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*Original Article*

# Effect of remazolam combined with hydromorphone postoperative analgesia on cognitive function in elderly patients undergoing hip replacement

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**Abstract:** Objective: To investigate the effect of remazolam combined with hydromorphone on postoperative cognitive function in elderly patients undergoing hip replacement. Methods: 184 elderly patients who underwent hip replacement in Sir Run Run Shaw hospital from January 2023 to January 2025 were retrospectively analyzed. According to the intraoperative anesthesia scheme, they were divided into an observation group (remazolam combined with postoperative hydromorphone analgesia) and a control group (propofol combined with postoperative hydromorphone analgesia). The intraoperative hemodynamics, anesthesia recovery, incidence of cognitive dysfunction (POD) within 7 days after operation, scores of mini-mental state examination (MMSE) and Montreal cognitive assessment (MoCA), visual analogue scale (VAS) score within 48 hours after operation, hydromorphone dosage, joint function score, adverse reactions, and analgesia satisfaction were compared between the two groups. Results: There was no significant difference in intraoperative hemodynamic indexes or post-anesthesia monitoring treatment room stay time between the two groups ($P > 0.05$), but the eye opening time and extubation time in the observation group were shorter ($P < 0.05$) and the incidence of POD in the observation group were lower than in the control group within 7 days after operation. The scores of MoCA and MMSE in the observation group were higher than those in the control group on the 1st and 3rd day after operation ($P < 0.05$), but there was no difference between the two groups on the 7th day after operation. There was no significant difference in VAS scores between the two groups at each time point after operation, but the cumulative dosage of hydromorphone in the observation group was higher at 6 hours and 24 hours after operation ($P < 0.05$), and there was no difference between the two groups at 48 hours. The analgesic satisfaction of the observation group was higher ($P < 0.05$). There was no significant difference in the incidence of adverse reactions or joint function scores between the two groups. Conclusion: Remazolam combined with hydromorphone for postoperative analgesia in elderly patients undergoing hip replacement can help reduce the incidence of early POD, promote anesthesia recovery, improve analgesia satisfaction, and does not increase adverse reactions.

**Keywords:** Remazolam, hydromorphone, elderly patients, hip replacement, cognitive function

## Introduction

Hip fracture is a common traumatic disease in elderly patients. It is also the main type of disease that affects the walking function of the elderly population. Surgical treatment is the main way to restore the walking function of the lower limbs [1, 2]. Although perioperative anesthesia management and surgical techniques are constantly improving, the incidence of complications has always been the main factor affecting the rapid recovery of patients. Postoperative delirium is one of the most common complications after hip replacement in elderly patients [3, 4]. The latest research shows that the incidence of POD in elderly patients after hip replacement is between 10% and 40%. On the one hand, POD seriously affects the postoperative rehabilitation process of patients, prolongs hospitalization time, and increases the burden of family and social care. On the other hand, it can result in permanent dysfunction [5, 6].

Current studies have confirmed that the mechanism of POD involves multiple factors such as surgical trauma, anesthetics, inflammatory response, pain stress, and sleep rhythm disorders [7]. Among these, anesthetics are important influencing factors. Traditional anesthetics such as propofol have rapid onset and rapid metabolism, but studies suggest that it may be involved in postoperative POD by affecting the γ-aminobutyric acid (GABA) system and inducing neuroinflammatory response. Therefore, optimizing the anesthesia program can reduce the occurrence of POD to a certain extent [8]. The literature has confirmed that remazolam not only has the characteristics of rapid onset, easy regulation of sedation depth, and weak respiratory and circulatory inhibition, but also has a rapid and stable recovery after surgery, which has gradually been applied in clinical practice. Theoretically, it is conducive to the prevention of postoperative cognitive dysfunction [9]. At the same time, scholars have made it clear that optimizing postoperative pain management can reduce the occurrence of cognitive dysfunction in patients, and hydromorphone has a good postoperative analgesic effect [10]. Based on the above theory, the purpose of this study was to investigate the effect of postoperative analgesia with remazolam combined with hydromorphone on postoperative POD in elderly patients undergoing hip replacement, in order to provide potential intervention targets for optimizing perioperative anesthesia management strategies and reducing the occurrence of POD in elderly patients to improve long-term prognosis.

## Patients and methods

*General information*

A retrospective analysis of 184 elderly patients who underwent hip replacement in Sir Run Run Shaw hospital from January 2023 to January 2025 was divided into an observation group (remazolam combined with hydromorphone for postoperative analgesia, n=98) and a control group (propofol combined with hydromorphone for postoperative analgesia, n=86) according to intraoperative anesthesia methods. This study was approved by the ethics committee of Sir Run Run Shaw hospital (ethical number: KYLL-20241108).

*Sample size*

The sample size was estimated based on the difference in MMSE scores on postoperative day 1 between the two groups. According to the pilot study/literature review [5], the mean MMSE score in the control group was $\mu 1=26.5$ with a standard deviation of $\sigma=2.5$ and that in the observation group was $\mu 2=28.0$. With a two-sided significance level of $\alpha=0.05$ and a power of $1-\beta=0.80$, the sample size was calculated using the formula for comparing two independent means:

$$n=2(Z\alpha/2+Z\beta)2\times\sigma 2/(\mu 1-\mu 2)^2$$

Where $Z\alpha/2=1.96$, $Z\beta=0.84$, $\sigma=2.5$, and $\mu 1-\mu 2=1.5$. The calculation yielded a required sample size of approximately nn=70 cases per group. Considering a 10%-20% dropout rate, the final sample size was determined to be at least 84 cases per group, with a total of 168 cases. This study actually included 184 patients, meeting the sample size requirement.

*Inclusion criteria*

1. Age ≥ 65 years; 2. American Society of Anesthesiologists (ASA) grade II-III; 3. Selective unilateral total hip arthroplasty; 4. Preoperative Mini-Mental State Examination (MMSE) score ≥ 24 points; 5. Those with complete clinical data; 6. First hip surgery.

*Exclusion criteria*

1. Preoperative cognitive dysfunction, mental illness, or history of neurodegenerative diseases; 2. Long-term use of sedative hypnotics, antipsychotics or opioids; 3. Patients allergic to benzodiazepines or opioids; 4. Severe complications (such as massive hemorrhage, cardiovascular and cerebrovascular accidents) or transfer to ICU; 5. Pregnant or lactating women; 6. Cardiovascular and cerebrovascular diseases.

*Data collection*

The general information of the patients was obtained by consulting the electronic system, including baseline data, liver and kidney function indicators, course of disease, and inflammatory factor change score. Anesthesia methods: The patients in both groups were fasted for 8 hours before operation, and did not take any drugs. After entering the operating room, venous access was established for all patients, and masks were used for pre-oxygenation. The oxygen flow rate was set to 6 L·min$^{-1}$. Philips MX450 Intelli Vue monitor (Philips China Investment Co., Ltd.) was used to monitor the patient's heart rate (HR), mean arterial pressure (MAP), oxygen saturation ($SpO_2$), body temperature and end-tidal carbon dioxide partial pressure ($PETCO_2$). In the anesthesia induction stage, the grouping administration scheme was adopted: the first dose of remazolam group was intravenously administered with benzodiazepine sedative remazolam besylate for injection (Yichang Renfu Pharmaceutical Co., Ltd., Sinopharm approval No.: H20200006, specification: 25 mg), and the dosage was 0.2-0.4 mg·kg$^{-1}$ according to body weight. The control group was treated with short-acting anesthetic propofol emulsion injection (Sichuan Guorui Pharmaceutical Co., Ltd., national standard H2003-0115, specification 20 mL: 0.2 g), according to 1.5-2.0 mg·kg$^{-1}$ dose standard. All subjects were injected with μ-opioid receptor agonist sufentanil (Yichang Renfu Pharmaceutical Co., Ltd., Sinopharm approval number H20054171, specification 50 μg/mL) 0.3-0.5 μg·kg$^{-1}$ and non-depolarizing muscle relaxant cisatracurium besilate injection (Nanjing Jianyou Biochemical Pharmaceutical Co., Ltd., Sinopharm approval number H20203700, specification 10 mg) 0.1-0.2 mg·kg$^{-1}$ to complete anesthesia induction after the establishment of basic anesthesia. After induction, the laryngeal mask was placed and connected to the HEINEN und LOWENSTEIN Leon PLUS anesthesia machine (Helen, Germany). Volume-controlled ventilation (VCV) was used. The tidal volume (VT) was set to 6-8 mL kg$^{-1}$, the ratio of inspiratory time to expiratory time was 1:2, and the respiratory rate (RR) was 12-16 times min-1. During the maintenance of anesthesia, the continuous infusion dose of remazolam in the remazolam group was 0.3-0.5 mg (kg·h)$^{-1}$, and the maintenance dose of propofol in the propofol group was 4-8 mg·(kg·h)$^{-1}$. Both groups were given remazolam (Yichang Renfu Pharmaceutical Co., Ltd., national drug approval H20030197, specification 1 mg each), and the infusion rate was 0.1-0.25 μg·(kg·min)$^{-1}$. After operation, all patients received patient-controlled intravenous analgesia with hydromorphone at a dose of 0.2 mg·kg$^{-1}$ and normal saline to prepare 100 mL. Analgesia pump parameters were set as follows: background infusion rate 2 mL·h$^{-1}$; a single pressing dose of 0.5 mL; the locking time was 15 min.

*Observation indicators*

Main outcome measures: The incidence of POD was compared between the two groups. Postoperative cognitive dysfunction (POD) was diagnosed by referring to the relevant guidelines within 7 days after operation and combining with the patient's daily consciousness state assessment (such as consciousness fuzzy assessment method). Postoperative cognitive dysfunction was compared between the two groups: the Mini-Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MoCA) Chinese version were used to evaluate [11]. MMSE total score of 30 points, < 24 points for cognitive dysfunction; moCA total score of 30 points, < 26 points for cognitive dysfunction [12]. Analgesia-related indicators were compared between the two groups: postoperative pain assessment combined with analgesic drug dosage. The method was as follows: Visual analogue scale (VAS) was used to evaluate the pain intensity of patients at rest after operation. The scale was a 10 cm long straight line, with 'painless' (0 point) at the left end and 'severe pain' (10 points) at the right end. The patients were instructed to mark the degree of pain and record the scores at 6, 12, 24, and 48 h after operation. The cumulative consumption of hydromorphone (mg) in the patient-controlled analgesia pump within 48 h after operation was recorded and directly read by the built-in electronic recording system of the analgesia pump.

Secondary observation indicators: Comparison of patient satisfaction between the two groups: 48 hours after surgery, the two groups of patients were assessed with a five-level Likert scale: 1 point (very dissatisfied), 2 points (dissatisfied), 3 points (general), 4 points (satisfied), 5 points (very satisfied). Comparison of postoperative joint function scores between the two group: Harris hip function score was used on the 7th day after operation, including pain, function, activity and deformity. The total score was 100 points, ≥ 90 points were excel-

**Table 1.** Comparison of baseline characteristics between the two groups of patients

| Indicator | Observation Group (n=98) | Control Group (n=86) | Statistical Value | *P* Value |
|---|---|---|---|---|
| Gender (Male/Female) | 52/46 | 48/38 | 0.22 | 0.637 |
| Age (years) | 72.4 ± 6.8 | 73.1 ± 7.2 | -0.73 | 0.468 |
| BMI (kg/m$^2$) | 24.3 ± 3.1 | 24.6 ± 3.4 | -0.68 | 0.498 |
| Education Level (n) | | | 1.48 | 0.478 |
| Primary School or Below | 18 | 16 | | |
| Middle/High School | 52 | 48 | | |
| College/University or Above | 28 | 22 | | |
| Coronary Artery Disease (n) | 22 | 20 | 0.05 | 0.823 |
| Smoking History (n) | 34 | 32 | 0.09 | 0.761 |
| Hypertension (n) | 58 | 52 | 0.08 | 0.777 |
| Diabetes (n) | 32 | 30 | 0.06 | 0.806 |
| ASA Classification (n) | | | 0.62 | 0.733 |
| Grade II | 60 | 56 | | |
| Grade III | 38 | 30 | | |

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

lent, 80-89 points were good, 70-79 points were medium, and < 70 points were poor.

*Data statistics*

SPSS 23.0 statistical software was used for data analysis. The measured data conforming to the normal distribution were expressed as mean ± standard deviation, and the counted data were expressed as number of cases (percentage). First, single factor analysis was carried out: independent sample t-test was used to compare the measurement data between groups, and chi-square test was used to compare the counted data. All analyses were considered significant at $P < 0.05$.

## Results

*Comparison of baseline data*

A total of 184 elderly patients undergoing hip replacement were included in this study, including 98 patients in the observation group (remazolam combined with hydromorphone) and 86 patients in the control group (propofol combined with hydromorphone). There was no significant difference in gender, age, body mass index (BMI), education level, coronary artery disease, smoking history, hypertension, diabetes or ASA classification between the two groups (all $P > 0.05$), suggesting that the baseline characteristics of the two groups were balanced and comparable (**Table 1**).

*Comparison of hemodynamic data between the two groups of elderly patients undergoing hip replacement*

The changes of hemodynamic data at different time points in the two groups were shown in **Table 2**. At T0 and T3, there was no significant difference in heart rate (HR) or mean arterial pressure (MAP) between the two groups (all $P > 0.05$). At T1 time point, there was no significant difference in HR between the two groups ($P > 0.05$). However, at T1 and T2 time points, the MAP of the observation group (remazolam combined with hydromorphone) was significantly higher than that of the control group (propofol combined with hydromorphone) (all $P < 0.05$); at T2 time point, HR in the observation group was also significantly higher than that of the control group ($P < 0.05$).

*Comparison of recovery room findings between the two groups of elderly patients undergoing hip replacement*

There was no significant difference in the post-anesthesia care unit (PACU) residence time between the two groups ($P > 0.05$). However, in terms of postoperative recovery and extubation, the eye opening time and extubation time of the observation group (remazolam combined with hydromorphone) were significantly shorter than those of the control group (propofol combined with hydromorphone, all $P < 0.001$), suggesting that remazolam can promote postoper-

**Table 2.** Comparison of intraoperative hemodynamic data at different time points between the two groups ($\overline{x} \pm s$)

| Indicator | Time Point | Observation Group (n=98) | Control Group (n=86) | t Value | *P* Value |
|---|---|---|---|---|---|
| HR (bpm) | T0 | 78.4 ± 8.2 | 77.9 ± 7.8 | 0.43 | 0.666 |
| | T1 | 85.3 ± 9.1 | 83.2 ± 8.7 | 1.59 | 0.114 |
| | T2 | 88.7 ± 9.5 | 85.1 ± 8.9 | 2.54 | 0.012 |
| | T3 | 80.2 ± 8.6 | 79.8 ± 8.3 | 0.33 | 0.740 |
| MAP (mmHg) | T0 | 92.5 ± 7.8 | 93.1 ± 8.2 | -0.52 | 0.606 |
| | T1 | 89.8 ± 8.4 | 86.3 ± 7.9 | 2.92 | 0.004 |
| | T2 | 87.6 ± 8.1 | 84.2 ± 7.8 | 2.78 | 0.006 |
| | T3 | 91.3 ± 7.9 | 90.8 ± 8.1 | 0.44 | 0.659 |

Note: HR: Heart rate; MAP: Mean Arterial Pressure.

**Table 3.** Comparison of post-anesthesia recovery times between the two groups

| Indicator | Observation Group (n=98) | Control Group (n=86) | t Value | *P* Value |
|---|---|---|---|---|
| PACU Stay Time (min) | 45.6 ± 8.3 | 46.8 ± 9.1 | -0.96 | 0.340 |
| Postoperative Eye-opening Time (min) | 8.2 ± 2.4 | 11.7 ± 3.1 | -8.67 | < 0.001 |
| Extubation Time (min) | 9.6 ± 2.8 | 13.2 ± 3.5 | -7.94 | < 0.001 |

Note: PACU: Post-Anesthesia Care Unit.

**Table 4.** Comparison of the incidence of postoperative cognitive dysfunction (POD) between the two groups

| Group | Total Cases (n) | POD Cases (n) | Incidence (%) | $\chi^2$ Value | *P* Value |
|---|---|---|---|---|---|
| Observation Group | 98 | 8 | 8.16 | 5.14 | 0.023 |
| Control Group | 86 | 16 | 18.60 | | |

Note: POD: Postoperative Cognitive Dysfunction.

ative anesthesia recovery and extubation in elderly patients with hip replacement (**Table 3**).

*Comparison of the incidence of postoperative POD between the two groups of patients*

The incidence of postoperative cognitive dysfunction (POD) in the observation group (Remazolam combined with Hydromorphone) was 8.16% (8/98), which was significantly lower than that of the control group (Propofol combined with Hydromorphone) 18.60% (16/86; P=0.023), suggesting that remazolam may have a protective effect on postoperative cognitive function in elderly patients with hip replacement (**Table 4**).

*Comparison of analgesia-related indexes between the two groups*

There was no significant difference in VAS scores between the two groups at each time point (6 h, 12 h, 24 h, 48 h) after operation (all P > 0.05). In terms of postoperative analgesic drug dosage, the cumulative consumption of hydromorphone in the observation group (Remazolam combined with hydromorphone) was significantly higher than that in the control group (propofol combined with hydromorphone) at 6 h and 24 h after operation (all P < 0.05) (see **Figure 1**).

*Comparison of postoperative cognitive function between the two groups of elderly patients undergoing hip replacement*

This study compared the effects of remazolam combined with hydromorphone (observation group, n=98) and propofol combined with hydromorphone (control group, n=86) on postoperative cognitive function. The results showed that there was no significant difference in preoperative MoCA and MMSE scores between the two groups (P > 0.05). At 24 hours after operation, the two scores of the observation group

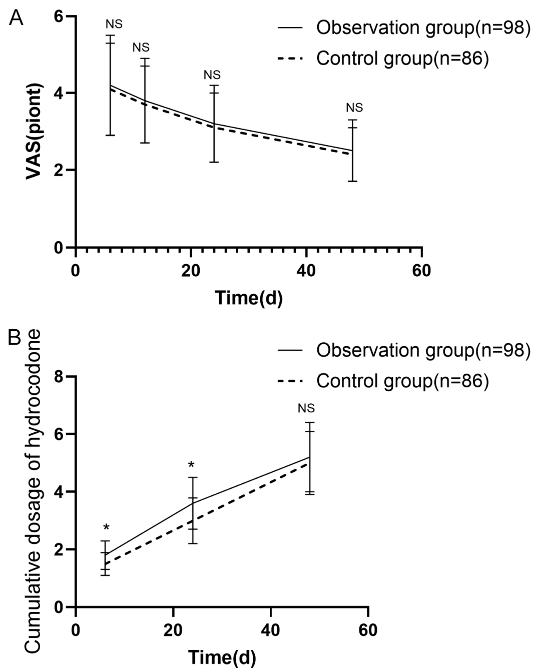


**Figure 1.** Comparison of postoperative pain score and dosage of hydromorphone between the two groups. A: VAS score between the two groups. B: Dosage of hydromorphone. VAS: Visual Analogue Scale.

were higher than those before operation (MoCA difference: 0.52 ± 1.20, MMSE difference: 0.43 ± 1.11), while the control group decreased significantly (MoCA difference: -1.74 ± 1.50, MMSE difference: -3.12 ± 1.31). The comparison between groups showed that the cognitive function score of the observation group was significantly higher than that of the control group at 24 hours after operation ($P < 0.01$). See **Table 5**.

*The joint scores of the two groups of patients after treatment*

This study compared the effects of remazolam combined with hydromorphone (observation group, n=98) and propofol combined with hydromorphone (control group, n=86) on the recovery of hip joint function. The results showed that there was no significant difference in Harris score of hip joint function between the two groups before operation. At 1 week and 1 month after operation, the scores of the two groups were significantly improved with time, but there was no significant difference between the two groups at 1 week or 1 month after operation. See **Table 6** and **Figure 2**.

*Comparison of patient satisfaction between the two groups*

In this study, the effects of remazolam combined with hydromorphone (observation group, n=98) and propofol combined with hydromorphone (control group, n=86) on postoperative analgesia satisfaction were compared. The results showed that the total satisfaction rate of the observation group was 86.7%, which was significantly higher than 75.6% in the control group (P=0.04). See **Table 7**.

*Comparison of the incidence of adverse reactions between the two groups*

In this study, the adverse reactions of remazolam combined with hydromorphone (observation group, n=98) and propofol combined with hydromorphone (control group, n=86) in postoperative analgesia were compared. The total incidence of adverse reactions was 26.5% in the observation group and 33.7% in the control group. There was no significant difference in the total incidence of adverse reactions between the two groups ($\chi^2$=1.25, P=0.264). There were no significant differences in the incidence of adverse reactions between the two groups, including nausea and vomiting, dizziness and drowsiness, respiratory depression and skin itching (all $P > 0.05$). See **Table 8**.

## Discussion

Hip arthroplasty in the elderly is the main treatment for hip joint diseases such as femoral neck fracture and femoral head necrosis in the elderly, which can quickly and effectively restore the joint function of patients [2]. However, elderly patients have physiological function degradation, often combined with a variety of basic diseases, poor tolerance to anesthesia, high risk of complications such as intraoperative hemodynamic fluctuations, postoperative cognitive dysfunction (POD), and delayed recovery, which seriously affect the surgical efficacy and prognosis of patients [3, 5]. Therefore, a safe and efficient anesthesia program, effective maintenance of intraoperative hemodynamic stability, and reduction of postoperative complications are important measures to improve the effect of anesthesia management in elderly hip replacement.

In the past, propofol combined with opioids was a common anesthesia regimen for elderly hip

**Table 5.** Comparison of cognitive function scores before and after surgery between the two groups

| Group | n | MoCA Score | | | MMSE Score | | |
|---|---|---|---|---|---|---|---|
| | | Preoperative | 24 h Postoperative | Difference | Preoperative | 24 h Postoperative | Difference |
| Observation Group | 98 | 22.50 ± 3.80 | 23.02 ± 4.15 | 0.52 ± 1.20 | 23.80 ± 3.50 | 24.23 ± 3.61 | 0.43 ± 1.11 |
| Control Group | 86 | 21.80 ± 3.60 | 20.06 ± 3.91 | -1.74 ± 1.50 | 22.91 ± 3.42 | 19.78 ± 3.33 | -3.12 ± 1.31 |
| t value | | 0.802 | 3.115 | 7.059 | 1.091 | 5.436 | 12.405 |
| *P* value | | 0.425 | 0.003 | < 0.001 | 0.279 | < 0.001 | < 0.001 |

Note: MoCA: Montreal Cognitive Assessment; MMSE: Mini-Mental State Examination.

**Table 6.** Comparison of hip joint function scores before and after surgery between the two groups

| Group | n | Preoperative Score | Score at 1 Week Postoperative | Score at 1 Month Postoperative |
|---|---|---|---|---|
| Observation Group | 98 | 45.2 ± 6.3 | 62.5 ± 7.8 | 78.9 ± 8.5 |
| Control Group | 86 | 44.8 ± 5.9 | 61.8 ± 8.2 | 77.6 ± 9.1 |
| t value | | 0.41 | 0.62 | 1.03 |
| *P* value | | 0.682 | 0.536 | 0.305 |

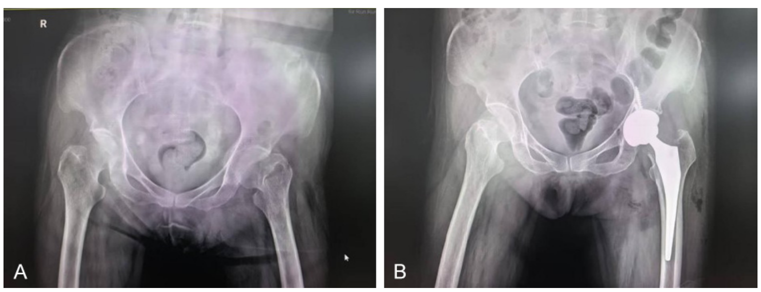


**Figure 2.** A: X-Ray pre-operation. B: Post-operation.

replacement. Propofol has a certain inhibitory effect on the cardiovascular system, which may increase the risk of intraoperative hemodynamic fluctuations, and the incidence of postoperative recovery delay and POD is high [13, 14]. As a new type of short-acting benzodiazepine, remazolam has the advantages of rapid onset, rapid metabolism and less effect on the cardiovascular system. It has been gradually applied for anesthesia in elderly patients. However, there are few studies on the efficacy and safety of remazolam combined with hydromorphone in elderly hip replacement. Therefore, this study compared the anesthetic effects of remazolam combined with hydromorphone and propofol combined with hydromorphone, plus various observation indicators, to explore its application value in elderly patients with hip replacement.

The guidelines point out that intraoperative hemodynamic stability is the core of anesthesia safety in elderly patients. The cardiovascular regulation ability of elderly patients decreases, and the fluctuation of intraoperative circulation is large, which may lead to serious complications such as postoperative myocardial ischemia and cerebral hypoperfusion, and increase the risk of surgery [15]. The results of this study showed that there was no significant difference in HR or MAP between the two groups before anesthesia induction and at the end of surgery, indicating that there was no significant difference in the hemodynamic effects of the two anesthesia regimens before anesthesia induction and at the end of surgery. At the same time, the results of this study showed that there was no significant difference in HR between the two groups after tracheal intubation/laryngeal mask placement, but MAP in the observation group was significantly higher than that of the control group. The HR and MAP of the observation group were significantly higher than those of the control group at 30 min after the start of the operation. The above results suggest that remazolam has less effect on hemodynamics in elderly patients and improves the safety of surgery [16, 17]. The underlying mechanism is as follows: Propofol can inhibit sympathetic nerve activity and expand peripheral blood vessels, resulting in decreased blood pressure and slowed heart rate, especially in elderly patients, due to its decreased vascular elasticity and decreased myocardial contractility. This inhibitory effect is more obvious and easily leads to intraoperative

**Table 7.** Comparison of postoperative analgesia satisfaction between the two groups [n (%)]

| Group | n | Very Satisfied | Satisfied | Neutral | Dissatisfied | Total Satisfaction Rate |
|---|---|---|---|---|---|---|
| Observation Group | 98 | 45 (45.9) | 40 (40.8) | 10 (10.2) | 3 (3.1) | 85 (86.7) |
| Control Group | 86 | 30 (34.9) | 35 (40.7) | 15 (17.4) | 6 (7.0) | 65 (75.6) |
| $\chi^2$ value | | | | | | 4.12 |
| *P* value | | | | | | 0.042 |

**Table 8.** Comparison of the incidence of postoperative adverse reactions between the two groups

| Group | n | Nausea/Vomiting | Dizziness/Somnolence | Respiratory Depression | Skin Pruritus | Total Adverse Reaction Rate |
|---|---|---|---|---|---|---|
| Observation Group | 98 | 12 (12.2) | 8 (8.2) | 2 (2.0) | 4 (4.1) | 26 (26.5) |
| Control Group | 86 | 15 (17.4) | 10 (11.6) | 1 (1.2) | 3 (3.5) | 29 (33.7) |
| $\chi^2$ value | | 1.02 | 0.62 | 0.21 | 0.05 | 1.25 |
| *P* value | | 0.312 | 0.431 | 0.646 | 0.823 | 0.264 |

hemodynamic fluctuations [18, 19]. Remazolam plays an anesthetic role mainly by activating the γ-aminobutyric acid receptor in the central nervous system. Its effect on the cardiovascular system is significantly milder than that of propofol. It can reduce the inhibition of sympathetic nerves while ensuring the depth of anesthesia and avoid excessive expansion of peripheral blood vessels, so as to better maintain myocardial perfusion and blood pressure stability. Similar studies have been reported in the past [20].

Postoperative recovery quality and recovery speed are important indicators to evaluate the advantages and disadvantages of elderly anesthesia programs. The metabolic capacity of elderly patients decreases, and the risk of accumulation of anesthetic drugs in the body is high, which can easily lead to delayed postoperative recovery and prolonged extubation time, and increase the risk of complications such as post-anesthesia care unit (PACU) stay and pulmonary infection. The results of this study showed that there was no significant difference in PACU residence time between the two groups, but the postoperative eye opening time and extubation time in the observation group were significantly shorter than those in the control group, suggesting that remazolam can significantly promote the postoperative anesthesia recovery and extubation process in elderly patients undergoing hip replacement, and improve the quality of postoperative recovery. The potential reasons are as follows: the metabolic half-life of propofol is relatively long, and the metabolic rate of propofol in elderly patients is slowed down, which is prone to drug accumulation, resulting in delayed postoperative recovery. As a short-acting benzodiazepine, remazolam has the characteristics of rapid onset, rapid metabolism and no obvious accumulation effect. It is mainly metabolized into inactive products through the liver and excreted through the kidney. The metabolic rate in elderly patients is less affected by age, liver and kidney function, and can be quickly removed from the body, thereby shortening the time of postoperative recovery and extubation. Similar research results have also been found in the past [21, 22].

It is reported in the literature that POD is a common neurological complication after hip replacement in the elderly. It is mainly manifested as a decline in cognitive function in the short term after surgery, including memory loss, inattention, and disorientation, which seriously affect the postoperative rehabilitation and quality of life of patients, and even increase the risk of long-term cognitive impairment [23]. The results of this study showed that the incidence of POD in the observation group was significantly lower than that in the control group. At the same time, the two cognitive function scores of the observation group at 24 hours after operation were slightly higher than those before operation, while the control group decreased significantly, and the cognitive function score of the observation group at 24 hours after operation was significantly higher than that of the control group, suggesting that remazolam can effectively reduce the incidence of postoperative POD in elderly patients with hip replacement, and has a protective effect on postoperative cognitive function. The possible mechanism is as follows: Propofol can cause postoperative cognitive impairment by inhibiting the cholinergic pathway of the central nervous system and affecting synaptic plasticity. Especially in elderly patients, due to the degeneration of brain nerve cells and the decrease of cholinergic function, the inhibitory effect of propofol on cognitive function is more obvious and it is easy to induce POD [24]. The inhibition of remazolam on the central nervous system is reversible, and it mainly acts on the limbic system of the brain, and has little effect on the cognitive-related cholinergic pathway, which can reduce the damage to nerve cell function. At the same time, remazolam can reduce the release of inflammatory factors (such as IL-6, TNF-α) by inhibiting the inflammatory stress response caused by surgical trauma. Excessive release of inflammatory factors is one of the important mechanisms leading to postoperative cognitive dysfunction, which can lead to cognitive decline by damaging the blood-brain barrier and affecting neurotransmitter metabolism [25]. In addition, the characteristics of rapid recovery of remazolam can reduce the duration of postoperative unconscious state, reduce the damage of cognitive function caused by cerebral hypoxia and cerebral hypoperfusion, further reduce the incidence of POD and protect postoperative cognitive function, which is consistent with the previous scholars' research results that remazolam can reduce the incidence of POD in elderly patients [26].

The effect of postoperative analgesia is an important factor affecting the recovery quality and satisfaction of elderly patients with hip replacement. Effective postoperative analgesia can reduce the pain of patients, reduce the stress response, and promote the rapid recovery of patients. The results of this study showed that there was no significant difference in VAS scores between the two groups at 6 h, 12 h, 24 h and 48 h after operation, suggesting that the postoperative analgesic effects of the two anesthesia schemes were comparable and could effectively relieve postoperative pain in elderly patients undergoing hip replacement. In terms of postoperative analgesic drug dosage, the cumulative consumption of hydromorphone in the observation group was significantly higher than that of the control group at 6 h and 24 h after operation, but there was no statistical difference in the total dosage at 48 h after operation. The reasons are as follows: Remazolam itself has a certain sedative effect, which can enhance the analgesic effect of hydromorphone. In the early postoperative period (6 h, 24 h), the observation group can quickly control the postoperative acute pain and avoid the stress response caused by pain stimulation by appropriately increasing the dosage of hydromorphone. With the gradual relief of pain, the dosage of hydromorphone can be gradually reduced, and finally there is no significant difference in the total dosage at 48 h after operation compared to the control group. At the same time, the results of this study showed that the total satisfaction rate of postoperative analgesia in the observation group was significantly higher than that in the control group, which was related to the faster postoperative recovery, lower incidence of POD and higher postoperative comfort of patients in the observation group, thus improving the satisfaction of postoperative analgesia, which was also consistent with the scholars' support for the anesthesia scheme of remazolam combined with hydromorphone [27].

The incidence of adverse reactions is an important index to evaluate the safety of anesthesia regimen. Elderly patients have weak physical function, poor tolerance to anesthetic drugs, and high risk of postoperative adverse reactions. Therefore, adverse reactions are important indicators for evaluating anesthesia regimen. The results of this study showed that there was no statistically significant difference in the total adverse reaction rate and the incidence of various adverse reactions between the two groups, suggesting that the anesthesia regimen of remazolam combined with hydromorphone and propofol combined with hydromorphone has the same safety in elderly patients undergoing hip replacement, which supports the previous scholars' research conclusions [28].

This study has several limitations. First, as a single-center retrospective study with a limited sample size, it did not employ methods such as propensity score matching to control for confounding factors. Although no statistical differences were found in baseline characteristics, potential selection bias cannot be entirely excluded. Second, the inclusion and exclusion criteria were not sufficiently refined; for example, "cerebrovascular disease" lacked severity stratification, and "unilateral total hip replacement" did not standardize surgical duration or approach, which may affect the robustness of the results. Third, the study only assessed short-term outcomes and did not track the long-term evolution of postoperative cognitive function or hip function, nor did it evaluate long-term adverse reactions. Fourth, the analysis of postoperative cognitive dysfunction (POD) was limited to its incidence, without severity stratification or exploration of the correlation between risk factors and anesthetic regimens, resulting in insufficient analytical depth. Fifth, although the observation group had higher cumulative hydromorphone dosages at 6 and 24 hours postoperatively, there was no difference in VAS scores. The study provided only a preliminary explanation for this finding without validation using factors such as pain tolerance or postoperative activity levels. Sixth, intraoperative inflammatory factors and neurotransmitters were not measured, limiting the exploration of the mechanisms by which remazolam protects cognitive function and maintains hemodynamic stability. Future multicenter, large-sample prospective studies with refined inclusion criteria, extended follow-up, and incorporation of pharmacoeconomic and mechanistic analyses are needed to validate the clinical value of this regimen.

In summary, remazolam combined with hydromorphone can better maintain intraoperative hemodynamic stability, significantly shorten postoperative recovery and extubation time, reduce the incidence of postoperative POD, protect postoperative cognitive function, and improve postoperative analgesia satisfaction.

## Disclosure of conflict of interest

None.

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