior patients with laparoscopic colorectal cancer surgery who were treated at our hospital between September 2018 and May 2020 were randomly assigned to receive a target-controlled infusion of 0.6mg/L of rocuronium bromide (low-dose group), 0.9mg/L of rocuronium bromide (middle-dose group), and 1.2mg/L of rocuronium bromide (high-dose group) to maintain skeletal muscle relaxation during surgery.

The original sample size calculation estimated that 30 patients in each group would be needed to detect a 3-point difference between groups in a 2-sided significance test with a power of 0.8 and an alpha error level of 0.05.

Prior to participation, all participants were provided with detailed information about the study, including its purpose, methods, potential risks, and benefits. They were given sufficient time to review the information and ask any questions they had. Informed consent was obtained from each participant, ensuring their voluntary participation and understanding of the study. The rights and privacy of the patients were respected throughout the study. Confidentiality measures were implemented to protect the privacy of participants' personal and medical information. Data collection and storage procedures were designed in compliance with relevant data protection regulations to safeguard participant confidentiality. The study adhered to established ethical guidelines, including the principles outlined in the Helsinki Declaration. These guidelines ensure the protection of participants' rights, welfare, and well-being. The research aimed to minimize any potential harm or discomfort to the participants while maximizing the potential benefits of the study. A detailed research plan, including the study's objectives, methods, participant recruitment, and data collection procedures, was submitted to the Hospital Ethics Committee for review. The committee assessed the ethical soundness of the research and approved the study protocol, ensuring that it aligned with ethical standards and regulations. Ethics number: JG-JU20180906.

Elderly patients undergoing laparoscopic rectal cancer surgery are typically of advanced age, with the majority being aged 65 and above and a higher proportion being male. They often present with concurrent chronic conditions such as hypertension and diabetes, which elevate the surgical risk. These patients face an increased risk of complications, including infections, bleeding, cardiac and pulmonary issues, as well as gastrointestinal problems. Preoperative factors may encompass compromised immune function and nutritional deficiencies. Consequently, rectal cancer surgery in the elderly necessitates special attention to preoperative assessment and risk management to ensure optimal surgical outcomes and recovery.

There were 18 males and 12 females in the low-dose group, aged 61-77 (68.34±5.26) years, with a weight of 49-85(60.27±7.48) kg; there were 13 cases of ASA classification grade I and 17 cases of grade II.

In the middle-dose group, there were 17 males and 13 females, aged 60-77 (68.41±5.30) years, with a weight of

49-84 (60.21±7.38) kg; there were 14 cases of ASA classification grade I and16 cases of grade II.

There were 19 males and 11 females in the high-dose group, aged 61-77 (68.41±5.32) years, with a weight of 48-85 (60.30±7.42) kg; there were 11 cases of ASA classification grade I and 19 cases of grade II.

Inclusion and exclusion criteria

Inclusion criteria: (1) patients who were over 65 years and met the relevant indications for surgery; (2) patients had normal communication ability; (3) patients were willing to cooperate with this study.

Exclusion criteria: (1) patients with severe mental illness or language communication disorders; (2) Patients with poor compliance and resistance to cooperate with this study; (3) patients with difficulties in venous access puncture or repeated puncture at the same site; (4) patients who failed to successfully complete the study as planned due to various interfering factors. (5) patients with allergy to relevant drugs; (6) patients on sedative and analgesic drugs; (7) patients with cardiopulmonary, hepatic, and renal insufficiency; (8) patients with cerebrovascular disease; (9) patients with forearm thrombophlebitis; (10) patients with chronic pain syndrome; (11) patients with neuropathic pain; (12) pregnant women.

Randomization: a computer-generated randomization sequence has been used. Each patient was assigned a unique identification number and then randomized using a randomization algorithm. This process assigns patients to different treatment groups, a rocuronium bromide concentration group and a control group, in a random manner.

The allocation of patients to the different groups was concealed to maintain blinding and prevent potential allocation bias. This was achieved through the use of sealed envelopes, central randomization through the involvement of an independent statistician responsible for the randomization process.

Methods

The process of laparoscopic surgery involves the following steps: Initially, an anesthesiologist assesses the patient's health condition, monitors vital signs, establishes an intravenous line, and gradually administers anesthesia drugs such as sedatives, analgesics, and muscle relaxants to induce unconsciousness, ensuring that the patient does not feel pain during the procedure. While under anesthesia, the surgeon inserts a laparoscope through small incisions and performs surgical procedures, such as tissue resection, hemostasis, and wound closure, all under the magnified view of a microscope. This laparoscopic technique reduces tissue damage and trauma, facilitating faster recovery. All patients underwent routine monitoring of electrocardiogram, heart rate, blood pressure, oxygen saturation, and end-tidal carbon dioxide partial pressure after admission to the operation room. The venous access was established, and Sodium Lactated Ringer's Injection was intravenously administered. The anesthesia induction and maintenance were identical in the three

groups. Anesthesia was performed with fentanyl 1.8 μg/kg, midazolam 0.04 mg/kg, propofol 1.4 mg/kg, and rocuronium 0.6 mg/kg. Anesthesia was maintained with 0.4-1.05 μg (/kg·min) of remifentanil and 0.05-0.15 mg (/kg·min) of propofol. The three groups of patients were treated with target-controlled infusion of rocuronium bromide 0.6 mg/L, 0.9 mg/L, and 1.2 mg/L, respectively, to maintain skeletal muscle relaxation during surgery.[13]

All patients received Gegen Qinlian Decoction. The ingredients included 15 g of Puerariae Lobatae Radix, 9 g of Scutellariae Radix, 9 g of Coptidis Rhizoma, and 6g of roasted licorice root. 15 g of Sanguisorbae Radix was added for blood in stool, 10 g of Paeoniae Radix Alba was added for severe abdominal pain, 9 g of Halloysitum Rubrum and 9 g of Chebulae Fructus were added for loose stool. The herbs were prepared by the hospital's pharmacy department. The herbs were decocted with water to obtain 400mL of filtrate and were administered with half in the morning and a half in the evening. The duration of treatment was 7d.

Observation indicators

(1) Monitoring of skeletal muscle relaxation: Achieving appropriate muscle relaxation helps ensure patient safety during surgery. It allows for proper positioning, manipulation, and access to the surgical site, reducing the risk of inadvertent injury or complications. In addition, adequate muscle relaxation promotes optimal surgical conditions by reducing muscle tone and tension. It improves the surgeon's visibility and facilitates precise instrument control, leading to more accurate surgical maneuvers and better outcomes. In laparoscopic surgery, a pneumoperitoneum (inflation of the abdomen with carbon dioxide gas) is created. This can cause elevated intra-abdominal pressure, which may affect respiratory mechanics and cardiovascular function. Proper muscle relaxation helps minimize the adverse effects of pneumoperitoneum on these physiological parameters.

The TOF-WATCH SX muscle relaxation tester is a device used to monitor and assess the level of skeletal muscle relaxation during surgery. It utilizes acceleromyography, a technique that measures the response of the thumb or hand muscles to nerve stimulation. The device delivers electrical impulses to the ulnar nerve, causing thumb twitch responses, which are then measured and analyzed.

The TOF-WATCH SX provides objective measurements of muscle response, specifically the Train-of-Four (TOF) ratio. This ratio represents the degree of muscle relaxation by comparing the strength of the fourth twitch response to the first twitch response. A TOF ratio close to 1 indicates adequate muscle relaxation, while a lower ratio suggests incomplete relaxation.

TOF-WATCH SX muscle relaxation tester was used to stimulate the patient's ulnar nerve to assess the neuromuscular conduction function of the patient. The action time and maintenance duration of rocuronium bromide in the three groups were monitored using the train of four stimulation (TOF). From the end of intravenous rocuronium bromide to

T1=0 is the onset time; the end of the injection to T1=25% is the time of action. The baseline value (TC) was considered when the height of the TOF's first twitch response (T1) was stable, around 100%. Intraoperative skeletal muscle relaxation conditions were classified as follows: Grade 1: T1/TC=0; In this grade, the skeletal muscles are deeply relaxed, resulting in a significant reduction or absence of muscle twitches in response to nerve stimulation.

Grade 2: 0<T1/TC≤10%; Grade 2 represents a moderate level of muscle relaxation. It is characterized by a partial reduction in muscle twitches in response to nerve stimulation.

Grade 3: T1/TC>10%; it indicates a shallow level of muscle relaxation. In this grade, muscle twitches are more prominent in response to nerve stimulation.

Grades 1 and 2 were regarded as satisfactory muscle relaxation conditions.

(2) Recovery time and index of skeletal muscle relaxation: The time lapse before the recovery of T1/TC to 25% was the recovery time.

(3) Extubation time and remifentanil consumption of the three groups of patients were also measured.

(4) Skeletal muscle relaxation effect: Using physiological parameters such as muscle tension, electromyography (EMG) activity, or joint range of motion to quantify muscle relaxation levels.

(5) Patient satisfaction: The patient satisfaction questionnaire in this study aims to assess the following aspects of treatment and patient experience. Pain management: This aspect focuses on evaluating the effectiveness of pain management strategies, such as medication administration, pain relief, and overall satisfaction with pain control during and after the treatment. Overall experience: This aspect encompasses the patient›s overall perception of their treatment experience, including factors such as communication with healthcare providers, information provided, perceived quality of care, and general satisfaction with the treatment received. Side effects and adverse events: This aspect assesses the occurrence and impact of any treatment-related side effects or adverse events experienced by the patients. It includes questions about the severity of side effects, their management, and the patient's satisfaction with the healthcare team's response to these issues. Communication and information: This aspect explores the quality and effectiveness of communication between healthcare providers and patients. It may include questions about the clarity of information provided, the level of involvement in decision-making, and satisfaction with the level of communication and information exchange. Treatment outcome: This aspect focuses on evaluating the patient's perception of treatment outcomes and expectations. It may include questions related to treatment effectiveness, improvement in symptoms or condition, and overall satisfaction with the treatment outcome. Follow-up care: This aspect assesses the patient's satisfaction with post-treatment follow-up care, including access to healthcare professionals, availability of support services, and overall satisfaction with the continuity of care.

Statistical analysis

SPSS 21.0 was utilized for data analysis software. Normally distributed measures were presented as mean plus or minus standard deviation ($\bar{x} \pm s$). The skeletal muscle relaxation recovery time and index and extubation time and remifentanil consumption was compared using t test or analysis of variance (ANOVA) to examine if there are significant differences in these scores among the low-dose, middle-dose, and high-dose groups. In the case of count data, the number of cases (rate) was utilized, and the skeletal muscle relaxation effect and satisfaction were analyzed using the chi-square test. Notably, missing data were handled through appropriate imputation methods to ensure robust statistical analyses. Statistical significance was set at $P < .05$.

RESULTS
Patient characteristics

The three groups of patients exhibited comparable patient characteristics ($P > .05$). There were no significant differences in baseline characteristics among the three groups of patients, such as age (68.34±5.26 vs 68.41±5.30 vs 68.41±5.32) (Table 1).

Skeletal muscle relaxation effect and satisfaction

Skeletal muscle relaxation pleasure was considerably higher in the middle- and high-dose groups than in the low-dose group. Patients in the middle-dose and high-dose groups showed significantly higher levels of satisfaction compared to the low-dose group (33% vs 100% vs 100%, $P < .05$) (Table 2).

This could be attributed to the deeper level of muscle relaxation achieved with higher doses of rocuronium bromide, which may have resulted in improved surgical conditions and reduced muscle movement during the procedure. Patients may have perceived this as a more effective and comfortable experience.

Skeletal muscle relaxation recovery time and index

The high-dose and middle-dose groups showed significantly prolonged recovery and index of skeletal muscle

Table 1. Baseline data

	Low-dose group (n=30)	Medium-dose group (n=30)	High-dose group (n=30)	t or χ^2	P value
Gender				-	>.05
Male	18	17	19		
Female	12	13	11		
Age (year)	$\bar{x} \pm s$	$\bar{x} \pm s$	$\bar{x} \pm s$		
Mean age (year)	68.34±5.26	68.41±5.30	68.41±5.32	-	>.05
Weight (kg)	$\bar{x} \pm s$	$\bar{x} \pm s$	$\bar{x} \pm s$		
Mean weight (kg)	60.27±7.48	60.21±7.38	60.30±7.42	-	>.05
ASA grade				-	>.05
I	13	14	11		
II	17	16	19		

Table 2. Comparison of skeletal muscle relaxation effects and satisfaction among the three groups of patients [n(%)]

Groups	Grade 1	Grade 2	Grade 3	Satisfactory rate (%)
Low-dose group (n=30)	0	10	20	10(33%)
Medium-dose group (n=30)	7	23	0	30(100%)
High-dose group (n=30)	21	9	0	30(100%)

compared to the low-dose group. The increase in dosage resulted in prolonged recovery and index of skeletal muscle (17.24±3.25 vs 19.38±3.23 vs 27.95±5.68; 18.47±3.32 vs 20.44±4.52 vs 23.75±4.85, all $P < .05$) (Table 3). The observed association between higher rocuronium bromide dosages and prolonged recovery times suggests that the deeper muscle relaxation achieved with higher doses takes longer to wear off. This may be due to the longer elimination half-life of rocuronium bromide at higher doses. Although patients experienced higher satisfaction with muscle relaxation, the trade-off was a longer recovery period before regaining normal muscle function.

Extubation time and remifentanil consumption

Extubation time and remifentanil dose were considerably lower in the middle-dose group than in the low-dose and high-dose groups (8.54±2.13 vs 6.41±1.74 vs 9.29±2.25; 2.32±0.86 vs 1.27±0.44 vs 2.85±0.97; all $P < .001$) (Table 4). The middle-dose group exhibited a shorter extubation time, indicating that patients recovered from anesthesia more quickly, enabling them to breathe independently and reducing their reliance on mechanical ventilation. Additionally, the middle-dose group administered a lower dose of remifentanil, signifying a reduced requirement for analgesic medication. The middle-dose group exhibited significantly reduced extubation times and lower remifentanil dosages compared to the other groups. This could be attributed to the optimal balance achieved in the middle-dose group, where muscle relaxation was sufficient for intubation and surgical conditions while allowing for a faster recovery compared to the high-dose group. The lower remifentanil dosages in the middle-dose group suggest that the depth of anesthesia may have been appropriately adjusted to complement the muscle relaxation achieved with the middle dose of rocuronium bromide.

DISCUSSION

Colorectal cancer is a complex disease influenced by various factors, including the tumor microenvironment and host immune response. The role of chronic inflammation and its impact on cancer progression and patient outcomes has been extensively studied. Chronic inflammation can contribute to the development and progression of colorectal cancer through multiple mechanisms, including the release of pro-inflammatory cytokines, activation of signaling pathways, and genomic instability.

Several studies have investigated the association between chronic inflammation, immune microenvironment, and survival outcomes in colorectal cancer. For instance, research has demonstrated that a tumor microenvironment rich in immune cells, such as tumor-infiltrating lymphocytes (TILs) and dendritic cells, is associated with improved prognosis and increased survival in colorectal cancer patients.[14] These findings suggest the importance of the immune response in influencing disease progression and patient outcomes.

Moreover, studies examining the immune microenvironment in colorectal cancer have highlighted the

Table 3. Comparison of skeletal muscle relaxation recovery time and index among the three groups of patients ($\bar{x} \pm s$)

Groups	skeletal muscle relaxation recovery time(min)	Skeletal muscle relaxation recovery index(min)
Low-dose group (n=30)	17.24±3.25	18.47±3.32
Medium-dose group (n=30)	19.38±3.23	20.44±4.52
High-dose group (n=30)	27.95±5.68	23.75±4.85
F	5.956	6.283
P value	<.001	<.001

Table 4. Comparison of extubation time and remifentanil consumption among the three groups of patients ($\bar{x} \pm s$)

Groups	Time to extubation after drug withdrawal(min)	Remifentanil dosage(mg)
Low-dose group (n=30)	8.54±2.13	2.32±0.86
Medium-dose group (n=30)	6.41±1.74	1.27±0.44
High-dose group (n=30)	9.29±2.25	2.85±0.97
F	6.954	9.781
P value	<.001	<.001

crucial role of inflammatory markers, such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and C-reactive protein (CRP), in predicting prognosis and treatment response. Elevated levels of these markers have been associated with poorer survival outcomes in colorectal cancer patients.[15,14] At present, surgical management remains the mainstay of treatment for colorectal cancer, in which open surgery is a mature technique with low surgical operation requirements and a wide range of indications.[15] However, the large incision and the presence of straining on the intestine in open surgery disrupt the intra-abdominal environment, resulting in significant postoperative stress, slow recovery, and multiple complications.[16] Laparoscopic surgery is a minimally invasive technique that involves making small incisions through which specialized surgical instruments and a camera (laparoscope) are inserted. This approach reduces trauma to the surrounding tissues, resulting in less postoperative pain and discomfort for patients. Reduced tissue trauma may contribute to improved muscle relaxation during surgery, as patients experience less muscle tension and spasm compared to open surgery. The laparoscopic camera provides high-definition visualization of the surgical field, allowing surgeons to view magnified images on a monitor. This enhanced visualization aids in precise identification and manipulation of anatomical structures, leading to improved surgical precision and accuracy. Better visualization may contribute to more effective muscle relaxation techniques, thereby enhancing patient satisfaction with the procedure. In addition, laparoscopic surgery typically involves less blood loss compared to open surgery. The use of specialized instruments, such as energy devices that seal blood vessels during the procedure, helps minimize bleeding. Reduced blood loss can contribute to better surgical conditions and muscle relaxation, as excessive bleeding and associated tissue swelling can impair visualization and limit the surgeon's ability to achieve optimal muscle relaxation. Moreover, laparoscopic surgery is associated with a quicker recovery and shorter hospital stay compared to open surgery. Minimally invasive techniques result in smaller incisions, reduced tissue damage, and faster wound healing. Patients

undergoing laparoscopic surgery often experience less postoperative pain, require fewer pain medications, and can resume normal activities sooner. Faster recovery and shorter hospital stays are important factors contributing to overall patient satisfaction.[17]

Laparoscopic radical resection of colorectal cancer is usually performed under general anesthesia. However, it has been reported that general anesthesia will increase the incidence of perioperative adverse reactions in patients.[18] In recent years, with the continuous development of anesthesiology in China, the novel target-controlled infusion technology, a new type of anesthesia drug delivery method based on the pharmacodynamic-pharmacokinetic theory, has captured extensive attention.[19] The most appropriate dosage strategy for patients may be identified by computer simulation of drug metabolism and effect in vivo, which allows the blood drug concentration or effect site concentration to be adequately maintained at the target concentration, thereby contributing to anesthesia maintenance and the timely alteration of the drug delivery system as per clinical demands.[20] The impaired hepatic and renal functions in elderly patients lower the plasma clearance rate of the drug and prolong the onset time and recovery time of muscle relaxation in patients, which is associated with less total water, skeletal muscle atrophy, decreased muscle composition, and increased fat ratio in elderly patients.[21] The intraoperative stability of breathing and blood circulation and the complete relaxation of muscles are essential for low intra-abdominal pressure and a good surgical field.[22] The onset time of rocuronium bromide of 1-2 minutes is significantly lower than that of other non-depolarizing muscle relaxants, which may be closely associated with the presynaptic effect of rocuronium bromide.[23] The onset and recovery rules of rocuronium bromide differ from those of other non-depolarizing muscle relaxants. Rocuronium bromide is a non-depolarizing neuromuscular blocking agent commonly used during surgery to induce muscle relaxation. It acts by competitively binding to the nicotinic acetylcholine receptors at the neuromuscular junction, thereby blocking the transmission of nerve impulses to the skeletal muscles. The degree of muscle relaxation achieved with rocuronium bromide depends on the dosage administered. In the context of elderly patients, several factors contribute to their altered response to muscle relaxants compared to younger individuals. Age-related changes in pharmacokinetics and pharmacodynamics play a significant role. Elderly patients generally exhibit decreased hepatic and renal function, which can affect the metabolism and elimination of rocuronium bromide. As a result, the duration of action of the drug may be prolonged in elderly individuals.

Clinical investigations have revealed that rocuronium bromide's neuromuscular blockade is established abiotically by binding to presynaptic receptors, and its extinction is completed via postsynaptic actions.[24] Additionally, the clinical use of target-controlled infusion features the following advantages: (1) it effectively maintains the blood concentration and physiological effect of the body; (2) it is highly controllable; (3) the probability of drug overdose or accumulation is relatively low;[25] (4) it quickly reaches the set target concentration that allows stable skeletal muscle relaxation during surgery, which improves patient safety and controllability of surgery.[26]

Due to the positive correlation between the adverse effects of rocuronium and its dose, high doses of rocuronium are more liable to adverse effects. Therefore, in the present study, a small dose was initially administered, and the bupropion dose was gradually incremented to obtain a more optimal dosage for rocuronium injection.[27] The results of the present study showed that target-controlled infusion of 0.6mg/L, 0.9mg/L, and 1.2mg/L of rocuronium bromide could provide muscle relaxation effects for patients, while the middle- and high-dose groups showed significantly higher patient satisfaction versus the low-dose group, suggesting that the maintenance of muscle relaxation in patients with doses of 0.9 mg/L and 1.2 mg/L yielded satisfactory skeletal muscle relaxation effects.[28] However, the recovery time and index of skeletal muscle of the patients were prolonged with the increase of the dosage, which suggests that the higher the dose of rocuronium bromide, the deeper the neuromuscular blockade of the patient during the operation, which led to a prolonged postoperative recovery of the patient. The pharmacokinetics of rocuronium bromide play a significant role in its elimination from the body. In elderly patients, age-related changes in hepatic and renal function can lead to a slower metabolism and clearance of the drug. As a result, higher doses of rocuronium bromide take longer to be eliminated, leading to prolonged effects and delayed recovery.

Redistribution: After administration, rocuronium bromide undergoes redistribution from the neuromuscular junction to other tissues, including plasma and fat. Higher doses of the drug can result in a larger amount of rocuronium bromide being redistributed and sequestered in these tissues. The slower release of the drug from these reservoirs contributes to the prolonged duration of action and delayed recovery.[29,30]

Target-controlled infusion (TCI) is an approach used for administering intravenous medications, including muscle relaxants, with the aim of enhancing patient safety and improving surgical outcomes. 1) Precise drug delivery: TCI utilizes computerized models and algorithms to calculate and control the infusion rate of medications, ensuring precise and individualized dosing. This approach takes into account patient-specific factors such as age, weight, and pharmacokinetic parameters to achieve the desired drug concentration in the target tissue. By providing accurate dosing, TCI minimizes the risk of underdosing or overdosing, leading to safer administration of muscle relaxants. 2) Reduced inter-patient variability: Traditional methods of administering muscle relaxants often rely on fixed-dose regimens, which may not adequately account for inter-patient variability in drug response. TCI, on the other hand,

adjusts the infusion rate based on real-time feedback, allowing for better control of drug concentration in the body. This individualized dosing approach reduces the risk of both inadequate muscle relaxation and excessive drug effects, resulting in improved safety and better surgical conditions. 3) Rapid onset and offset of action: TCI allows for precise titration of drug concentration, enabling a more rapid onset and offset of action compared to traditional methods. By achieving the desired drug concentration in the target tissue more efficiently, TCI can facilitate faster induction of muscle relaxation at the beginning of the procedure and a quicker recovery at the end. This can contribute to shorter anesthesia duration, reduced exposure to anesthetics, and potentially improved postoperative outcomes. 4) Continuous monitoring and adjustment: TCI systems typically incorporate continuous pharmacokinetic monitoring, which allows anesthesiologists to continuously assess drug levels in real-time. This monitoring enables prompt adjustments to the infusion rate, ensuring that the desired drug concentration is maintained throughout the procedure. The ability to make timely dose adjustments based on individual patient response enhances the controllability and safety of muscle relaxation, minimizing the risk of adverse events.

Furthermore, the results of the current study showed that the extubation time and remifentanil consumption of 0.9 mg/L (medium-dose group) were significantly lower than 0.6 mg/L (low-dose group) and 1.2 mg/L (high-dose group), indicating that 0.9 mg/L (medium-dose group) of rocuronium bromide resulted in favorable skeletal muscle relaxation effects. Moreover, the dose of 0.9 mg/L does not prolong the recovery of patients after surgery and reduces the use of remifentanil.[31] In addition, Gegen Qinlian Decoction was administered to patients in this study after surgery. In TCM, this disease is classified as an intestinal toxin" and clinical symptoms include internal dampness and heat. Gegen Qinlian Decoction is a classic formula for clearing heat and detoxifying toxins and has clear anti-tumor effects to inhibit colorectal tumor growth.

The components of Gegen Qinlian Decoction have been studied individually and have shown certain pharmacological properties that could potentially affect outcomes in surgical or anesthesia settings. Coptidis Rhizoma and Rhizoma Coptidis are rich sources of berberine, a bioactive alkaloid with antimicrobial, anti-inflammatory, and antioxidant properties. Berberine has been investigated for its potential effects on various physiological pathways, including modulation of the immune response and reduction of oxidative stress. These properties may have implications for postoperative recovery and tissue healing. Radix Scutellariae, derived from Scutellaria baicalensis, contains flavonoids such as baicalin and baicalein. These compounds have demonstrated anti-inflammatory and antioxidant effects in experimental studies. The anti-inflammatory properties of Scutellaria baicalensis may be relevant in mitigating surgical inflammation and promoting recovery.

These research findings have significant implications for anesthesia practices and the care of elderly patients. Proper

dosage selection of rocuronium bromide can improve patients' postoperative experiences, with the middle-dose group demonstrating distinct advantages. Elderly patients also benefit, as reflected in improved skeletal muscle relaxation and reduced medication use, ultimately enhancing postoperative satisfaction. This underscores the value of personalized treatment, aiming to elevate the quality of surgical care and provide safer, more effective, and satisfactory medical services.

This study underscores the importance of moderate and high-dose rocuronium in enhancing patient satisfaction and skeletal muscle relaxation. It has a positive impact on anesthesia practice and surgical care for elderly patients. Selecting the appropriate rocuronium dosage can improve the surgical experience, especially in elderly patients. This contributes to the improvement of surgical care quality and the provision of safer and more effective medical services.

To enhance generalizability, it is important to conduct studies that include diverse populations and settings. Large-scale, multicenter studies that involve participants from various demographic backgrounds can provide more representative data and contribute to generalizability. Future research plans: 1) Larger sample sizes: Conducting studies with larger sample sizes can increase the statistical power and precision of the findings. This allows for more accurate estimation of treatment effects and generalizability to broader populations. Larger sample sizes are particularly important for investigating rare outcomes or subgroups within the population. 2) Multicenter studies: Collaborative multicenter studies involve multiple institutions or research centers, enabling the recruitment of participants from diverse geographical locations and healthcare settings. Multicenter studies provide opportunities to validate findings across different populations and healthcare systems, enhancing the generalizability of research outcomes. 3) Pharmacokinetic investigations: Pharmacokinetic studies play a crucial role in understanding the absorption, distribution, metabolism, and elimination of medications. Investigating the pharmacokinetics of drugs, including muscle relaxants, in different patient populations can help identify potential variations in drug response and guide dosing strategies. Pharmacokinetic investigations can provide valuable insights into inter-individual variability, age-related changes, and factors influencing drug metabolism, ultimately informing personalized and targeted therapeutic approaches.

In conclusion, an infusion dosage of 0.9mg/L of rocuronium bromide may be feasible for senior patients undergoing laparoscopic rectal cancer surgery. It retains appropriate skeletal muscular relaxation, shortens postoperative recovery, and obviates the need for remifentanil, which demonstrates good potential for clinical promotion. When considering the use of 0.9 mg/L of rocuronium bromide in elderly patients undergoing laparoscopic rectal cancer surgery, clinicians should weigh the potential benefits of adequate muscle relaxation and reduced complications against the challenges associated with prolonged recovery

times. Individualized dosing, close monitoring, and appropriate use of reversal agents can help mitigate the risks and optimize patient outcomes.

AUTHOR CONTRIBUTIONS
Xuan Guo drafted and revised the manuscript. Jing Li , Liye Yang , Feifei Wu , Xiang Li, conceived and designed this article, in charge of syntax modification and revise of the manuscript. All the authors have read and agreed to the final version manuscript.

DATA AVAILABILITY STATEMENT
All data generated or ed during this study are included in this published article.

Consent for publication
All authors have read and approved this manuscript to be considered for publication.

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