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INVESTIGATING NEUROPROTECTIVE STRATEGIES OF REMIMAZOLAM TOSILATE IN ELDERLY ATHLETES UNDERGOING ENDOSCOPIC SURGERY FOR COLORECTAL TUMORS

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ABSTRACT

Background: Endoscopic surgery for colorectal tumors often involves CO_2 pneumoperitoneum and a supine head-down position, which may increase the risk of cerebral hypoxia, edema, stroke, and postoperative cognitive dysfunction, particularly in elderly athletes whose vascular health may already be compromised by age and physical stress from long-term sports participation. Protecting brain function during and after surgery is thus crucial for maintaining postoperative cognitive and physical performance levels in this population. **Objective:** This study aims to evaluate the effects of Remimazolam Tosilate on brain protection and cognitive function in elderly athletes undergoing endoscopic surgery for colorectal tumors, assessing its efficacy and safety compared to traditional anesthetics. **Methods:** From July 2021 to October 2022, sixty elderly athletic patients diagnosed with colorectal tumors were randomly divided into three anesthetic groups at our hospital. These included a Sevoflurane group (Sevoflurane + Fentanyl induction + Remifentanil maintenance), a Propofol group (Propofol + Fentanyl induction + Remifentanil maintenance), and a Remimazolam Tosilate group (Remimazolam Tosilate + Fentanyl induction + Remifentanil maintenance), with twenty patients in each group. We compared early brain function injury indices, clinical examination outcomes, and cognitive functions across the groups. **Results:** Measurements such as serum neuron-specific enolase (NSE), S100 protein, myelin basic protein (MBP), arterial and jugular bulb oxygen partial pressures, carbon

dioxide levels, hemoglobin content, oxygen saturation, blood glucose, and lactic acid levels indicated that the Remimazolam Tosilate group experienced better outcomes than those receiving Sevoflurane or Propofol. **Conclusion:** Remimazolam Tosilate offers significant neuroprotective benefits during endoscopic colorectal surgery in elderly athletes, enhancing postoperative cognitive function and potentially facilitating quicker cognitive and physical recovery. This study underscores the importance of tailored anesthetic approaches to support the unique needs of elderly athletes undergoing significant surgical interventions**.**

KEYWORDS: Colorectal neoplasms in the elderly; Remimazolam Tosilate; Brain protection; Postoperative cognitive function; Endoscopic surgery

1. INTRODUCTION

The management of perioperative brain health in elderly athletes undergoing endoscopic surgery for colorectal tumors presents a unique clinical challenge. The specific physiological demands of athletes, combined with the effects of aging, make it imperative to choose anesthetic techniques that minimize cognitive and neurological risks while promoting rapid recovery (Schöb et al., 1996). This is particularly relevant in sports medicine, where maintaining cognitive function is crucial for the athlete's ability to return to sport and perform at high levels. Colorectal cancer surgery often involves the use of CO_2 pneumoperitoneum and a supine head-down, foot-up truncal position to improve surgical access (Johncilla & Yantiss, 2020). While effective, these techniques can compromise cerebral blood flow, potentially leading to cerebral hypoxia, edema, and even long-term cognitive dysfunction. Such complications are of great concern for the elderly, and the risks may be further pronounced in elderly athletes whose careers depend on both physical and cognitive health (Das et al., 2020). The choice of anesthetic agents in this context is critical, as some can exacerbate the risk of postoperative cognitive dysfunction (POCD) (Borahay et al., 2013). Traditional agents like sevoflurane and propofol have been extensively used in the general population, but their effects on the brains of elderly athletes—who may have different baseline cerebral blood flow and metabolic needs due to their training histories—have not been adequately explored. Remimazolam Tosilate, a newer anesthetic agent, shows promise in providing effective sedation while potentially mitigating some of the adverse effects on brain function seen with other agents. Its pharmacological profile suggests that it could offer advantages in terms of stability of cerebral hemodynamics and reduced incidence of POCD, which is particularly valuable in athletes who need to maintain high levels of mental clarity and quick reflexes post-surgery (Mathey et al., 2021). This study aims to directly compare the impact of Remimazolam Tosilate with that of sevoflurane and propofol on the brain protection and cognitive function of elderly athletes undergoing endoscopic surgery for colorectal tumors. By focusing on a cohort of athletes,

we hope to illuminate whether the neuroprotective properties of Remimazolam Tosilate translate into meaningful benefits in terms of cognitive recovery and overall postoperative outcomes (Bell & Pai, 2022). Understanding these dynamics is essential not only for optimizing surgical care but also for developing postoperative rehabilitation protocols that align with the athletes' needs for a quick return to training and competition (Hissong & Pittman, 2020; Rafii, 2022; Thimme & von Bergwelt-Baildon, 2021). This research, therefore, not only addresses a gap in the existing medical literature but also serves a practical need within the realm of sports medicine, potentially influencing how anesthesia is approached in elderly athletic populations undergoing complex surgical procedures.

2. Patients and methods

2.1 General information

During July 2021 to October 2022, sixty elderly patients with colorectal tumor cured in our hospital were enrolled as subjects. According to the inclusion criteria and exclusion criteria, they were arbitrarily classified into three groups, including sevoflurane group (sevoflurane combined with fentanyl induction + remifentanil maintenance anesthesia), propofol group (propofol combined with fentanyl induction + remifentanil maintenance anesthesia), Remimazolam Tosilate group (Remimazolam Tosilate+fentanyl induction + remifentanil maintenance anesthesia. There were 20 patients in each group. During the trial, all patients signed the informed consent form, which was approved by our hospital's Medical Ethics Council.

2.1.1 Inclusion criteria

All the enrolled cases were diagnosed as colorectal tumors, and the diagnostic criteria were referred to the relevant literature (Beech & Hechtman, 2021; Eberhardt et al., 2020). All patients were treated by laparoscopic surgery, and those who met the following criteria could be included in the study. Body mass index (BMI) was 18-24 kg/m^2; Completion of pre-operative examination; Hemoglobin > 90g/L and fasting blood glucose < 10mmol/L before operation; American Association of Anesthesiologists (ASA) patients were classified as I—III; The age of the patients was 65 to 85 years old; The sex of the patient was not limited. There were no serious cardiovascular diseases, chronic obstructive pulmonary diseases, severe hepatorenal insufficiency, endocrine and metabolic diseases, central nervous system diseases, mental diseases, intelligence, and hearing impairment.

2.1.2 Exclusion criteria

1) patients with severe cardiovascular diseases, chronic obstructive pulmonary disease, severe hepatorenal insufficiency, endocrine and metabolic

diseases, and central nervous system diseases; 2) patients were allergic to narcotic drugs in this study; 3) the patients had long-term use of immunosuppressants, sedatives, antidepressants, antianxiety drugs, and glucocorticoids; 4) the patients had other virus infections; 5) the patients had mental illness or mental retardation, hearing impairment, who were unable to cooperate with anesthesia; 6) the patients had a history of alcohol or drug abuse. Calculation formula of sample size:

$$n = 2 \times \left[\frac{(u_\alpha + u_\beta \times \sigma)}{\delta}\right]^2$$

U α-the u value corresponding to the level α; U value corresponding to u β- Ⅱ error probability β; δ -the difference between the two population averages, δ = μ 1-μ 2; σ -overall standard deviation. Take the bilateral α as 0.05, β as 0.1, and look up the table to get u0.05/2 = 1.97, u0.1 = 1.283. NSE was taken as the effect index, and set the parameters: δ=3.44, n1= n2= 45, S1= 5.25, S2= 6.33.

2.2 Preoperative preparation

All patients were visited the day before the operation, evaluated the status of the patients, judged whether the patients met the criteria of the subjects, and signed the informed consent form. At the same time, the general conditions such as age, height, weight, BMI, ASA grade and history were recorded. The patients were told to fast for 6 hours and drink for 2 hours before operation.

2.3 Anesthetic methods

After entering the room, the patients lay flat on the operating bed and were given routine monitoring, such as electrocardiogram (ECGE), non-invasive blood pressure (NIBP), heart rate (HR), pulse, blood oxygen saturation (SpO2), muscle relaxation monitoring, the bispectral index (BIS) and peripheral venous pathway was established. After the patient's vital signs were stable, the patient's peripheral blood 2ml was extracted at T0 (after entering the room), stored in a vacuum test tube containing EDTAK2 anticoagulant, and stored in a 4 °C refrigerator. At the same time, the vital signs of the patients immediately after blood sampling were recorded.

2.4 Anesthesia induction

After entering the operating room, the patients' blood pressure, electrocardiogram and pulse oxygen saturation were monitored routinely, and the BIS level was monitored by BIS index monitor (ASPECT medical system sprinter forA-200, Aspect company). Propofol group was infused with propofol

by TCI infusion system (Graseby3500 micropump), Marsh pharmacokinetic model was used to input patient's age and body weight, and propofol was infused with 3.5-4.0ug/mL plasma target-controlled concentration until the patient's consciousness disappeared (eyelash reflex disappeared). Intravenous injection of fentanyl 3ug/kg and 0.2mg/kg of atracurium benzenesulfonate. Sevoflurane group inhaled 6% sevoflurane with a mask, oxygen flow was 2.0L/min, until consciousness disappeared (eyelash reflex disappeared), intravenous injection of fentanyl 3ug/kg and cis-atracurium benzenesulfonate 0.2mg/kg. In the Remimazolam Tosilate group, 6-12mg/kg·h was infused intravenously until the patient lost consciousness (eyelash reflex disappeared), fentanyl 3ug/kg and atracurium cis-besylate 0.2mg/kg were injected intravenously.

After muscle relaxation took effect, endotracheal intubation was performed under clear vision, and the ventilator was connected. According to the patient's weight, the initial tidal volume was set to 10ml / min, I: E=1:2, and mechanical ventilation was performed. Anesthesia management and maintenance: After anesthesia induction, bilateral prefrontal monitoring was performed to monitor cerebral oxygen saturation (rS02) (near infrared spectrometer INVOS5100Soma.neti, USA). Left radial artery catheterization was carried out to monitor invasive blood pressure, and the mean arterial pressure was less than 20% higher than the basic value during operation to avoid the effect of large fluctuation of blood pressure on craniocerebral function. Under ultrasound guidance, an 18G single-lumen deep vein catheter was enrolled for right internal jugular vein puncture placement; an 18G single-lumen deep vein catheter was used for retrograde placement of the left internal jugular vein. The depth of the catheter was the distance from the puncture point to the ipsilateral mastoid (about 10~14cm). After reaching the predetermined depth, I ml (pre-5ml blood transfusion) was collected slowly for blood gas analysis to determine whether the tip of the catheter reached the jugular bulb, and then connected with tee and pressure measuring device. The jugular bulb was the dilated part of the internal jugular vein at the base of the skull. The body surface projection was equivalent to the position of the mastoid, and the blood flew back from the intracranial sigmoid sinus to the jugular bulb. This site did not contain blood returning from the extracranial veins and it is ideal for monitoring the overall balance of brain oxygen supply and demand and brain oxygen saturation.

During the operation, the end-expiratory carbon dioxide (PETCO$_2$) 35~45mmHg was maintained, the tidal volume and frequency were adjusted according to the PETCO$_2$, the BIS was maintained between 40 and 60 during the operation, the nasopharyngeal temperature was monitored by bilateral forehead monitoring rS02, and the warming device was used to ensure the temperature rise and fall within 1 ℃ (36.5° ±1 °). Propofol group received propofol plasma target control of 3.5-4.0μg/mL+ remifentanil 0.1-0.2ug/kg·min,

sevoflurane group-maintained sevoflurane 1.0-2.0 MAC + remifentanil 0.1-0.2ug/ kg ·min during operation. In the Remimazolam Tosilate group, 1mg/ kg ·h + remifentanil 0.1-0.2ug/ kg ·min was maintained during operation, which could be adjusted as needed, and cis atracurium was given during operation. 0.1mg fentanyl and 5mg tropisetron were injected intravenously half an hour before the end of the operation. Postoperative patient-controlled analgesia with sufentanil 2-6μg/kg analgesia pump was used.

2.5 Surgical position

An establishment of pneumoperitoneum (pneumoperitoneum pressure = 12-15 mmHg) was performed in the supine position with the head hanging down (supine + head low + foot high + pneumoperitoneum position) at 30 degrees.

2.6 Observation index

2.6.1 Laboratory examination index (related index of early brain function damage)

The indexes of laboratory examination were NSE, S100 protein and MBP. Blood samples were collected from the bulbar part of the internal jugular vein, and the concentrations of NSE, S100 protein and MBP were determined by enzyme-linked immunosorbent assay (ELISA). All patients were examined at four time points: 5 min after general anesthesia intubation, 60min (T1) and 180min (T2) after CO_2 pneumoperitoneum and Trendelenburg position, and 15min (T3) after pneumoperitoneum deflation.

2.6.2 Clinical examination index

All patients were examined at four time points: 5min (T0) after routine general anesthesia intubation, 60min (T1) and 180min (T2) after CO_2 pneumoperitoneum and Trendelenburg position, and 15min (T3) after aero peritoneum. The monitoring values of cerebral oxygen saturation were recorded, and the blood samples of radial artery and jugular bulb were collected for blood gas analysis. Arterial and jugular bulb oxygen partial pressure, carbon dioxide partial pressure, hemoglobin content, blood oxygen saturation, blood glucose and blood lactic acid were recorded. Calculated according to Fick formula: Cerebral arteriovenous oxygen content difference (Da-j02) = arterial blood oxygen content (Ca02)-jugular blood oxygen content (Cjv02); $Ca0_2$=1.36×Hb×Sa02+O.003×Pa02; $Cjv0_2$=1.36×Hb×Sjv02+0.003×Pjv02.

2.6.3 Cognitive function assessment

The scores of mini mental state scale (MMSE) were measured 1 day before operation and 1 day, 4 days and 7 days after operation. The MMSE has

been one of the most influential screening tools for cognitive impairment and is widely used in the Epidemiological Survey of Mental Disorders in the United States (ECA), including the Composite International Diagnostic Test recommended by the World Health Organization (WHO). This test can provide an overall survey of orientation, attention, numeracy, memory, language, and memory, with a maximum score of 30. A score between 24-27 is considered a mild cognitive impairment, between 19-23 moderate cognitive impairment, and between 0-18 severe cognitive impairment. The MMSE was used to compare the post- and pre-surgery basic values, and cognitive decline was considered if the score was 2 points lower than the pre-surgery basic value (Correa et al., 2021).

2.7 Statistical analysis

SPSS21.0 statistical software was used to analyze the data. The measurement data of non-normal distribution are expressed as median/quartile, nonparametric statistical rank-sum test was used for comparison between the two groups. The nonparametric test analysis was adopted for multi-group comparison, and repeated measurement analysis of variance was adopted for repeated measurement data. The counting data were represented by n (%), and analyzed by $\chi 2$ test. Statistically remarkable differences were observed (P<0.05).

3. Results

3.1 A comparison of general situations

No remarkable difference was found in the general data of patients in the Remimazolam Tosilate group compared with those in the sevoflurane group (P>0.05) and those in the propofol group (P>0.05). See Table 1 for all data results.

Table 1: General data among three groups

GROUP	N	AGE (YEARS)	(GENDER (MALE / FEMALE)	BMI(KG/M^2)	ASA(Ⅰ/Ⅱ)
SEVOFLURANE GROUP	20	53.2±10.4	12/8	22.5±3.0	12/8
PROPOFOL GROUP	20	54.5±9.5	11/9	23.4±3.3	15/5
REMIMAZOLAM TOSILATE GROUP	20	53.8±8.6	9/11	21.5±3.2	13/7
F		0.115	0.169	0.618	0.642
P		P＞0.05	P＞0.05	P＞0.05	P＞0.05

3.2 Comparison of NSE at different time points in three groups during operation

Compared with sevoflurane group and propofol group, no remarkable

difference was found in NSE level during 5min intubation among the three groups at different time points (P>0.05). The NSE levels in the Remimazolam Tosilate group were lower compared to the sevoflurane group and propofol group at 60min and 180min after CO_2 pneumoperitoneum and Trendelenburg position, and at 15min after pneumoperitoneum deflation in supine position (P<0.01). See Table 2 for all data results.

Table 2: The NSE levels in three groups of patients $[\bar{x}±s，μg/L]$

GROUP	N	T0	T1	T2	T3
SEVOFLURANE GROUP	20	5.14±0.42	9.82±1.15	7.93±1.51	8.32±3.56
PROPOFOL GROUP	20	5.16±0.37	7.24±1.26	6.28±0.94	6.32±3.95
REMIMAZOLAM TOSILATE GROUP	20	5.15±0.38	6.89±1.35	6.19±1.35	5.32±2.52
COMPARISON BETWEEN GROUPS	F=9.841，P＜0.05				
COMPARISON AT DIFFERENT TIME POINTS	F=48.583，P＜0.05				
INTERGROUP × TIME	F=14.125，P＜0.05				

3.3 The S100 protein levels in three groups at different time points during operation

Compared with sevoflurane group and propofol group, no remarkable difference was found in the level of S100 protein at different time points among the three groups during intubation of 5min(P>0.05). S100 protein levels in the Remimazolam Tosilate group were lower compared to the sevoflurane group and propofol group 60min and 180min after CO_2 pneumoperitoneum and Trendelenburg position, and 15min after pneumoperitoneum deflation in supine position, with remarkable differences (P<0.01, Table 3).

Table 3: The S100 levels in three groups of patients $[\bar{x}±s，μg/L]$

GROUP	N	T0	T1	T2	T3
SEVOFLURANE GROUP	20	77.58±18.47	156.13±37.23	137.53±26.56	120.52±18.65
PROPOFOL GROUP	20	76.23±19.65	163.23±36.58	136.28±30.56	106.62±13.05
REMIMAZOLAM TOSILATE GROUP	20	78.53±19.83	136.89±31.35	110.56±26.63	89.74±16.92
COMPARISON BETWEEN GROUPS	F=11.434，P＜0.05				
COMPARISON AT DIFFERENT TIME POINTS	F=16.863，P＜0.05				
INTERGROUP × TIME	F=22.313，P＜0.05				

3.4 The MBP concentration in three groups at different time points during operation

Compared with sevoflurane group and propofol group, no remarkable difference was found in MBP level during 5min intubation among the three groups at different time points (P > 0.05). The MBP levels of the Remimazolam Tosilate group at 60min and 180min after CO_2 pneumoperitoneum and Trendelenburg position, and at 15min after pneumoperitoneum deflation in supine position were remarkably lower compared to sevoflurane group and propofol group (P<0.01, Fig. 1).
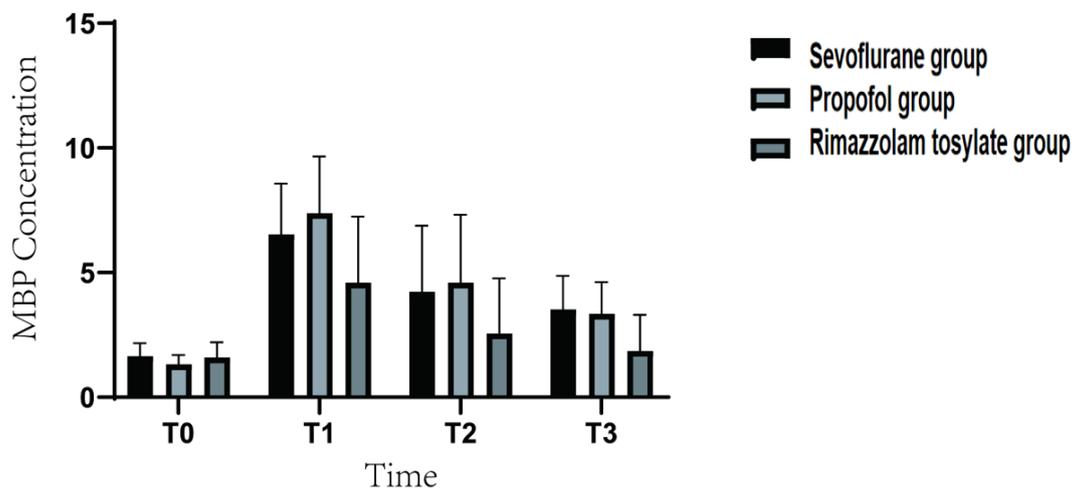

Figure 1: The MBP concentration between the two groups〔±s，μg/L〕

3.5 The arterial blood and jugular bulb oxygen partial pressure at different time points among the three groups

Compared with sevoflurane group and propofol group, there exhibited no remarkable difference 5min arterial oxygen partial pressure between the three groups at different time points (P>0.05). The arterial partial pressure of oxygen in the Remimazolam Tosilate group was higher compared to the sevoflurane group and propofol group 60min and 180min after CO_2 pneumoperitoneum and Trendelenburg position, and 15min after pneumoperitoneum deflation in supine position, with remarkable differences (P<0.01).

Compared with sevoflurane group and propofol group, there exhibited no remarkable difference in the partial pressure of jugular vein oxygen when the patients were intubated for 5 minutes (P>0.05). The partial pressure of jugular vein oxygen in the group of Remimazolam Tosilate at 60min and 180min after CO_2 pneumoperitoneum and Trendelenburg position, and at 15min after pneumoperitoneum in supine position were higher compared to the group of sevoflurane and propofol (P<0.01, Table 4).

Table 4: The partial pressure of oxygen in arterial blood and jugular bulb $[\bar{x} \pm s，mmHg]$

CATEGORY	N	Position	T0	T1	T2	T3
SEVOFLURANE GROUP	20	Arterial blood	214.7±17.4	184.3±14.1	184.9±8.9	180.0±12.6
PROPOFOL GROUP	20		225.4±17.4	178.3±12.2	182.9±12.5	182.8±13.5
REMIMAZOLAM TOSILATE GROUP	20		226.2±18.5	198.3±13.2	202±15.2	211±16.2
COMPARISON BETWEEN GROUPS			F=32.585，P＜0.05			
COMPARISON AT DIFFERENT TIME POINTS			F=17.381，P＜0.05			
INTERGROUP × TIME			F=15.645，P＜0.05			
SEVOFLURANE GROUP	20	Jugular bulb	60.86±3.64	68.93±4.91	75.91±3.91	80.75±3.95
PROPOFOL GROUP	20		65.91±3.91	78.72±2.97	86.91±3.95	90.83±3.42
REMIMAZOLAM TOSILATE GROUP	20		63.91±2.65	88.21±3.65	98.31±3.69	108.64±3.27
COMPARISON BETWEEN GROUPS			F=9.752，P＜0.05			
COMPARISON AT DIFFERENT TIME POINTS			F=4.866，P＜0.05			
INTERGROUP × TIME			F=12.845，P＜0.05			

3.6 Comparison of arterial blood carbon dioxide partial pressure at different time points among the three groups

Compared with sevoflurane group and propofol group, no remarkable difference was found in arterial partial pressure of carbon dioxide in the three groups at different time points (P>0.05). The partial pressure of arterial blood carbon dioxide in the Remimazolam Tosilate group was lower compared to the sevoflurane group and propofol group 60min and 180min after CO_2 pneumoperitoneum and Trendelenburg position, and 15min after pneumoperitoneum deflation in supine position (P<0.01, Table 5).

Table 5: The arterial blood carbon dioxide partial pressure among three groups of patients $[\bar{x} \pm s，mmHg]$

CATEGORY	N	T0	T1	T2	T3
SEVOFLURANE GROUP	20	34.87±3.85	37.66±4.32	39.60±4.12	40.13±4.12
PROPOFOL GROUP	20	35.13±2.99	36.13±2.53	39.86±2.56	40.33±2.38
REMIMAZOLAM TOSILATE GROUP	20	35.21±3.24	35.33±3.64	37.17±3.83	38.29±2.46
COMPARISON BETWEEN GROUPS		F=9.752，P＜0.05			
COMPARISON AT DIFFERENT TIME POINTS		F=15.232，P＜0.05			
INTERGROUP × TIME		F=12.812，P＜0.05			

3.7 The hemoglobin content in three groups at different time points during operation

Compared with sevoflurane group and propofol group, there exhibited no remarkable difference 5min hemoglobin content between the three groups at different time points (P>0.05). The hemoglobin content of Remimazolam Tosilate group was higher compared to sevoflurane group and propofol group 60min and 180min after CO_2 pneumoperitoneum and Trendelenburg position, and 15min after pneumoperitoneum deflation in supine position, with remarkable differences (P<0.01, Fig.2).
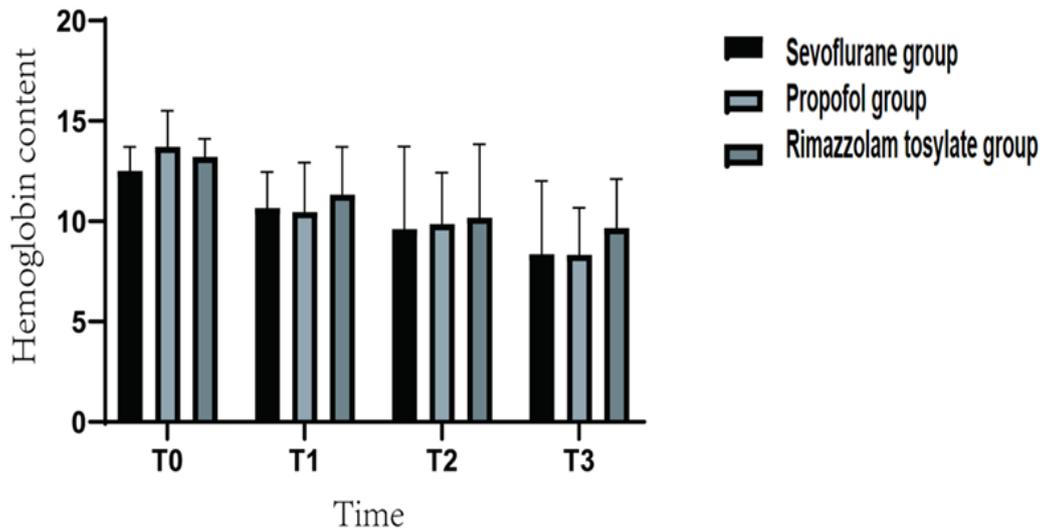

Figure 2: The hemoglobin concentration in three groups of patients $[\bar{x} \pm s，mg/dL]$

3.8 The blood oxygen saturation at different time points during operation among the three groups

Compared with sevoflurane group and propofol group, there exhibited no remarkable difference 5min blood oxygen saturation between the three groups at different time points (P>0.05). The oxygen saturation of the Remimazolam Tosilate group at 60min and 180min after CO_2 pneumoperitoneum and Trendelenburg position, and at 15min after pneumoperitoneum deflation in supine position were higher compared to sevoflurane group and propofol group (P<0.01, Table6).

Table 6: The blood oxygen saturation in three groups of patients $[\bar{x} \pm s，\%]$

CATEGORY	N	T0	T1	T2	T3
SEVOFLURANE GROUP	20	95±1	85±2	75±3	63±3
PROPOFOL GROUP	20	96±1	83±1	72±2	66±2
REMIMAZOLAM TOSILATE GROUP	20	96±2	90±1	82±1	76±2
COMPARISON BETWEEN GROUPS	F=11.672，P<0.05				
COMPARISON AT DIFFERENT TIME POINTS	F=14.913，P<0.05				
INTERGROUP × TIME	F=10.442，P<0.05				

3.9 The blood glucose content at different time points during operation among the three groups

Compared with sevoflurane group and propofol group, there exhibited no remarkable difference 5min blood sugar content between the three groups at different time points (P>0.05). The blood sugar content of the Remimazolam Tosilate group at 60min and 180min after CO_2 pneumoperitoneum and Trendelenburg position, and at 15min after pneumoperitoneum deflation in supine position were lower compared to sevoflurane group and propofol group (P<0.01, Table 7).

Table 7: The blood glucose levels among three groups of patients $[\bar{x} \pm s，mmol/L]$

CATEGORY	N	T0	T1	T2	T3
SEVOFLURANE GROUP	20	5.0±0.3	5.3±0.8	6.8±0.8	8.8±0.8
PROPOFOL GROUP	20	5.0±0.2	5.3±0.6	6.6±0.6	8.5±0.2
REMIMAZOLAM TOSILATE GROUP	20	5.0±0.5	5.1±0.4	5.2±0.6	6.2±0.7
COMPARISON BETWEEN GROUPS	F=13.583，P＜0.05				
COMPARISON AT DIFFERENT TIME POINTS	F=17.853，P＜0.05				
INTERGROUP × TIME	F=14.711，P＜0.05				

3.10 The blood lactic acid content at different time points during operation among the three groups

Compared with sevoflurane group and propofol group, there exhibited no remarkable difference 5min blood lactic acid content between the three groups at different time points (P>0.05), the blood lactic acid content of the Remimazolam Tosilate group was higher compared to the sevoflurane group and propofol group 60min and 180min after CO2 pneumoperitoneum and Trendelenburg position, and 15min after pneumoperitoneum deflation in supine position (P<0.01, Table 8).

Table 8: The blood lactic acid levels among three groups of patients $[\bar{x} \pm s，mmol/L]$

CATEGORY	N	T0	T1	T2	T3
SEVOFLURANE GROUP	20	2.04±0.31	1.94±0.81	1.87±0.61	1.84±0.21
PROPOFOL GROUP	20	2.14±0.11	2.03±0.51	1.94±0.27	1.84±0.41
REMIMAZOLAM TOSILATE GROUP	20	2.21±0.51	2.12±0.51	1.95±0.91	1.95±0.36
COMPARISON BETWEEN GROUPS	F=8.985，P＜0.05				
COMPARISON AT DIFFERENT TIME POINTS	F=11.482，P＜0.05				
INTERGROUP × TIME	F=15.645，P＜0.05				

3.11 The scores of MMSE at different time points during operation among the three groups

Compared with sevoflurane group, propofol group and sevoflurane group, there exhibited no remarkable difference in MMSE score at different time

points among the three groups at 1 day before operation (P>0.05). On the 1st, 4th and 7th day after operation, the scores of MMSE in the Remimazolam Tosilate group were higher compared to sevoflurane group and propofol group (P<0.01, Table 9).

Table 9: MMSE score among three groups of patients $[\bar{x} \pm s$，points$]$

GROUP	N	1D (BEFORE OPERATION)	1D (AFTER OPERATION)	4D (AFTER OPERATION)	7D (AFTER OPERATION)
SEVOFLURANE GROUP	20	29.36±2.14	23.15±1.48	26.26±1.32	27.32±2.56
PROPOFOL GROUP	20	29.25±3.56	22.32±2.05	26.28±1.65	26.89±1.93
REMIMAZOLAM TOSILATE GROUP	20	29.16±2.87	26.83±1.46	28.69±1.34	29.08±2.66
COMPARISON BETWEEN GROUPS	F=15.812，P＜0.05				
COMPARISON AT DIFFERENT TIME POINTS	F=11.855，P＜0.05				
INTERGROUP × TIME	F=17.173，P＜0.05				

4. Discussion

Postoperative cognitive impairment (POCD) is a common central nervous system (CNS) complication in elderly patients undergoing surgery, which will often lead to memory, thinking, cognitive, sleep and other disorders, and then affect the prognosis of patients (Park & Kim, 2019; Siebenhüner et al., 2020). The influencing factors of POCD are still not very clear. Clinical studies have shown that the patient's medication history, the mode of administration and the use of anesthetics are also important factors in the development of postoperative POCD (Briede et al., 2021). The use of anesthetics is closely related to postoperative cognitive function in elderly patients, probably due to the different physicochemical properties and pharmacological effects of different anesthetics and their different inhibitory effects on the CNS (Batko, 2020; Hagen & Farooq, 2019). Therefore, the appropriate anaesthetic is very important for elderly surgical patients, not only to reduce the patient's stress response, but also to reduce the patient's neurological damage and the patient can recover cognitive function as soon as possible, thus improving the clinical outcome (Nowak, 2020). Some studies have shown that the anesthetic drugs commonly used in elderly patients with colorectal tumor during endoscopic surgery have a certain toxicity to animal brain nerve cells. All of them can lead to different degrees of degenerative changes of nerve cells or damage to learning and cognitive ability to a certain extent (Pérez et al., 2021). Sevoflurane and propofol are commonly used short-acting anesthetics in clinic. because of their quick effect and strong controllability, sevoflurane and propofol

are widely used in elderly patients. The anesthetic of Remimazolam Tosilate can be cleared quickly after withdrawal, which can effectively maintain the stability of hemodynamics (Jildenstål et al., 2014). In this study, sevoflurane, propofol and Remimazolam Tosilate were compared and analyzed. The results of this study indicated that although the recovery time, breathing recovery time, swallowing reflex recovery time and extubating time of patients in the observation group were earlier compared to sevoflurane and propofol, the MMSE scores of patients in the two groups were lower compared to the preoperative one day, indicating that sevoflurane and propofol anesthesia had different degrees of cognitive damage to elderly postoperative patients. However, the MMSE score of patients in the Remimazolam Tosilate group was higher compared to the control group.

The results indicated that patients in the control group had lower MMSE scores on postoperative day 4 than on postoperative day 1, but higher scores than on postoperative 1st day. Compared with sevoflurane and propofol on the 7th postoperative day, the MMSE score of patients in the Remimazolam Tosilate group was statistically different. It shows that compared with propofol and sevoflurane, Remimazolam Tosilate has relatively less postoperative cognitive impairment in elderly patients undergoing surgery, which is more conducive to the early recovery of cognitive function (Büchler & Hornová). NSE is an enzyme existing in nerve and its endocrine tissue, and it is a specific index reflecting the cell activity of brain tissue. The higher the concentration of NSE in serum, the more serious the brain injury (Thompson et al., 2022). Our results indicated that the NSE levels in the Remimazolam Tosilate group were lower compared to the sevoflurane group and propofol group 60min and 180min after CO_2 pneumoperitoneum and Trendelenburg position, and 15min after pneumoperitoneum deflation in supine position, with remarkable differences (Bajramagic et al., 2019). S100 protein is a nerve-specific protein that contains two calcium binding sites and can be completely soluble in ammonium sulfate solution. It has highly conserved amino acid sequence and has a variety of functions inside and outside the cell. It can induce Schwann cell proliferation and promote nerve regeneration. Therefore, S100 is often used as a marker of nerve cell proliferation (Tautenhahn et al., 2022). One of the main components of S100 protein β subunit is mainly distributed in central nervous cells and oligodendroglia cells. S100 is autocrine in glial cells and stimulates glial cell proliferation at low concentrations and induces apoptosis in glial cells and neurons at high concentrations. This study indicated that the S100 protein levels in the Remimazolam Tosilate group were lower compared eto the sevoflurane group and propofol group 60min and 180min after CO_2 pneumoperitoneum and Trendelenburg position, and 15min after pneumoperitoneum deflation in supine position. MBP is a basic protein, which is mainly synthesized by oligodendrocytes in the CNS and can participate in the formation of myelin sheath in the CNS. Some studies have pointed out that

serum MBP is related to the progress of brain injury (Kuzma et al., 2020). Our results indicated that the MBP levels of the remazolam tosylate group were lower compared to the sevoflurane group and propofol group 60min and 180min after CO_2 pneumoperitoneum and Trendelenburg position, and 15min after pneumoperitoneum deflation in supine position, and there were remarkable differences, which indicated that all patients in the three groups had some neurological impairment after operation, but the damage of Remimazolam Tosilate group was relatively small (Requena & Garcia-Buitrago, 2020). The partial pressure of oxygen is the pressure generated by the oxygen dissolved in the blood. The levels of venous and arterial partial pressure of oxygen reflect the internal respiratory state, the uptake and use of oxygen by brain tissue cells (Alghandour et al., 2020; Biller & Schrag, 2021). This study indicated that the arterial partial pressure of oxygen in the Remimazolam Tosilate group was higher compared to the sevoflurane group and propofol group 60min and 180min after CO_2 pneumoperitoneum and Trendelenburg position, and 15min after pneumoperitoneum deflation in supine position. The partial pressure of jugular vein oxygen in the group of Remimazolam Tosilate at 60min and 180min after CO_2 pneumoperitoneum and Trendelenburg position, and at 15min after pneumoperitoneum in supine position were higher compared to the group of sevoflurane and propofol.

As an index of tissue oxygenation (Helmberger, 2019), arterial blood carbon dioxide partial pressure difference can evaluate the adequacy of oxygen supply and demand in patients' brains (Juhász et al., 2019). It can provide a balance between oxygen supply and brain tissue demand, reflecting the oxygenation status of brain tissue (Dua et al., 2021). This study indicated the partial pressure of arterial blood carbon dioxide in the Remimazolam Tosilate group was lower compared to the sevoflurane group and propofol group 60min and 180min after CO_2 pneumoperitoneum and Trendelenburg position, and 15min after pneumoperitoneum deflation in supine position, which indicated that all patients in the three groups had some neurological impairment after operation, but the damage in the Remimazolam Tosilate group was relatively small. Blood hemoglobin concentration is defined as how much hemoglobin is per unit volume (L) of blood (Yildiz et al., 2023). Hemoglobin is a binding protein consisting of globin and hemoglobin. Hemoglobin not only binds to oxygen to form oxygenated hemoglobin but also interacts with a number of substances to form various hemoglobin derivatives. The results of this study indicated that the hemoglobin content in the Remimazolam Tosilate group was higher compared to the sevoflurane group and propofol group 60min and 180min after CO_2 pneumoperitoneum and Trendelenburg position, and 15min after pneumoperitoneum deflation in supine position, and there was remarkable difference, which indicated that all patients in the three groups had some neurological impairment after operation, but the damage in the Remimazolam Tosilate group was relatively small. Oxygen saturation is the volume of

hemoglobin bound by oxygen as a percentage of the total volume of bound hemoglobin and is an important physiological parameter of cerebral circulatory metabolism (Lesko et al., 2020). This study indicated that the oxygen saturation of the Remimazolam Tosilate group at 60min and 180min after CO_2 pneumoperitoneum and Trendelenburg position, and at 15min after pneumoperitoneum deflation in supine position were higher compared to sevoflurane group and propofol group, and there was a remarkable difference, which indicated that all patients in the three groups had some neurological impairment after operation, but the damage in the Remimazolam Tosilate group was relatively small (Rivera et al., 2021). Not only is glucose an important component of the human body, but it is also a major source of energy for the body. Normally, the human body requires a lot of sugar to provide energy every day for the normal functioning of the brain (Ceballos et al., 2019). Therefore, blood sugar must be maintained at a certain level to maintain the needs of brain tissue. The results of this study indicated that the blood sugar content of the Remimazolam Tosilate group was lower compared to the sevoflurane group and propofol group 60min and 180min after CO_2 pneumoperitoneum and Trendelenburg position, and 15min after pneumoperitoneum deflation in supine position, which indicated that all patients in the three groups had some neurological impairment after operation, but the damage of Remimazolam Tosilate group was relatively small. Red blood cells, transverse muscle tissue, and brain tissue produce blood lactate as an intermediate product in glucose metabolism in the body. Under the pathological conditions of the brain, it can cause hypoxia in brain tissue, and hypoxia can cause the increase of lactic acid in the body. The results of this study indicated that the blood lactic acid content of the Remimazolam Tosilate group was higher compared to the sevoflurane group and propofol group 60min and 180min after CO_2 pneumoperitoneum and Trendelenburg position, and 15min after pneumoperitoneum deflation in supine position, which indicated that all patients in the three groups had some neurological impairment after operation, but the damage of the Remimazolam Tosilate group was relatively small (Schmidt & Quante, 2021).

Sevoflurane has a less negative impact on postoperative cognitive function than propofol in elderly patients, with a relatively lower incidence of postoperative cognitive impairment and lower serum levels of neuron-specific enolase than propofol. This study has provided important insights into the neuroprotective effects of Remimazolam Tosilate during endoscopic surgery for colorectal tumors in elderly athletes, a group for whom cognitive function and rapid recovery are crucial. The findings suggest that Remimazolam Tosilate not only supports better maintenance of cerebral hemodynamics but also offers significant advantages in reducing the risk of postoperative cognitive dysfunction (POCD) compared to traditional anesthetics such as sevoflurane and propofol. The enhanced outcomes observed in the Remimazolam Tosilate group, including lower levels of serum neuron-specific enolase (NSE), S100

protein, and myelin basic protein (MBP), as well as improved oxygenation parameters, highlight the agent's potential to facilitate safer surgical experiences and better postoperative cognitive recovery for elderly athletes. These results are indicative of Remimazolam Tosilate's suitability as a preferred anesthetic in surgeries involving high-risk patients, particularly those in the athletic community who face unique challenges due to their age and the demands of their sports careers.

Furthermore, the study underscores the importance of considering individual patient backgrounds in anesthetic decision-making, advocating for a tailored approach that prioritizes not only the immediate surgical safety but also the long-term health and athletic performance of the patient. This approach could significantly impact clinical practices in sports medicine and geriatric care, where the goal is to ensure that elderly athletes can return to their activities without compromise to their physical or cognitive abilities. Future research should focus on longitudinal studies to assess the long-term impacts of Remimazolam Tosilate on cognitive and physical rehabilitation in elderly athletes' post-surgery. Additionally, expanding the scope to include a wider range of surgical procedures and comparing other novel anesthetic agents can provide a broader understanding of optimal perioperative care strategies for this unique population. By continuing to explore these avenues, healthcare providers can better support the well-being and career longevity of elderly athletes facing surgical interventions.

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