

ORIGINAL ARTICLE

A subanesthetic dose of esketamine combined with hip peripheral nerve block has good sedative and analgesic effects in elderly patients undergoing total hip arthroplasty: A randomized-controlled trial

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Total hip arthroplasty (THA) is more common in elderly patients who suffer from coronary heart disease, hypertension, diabetes and respiratory diseases, among other chronic illnesses.^[1] The functions of various internal organs in those patients also decline with age; therefore, the risk of surgical treatment and anesthesia is high. To improve the survival rate of elderly patients with hip fractures and reduce the incidence of perioperative adverse events, the choice of anesthesia is a challenge to anesthesiologists. Current studies have shown that spinal anesthesia, general anesthesia, peripheral nerve blocks (PNBs) and other methods can be applied in THA surgery. However, these methods

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ABSTRACT

Objectives: This study aims to observe the postoperative anesthetic effect of esketamine combined with hip capsule peripheral nerve block (PNB) in elderly patients undergoing total hip arthroplasty (THA).

Patients and methods: A total of 120 elderly patients (67 males, 53 females; mean age: 72.5±6.1 years; range, 60 to 89 years) who underwent THA between January 2020 and May 2021 were randomly divided into three groups including 40 patients in each group. The observation group (Group A) was treated with a subanesthetic dose of esketamine combined with hip capsule PNB; control group (Group B) was treated with a subanesthetic dose of esketamine divided with a subanesthetic dose of esketamine combined with a subanesthetic dose of esketamine combined with a subanesthetic dose of esketamine for general anesthesia. The onset time of anesthesia, duration of block, postoperative recovery time, postoperative extubation time, mean arterial pressure (MAP), heart rate (HR) indexes, Visual Analog Scale (VAS) and Ramsay Sedation Scale (RSS) scores were recorded.

Results: The onset time of anesthesia, duration of block, postoperative recovery time and postoperative extubation time in Group A were significantly lower than those in Groups B and C (p<0.001). Compared to Groups B and C, the MAP was higher at T1-T3 and the HR was significantly higher at T0-T1 (p<0.05) in Group A. The VAS scores after the operation in Group A were significantly lower than those in Groups B and C (p<0.001), and the RSS scores after the operation were significantly higher in this group than in Groups B and C (p<0.001).

Conclusion: A subanesthetic dose of esketamine combined with hip capsule PNB for elderly patients undergoing THA has better postoperative analgesic effects.

Keywords: Elderly, esketamine, hip capsule peripheral nerve block, total hip arthroplasty.

have certain advantages and disadvantages. To illustrate, spinal anesthesia can cause changes in blood pressure and heart rate (HR) and hemodynamic

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instability.^[2] Traditional general anesthesia uses opioids more frequently, and excessive doses tend to affect the circulatory system of patients which, in turn, leads to serious adverse effects.^[3]

In THA, the nerves involved in regional anesthesia/analgesia are complex and can be divided into cutaneous, muscular and articular branches. In recent years, hip pericapsular nerve group (PENG) block, as a new regional block method, has been gradually applied to THA, and it has been more effective in improving the degree of pain.^[4] It has been anatomically confirmed that the PNB method is to stain both the femoral nerve and the articular branch of the obturator nerve by injecting the stain between the psoas tendon and the pubic bone.^[5] Esketamine is a chiral cyclohexanone derivative that acts as the dextrose monomer of ketamine and interacts with a variety of receptors, mainly by blocking the N-methyl-D-aspartate receptor (NMDA) to exert sedative and analgesic effects. It has been shown to have a higher affinity for NMDA receptors and opioid μ receptors, and it has a four-fold higher affinity for NMDA receptors than ketamine. Esketamine is also able to non-competitively antagonize NMDA receptors and inhibit their receptor channel opening.^[6] A subanesthetic dose is a dose that is lower than anesthesia. Patients who undergo subanesthesia doses cannot achieve the required depth of anesthesia, but can have a mild sedation effect. Low-dose esketamine can have a good sedative and analgesic effect, and higher doses have better anesthetic effects, accompanied by mild cardiovascular excitation.^[7] Esketamine can reduce the stimulation and psychological effects on the heart of elderly patients and have better analgesic and sedative effects, and nerve block anesthesia has a smaller effect on hemodynamics. In addition, the use of opioids in the perioperative period is closely related to postoperative analgesia and the sedation of patients and rehabilitation prognosis. Clinical studies have shown that the use of esketamine is significantly associated with the improvement of postoperative analgesia and pain.^[8] Therefore, low-dose esketamine can effectively reduce the use of opioids in the intraoperative period, thereby reducing the postoperative analgesia needs, increasing the intensity of pain and accelerating recovery.^[9]

The clinical application of esketamine combined with PENG in THA in elderly patients is relatively rare. It is important to consider the risks of surgery and anesthesia in elderly patients, as well as the requirements for hemodynamic stationarity during surgery. In the present study, we, therefore, aimed to compare and analyze the clinical effects of esketamine combined with PENG anesthesia and traditional lumbar plexus block anesthesia to provide a reference for the future clinical application of this method.

PATIENTS AND METHODS

Study design

This single-center, prospective, randomizedcontrolled study was conducted at Changzhou Hospital Affiliated to Nanjing University of Chinese Medicine, Department of Anesthesiology between January 2020 and May 2021. A total of 120 patients (67 males, 53 females; mean age: 72.5±6.1 years; range, 60 to 89 years) who were scheduled to undergo hip arthroplasty were recruited, and block randomization was adopted for 1:1 random grouping. The patients were divided into three groups including 40 patients in each group, and the independent variable was the type of neuroleptic used in combination with a subanesthetic dose of esketamine. The observation group (Group A) was treated with a subanesthetic dose of esketamine combined with PENG; the control group (Group B) was treated with a subanesthetic dose of esketamine combined with lumbar plexus block; and the control group (Group C) was treated with a subanesthetic dose of esketamine for general anesthesia. Inclusion criteria were as follows: patients aged ≥ 60 years; American Society of Anesthesiologists (ASA) Class II-III; and having no serious coronary heart disease, hypertension, diabetes and related complications, liver and kidney function damage or mental illness. Exclusion criteria were as follows: allergy to ketamine; abnormal coagulation function; mental system diseases or cognitive dysfunction; and severe liver and kidney dysfunction.

Comparisons were conducted on the preoperative baseline data among the three groups: the onset time of anesthesia, duration of block, postoperative recovery time, postoperative extubation time, the mean arterial pressure (MAP) and HR indexes and the Visual Analog Scale (VAS) and Ramsay Sedation Scale (RSS) scores after surgery, as well as the incidence of postoperative adverse reactions. Data were collected by the anesthesiologist responsible and by nurses involved in patient care during hospital admission, and the clinical research assistants collated and analyzed the data. The nurses and the research assistant were blinded to the type of anesthesia.

Overall patient data

Intervention

According to the latest ASA guidelines, all patients fasted for 6 to 8 h and were banned from drinking for 4 h before surgery. After entering the operating room, peripheral upper limbs and venous access were routinely opened. The electrocardiogram, bispectral index, MAP, HR, pulse oximetry, respiratory rate and body temperature were routinely monitored, and the MAP and HR, after 10 min of patient calming, were recorded as baseline MAP and HR. No cases of nerve block failure, incomplete block, nerve injury, hematoma and other conditions occurred during this study.

Anesthesia methods

A subanesthetic dose of esketamine combined with PENG was used in Group A. In the supine position, the groin area was exposed using povidone-iodine, and a sterile towel was used for skin disinfection. The ultrasonic convex array probe (2 to 5 MHz) was used to place the probe parallel to the inguinal ligament. One end pointed to the anterior inferior iliac spine, and the two bony protrusions, namely the anterior inferior iliac spine and the pubic symphysis of the exoskeleton, were clearly displayed (Figure 1a). The needle was injected from the outside to the inside using the plane method. When the tip of the needle reached the lower part of the psoas major muscle bond and the surface of the pubic bone, a small amount of normal saline was injected. After confirming the diffusion of the liquid on the surface of the pubic bone and below the tendon, 0.375% 20 mL of ropivacaine was injected.

administered The patients were, then, local anesthesia and punctured through the left radial artery for invasive arterial blood pressure monitoring. For anesthesia induction, Group A was administered 0.2 mg/kg of intravenous injection of ketamine (Jiangsu Hengrui Pharmaceutical Co., Ltd., 2 mL: 50 mg), 0.3 μ g/kg of sufentanil (Yichang Renfu Pharmaceutical Co., Ltd., 1 mL: 50 µg), 0.3 mg/kg of cyclophenol (Jiangsu Enhua Pharmaceutical Co., Ltd., 10 mL: 20 mg), 2 mg of midazolam and 0.6 mg/kg of rocuronium bromide. Endotracheal intubation was performed 2 min after the induction of anesthesia. After intubation, a Datex-Ohmeda 7100 ventilator (Shanghai Jumu Medical Equipment Co., Ltd., Pudong New Area, Shanghai) was used to control breathing during anesthesia. Anesthesia was maintained with 1 to 2% sevoflurane inhalation, the remifentanil infusion rate was 0.2 to 0.3 µg/kg·min and sevoflurane was discontinued 30 min before the end of the operation. A patient-controlled intravenous analgesia (PCIA) pump was given for postoperative analgesia. The PCIA formula was as follows: sufentanil 100 ug + ondansetron 8 mg + ketorolac tromethamine 60 mg + saline to 100 mL, pump speed at 2 mL/h, an automatic single dose at 3 mL and lock time at 20 min.

In Group B, a subanesthetic dose of esketamine combined with lumbar plexus block was used. The patients were placed in the healthy lateral decubitus position and ultrasound-guided puncture was performed 4 cm beside the third and fourth lumbar vertebrae (Figure 1b, c). The frequency of the ultrasound probe was 2 to 5 MHz, and the probe was adjusted until the images below the transverse processes of the third-to-fifth lumbar vertebrae and the psoas muscle were clearly



FIGURE 1. (a) The two bony protrusions, namely the anterior inferior iliac spine and the pubic symphysis of the exoskeleton, were clearly displayed; (b and c) Ultrasound-guided puncture after subanesthetic dose of esketamine combined with nerve block. The patient was placed in the healthy lateral decubitus position and ultrasound-guided puncture was performed 4 cm beside the third and fourth lumbar vertebrae.

displayed. The needle was inserted close to the probe and retracted in the lumbar plexus, and sufentanil 0.5 μ g/kg, propofol 1.5 mg/kg and rocuronium 0.6 mg/kg were injected after no blood extraction. General anesthesia was, then, performed using a subanesthetic dose of esketamine, and the same maintenance and postoperative analgesic measures in Group A were used.

In Group C, general anesthesia was performed with a subanesthetic dose of esketamine. The same maintenance and postoperative analgesia measures as in Group A were used.

Main outcome indicators

Primary outcome measures were as follows:

- 1. Anesthesia indicators: onset time of anesthesia, duration of block, postoperative recovery time and postoperative extubation time.
- 2. Vital signs: the MAP and HR before anesthesia (T0), during skin incision (T1), 30 min after the start of surgery (T2) and at the end of surgery (T3).
- VAS: VAS score at 0.5, 2, 6, 12 and 24 h after the operation (0 no pain; 0-4 mild pain; 4-7 moderate pain; 7-10 severe pain).^[10]

Secondary outcome measures were as follows:

- RSS: RSS at 0.5, 2, 6, 12 and 24 h after surgery (0-6 points: 1 point for insufficient sedation, 2-4 points for good sedation and 5-6 points for excessive sedation).^[11]
- Adverse reactions: the incidence of postoperative delirium, nausea and vomiting, drowsiness, skin itching and other adverse reactions.

Statistical analysis

Power analysis and sample size calculation were performed using the PASS version 14.0 (NCSS, LLC Statistical software, Kaysville, Utah, USA). It was calculated that with a sample size of at least 51 patients, the study would have 80% power to identify higher patient satisfaction among patients receiving a subanesthetic dose of esketamine combined with sufentanil treatment than among those receiving the control treatment (86.67% *vs.* 63.33%) at a two-sided 5% significance level.

Statistical analysis was performed using the IBM SPSS version 26.0 software (IBM Corp., Armonk, NY, USA). The normality test of quantitative data was performed using K-S test (p=0.05). Quantitative data conforming to normal distribution were expressed in mean \pm standard deviation, while qualitative data were expressed in number and frequency. Analysis of variance (ANOVA) was used for multiple comparisons. The chi-square test or exact probability method was used for comparison between the groups. A *p* value <0.05 was considered statistically significant.

RESULTS

There was no significant difference in age, sex, body mass index (BMI), ASA class, and operation time among the three groups (p>0.05), indicating that the overall data of the three groups were comparable (Table I).

However, there were significant differences in each anesthesia index among the three groups ($p \le 0.001$). The onset time of anesthesia, duration of block, postoperative recovery time and postoperative extubation time in Group A were significantly lower than those in Groups B and C (Table II).

TABLE I Baseline data of patients								
	Group A		Group B		Group C			
	n	Mean±SD	n	Mean±SD	n	Mean±SD	t/F	p
Age (year)		71.4±6.5		73.2±7.6		72.8±6.9	2.264	0.248
Sex							0.473	0.789
Male	21		22		24			
Female	19		18		16			
Body mass index (kg/m ²)		22.5±2.4		21.3±1.9		22.1±2.0	1.678	0.452
American Society of Anesthesiologists							0.897	0.639
Grade 2	23			26		22		
Grade 3	17			14		18		
Procedure time (min)		113.5±11.4		124.8±12.6		118.3±11.9	2.423	0.514
SD: Standard deviation.								

TABLE II Comparison of anesthesia indicators among patient groups								
	Group A	Group B	Group C	_				
	Mean±SD	Mean±SD	Mean±SD	F	p			
Onset of anesthesia (min)	3.5±1.5	3.8±1.9	4.1±2.0	5.784	0.001			
Duration of block (min)	323.7±14.6	352.3±12.5	376.9±11.3	12.465	<0.001			
Postoperative recovery time (min)	11.3±3.5	15.7±2.1	16.8±2.4	6.574	<0.001			
Postoperative extubation time (min)	12.5±3.3	18.3±5.8	19.2±7.6	10.347	<0.001			
SD: Standard deviation.								

TABLE III						
Comparison of vital sign indicators at different time points among patient groups						
	Group A	Group B	Group C			
	Mean±SD	Mean±SD	Mean±SD	F	p	
Mean arterial pressure (mmHg)						
To	95.7±12.2	95.4±12.4	92.6±10.3	30.452	<0.001	
T ₁	93.5±11.3	88.3±9.2*	87.4±9.0*	28.345	<0.001	
T ₂	90.6±9.8	84.6±8.4*	84.2±8.0*	32.59	<0.001	
T ₃	89.8±8.4	81.5±7.8*	80.4±8.2*	29.648	<0.001	
Heart rate (time/min)						
To	84.4±8.3	83.5±9.4	83.0±9.2	25.476	0.001	
T ₁	80.3±7.9	78.2±8.3	78.4±7.4*	22.862	<0.001	
T ₂	78.7±7.2	82.3±8.7	77.6±9.1*	21.743	<0.001	
T ₃	77.2±6.5	78.4±9.1	75.6±9.5*	19.445	<0.001	
SD: Standard deviation; * Compared to T ₀ ; p<0.05.						

TABLE IV								
Comparison of VAS score and RSS scores at different time points between the two groups								
	Group A	Group B	Group C					
	Mean±SD	Mean±SD	Mean±SD	F	p			
Visual Analog Scale score (h)								
0.5	2.5±0.6	3.9±0.8	4.0±1.2	6.025	0.342			
2	2.7±0.7	4.6±0.7	4.7±0.9	3.427	<0.001			
6	4.3±0.6	5.2±0.5	5.3±0.8	4.234	<0.001			
12	3.1±0.5	3.8±0.6	4.1±1.3	2.485	<0.001			
24	2.3±0.4	2.4±0.3	2.6±0.5	1.348	0.942			
Ramsay score (h)								
0.5	4.3±0.7	2.3±0.5	2.4±0.4	3.412	<0.001			
2	4.1±0.5	3.2±0.4	3.3±0.3	4.384	<0.001			
6	2.4±0.2	2.1±0.3	1.8±0.6	2.564	<0.001			
12	1.9±0.3	1.8±0.4	1.6±0.9	1.385	<0.001			
24	1.7±0.3	1.6±0.2	1.8±0.8	1.572	0.564			
VAS: Visual Analog Scale: BSS: Ramsay Sedation Scale: SD: Standard deviation								

TABLE V Comparison of the incidence rate of postoperative adverse reactions among patient groups (%)								
	Group A		Group B		Group C			
Adverse reactions	n	%	n	%	n	%	χ²	p
Delirium	2	5.0	4	10.0	5	12.5	1.401	0.496
Nausea and Vomiting	10	25.0	21	52.5	24	60.0	10.943	0.004
Lethargy	3	7.5	5	12.5	4	10.0	0.556	0.757
Pruritus	1	2.5	3	7.5	7	17.5	5.605	0.061

Compared to T0, the MAP at T1-T3 in Group A gradually decreased, but its decreasing trend was not statistically significant (p>0.05). The MAP at T1-T3 in Group B significantly decreased compared to T0 (p<0.05), and the MAP at T1-T3 in Group C significantly decreased compared with T0 (p<0.05). There were significant differences in the MAP among the three groups at each time point (p<0.001), and the MAP was higher in Group A at T1-T3 compared to Groups C and B.

Compared to T0, the HR gradually decreased from T1 to T3 in Group A, but its decreasing trend was not statistically significant (p>0.05), and the HR change from T1 to T3 in Group C was statistically significant (p<0.05). There were significant differences in the HR among the three groups at each time point (p<0.001). Compared to Group C, the HR at T0-T3 was significantly higher in Group A (p<0.05). Compared to Group B, the HR at T0-T1 was higher, and it was lower in Group A at T2-T3 (Table III).

There were significant differences in the VAS scores among the three groups at each time point, except at 0.5 and 24 h (p<0.001). The VAS scores at 2, 6, and 12 h after the operation in Group A were significantly lower than those in Groups B and C.

There were significant differences in the RSS scores among the three groups at each time point, except at 24 h (p<0.001). The RSS at 0.5, 2, 6 and 12 h after surgery were significantly higher in Group A than in Groups B and C (Table IV).

Except for the incidence of nausea and vomiting, there was no significant difference in the detection rate of postoperative adverse reactions among the three groups (p>0.05). Patients in Group C had a significantly higher incidence of nausea and vomiting compared to Groups A and B (60% vs. 52.5% vs. 25.0%) (Table V).

DISCUSSION

With the rising ageing population in China, hip fractures and other elderly diseases have become more

common. As a common surgical treatment for hip fractures, THA has good function and low revision rates. However, the requirements and damage of surgical treatment to the physiological function of patients also bring challenges: preoperative fasting and drinking, intraoperative bleeding, and hip tissue damage. As elderly patients have more underlying diseases such as concomitant coronary heart disease, diabetes, hypertension, the risk of surgery and anesthesia is greater than in other populations. In addition, THA produces a certain degree of pain, and some elderly patients experience anxiety, panic and other emotions, and postoperative recovery is less optimistic.^[12] To improve the survival rate of elderly patients with hip fractures, improve the quality of postoperative recovery and reduce the incidence of postoperative pain, the choice of anesthesia is critical. The reason for this is not only to maintain stable hemodynamics such as MAP and HR during surgery, but also to do a good job of adequate preoperative and postoperative analgesia. Peripheral nerve blockades have a prominent role in modern anesthesia. The femoral nerve is the most important and easiest nerve to find, and anesthesia of other nerve fibers may theoretically improve analgesia without significantly increasing costs and time.[13]

Currently, traditional intravenous inhalation combined with general anesthesia can meet the surgical needs of patients with hip fractures. However, as elderly patients account for a relatively large proportion, unreasonable anesthesia can easily cause fluctuations in the vital signs of patients, thereby increasing the risk of anesthesia surgery and the occurrence of postoperative complications. Therefore, it is necessary to select appropriate vasoactive drugs to maintain intraoperative hemodynamic stability and analgesic and sedative effects, reduce the occurrence of postoperative adverse reactions in patients and shorten recovery time. Esketamine is a new anesthetic with analgesic and sedative effects; it has twice the intensity of analgesia compared to ketamine and is administered at half the dose of ketamine, when the same anesthetic effect is required.^[14] The adverse effects of ketamine drugs are dose-related, and subanesthetic doses of ketamine refer to intravenous doses ≤0.5 mg/kg.^[15] Furthermore, their plasma concentrations are usually high considering the analgesic intensity ratio of ketamine to esketamine, the decline of organ function in elderly patients and the decrease of drug metabolism ability.^[16] In middle-aged and elderly patients undergoing surgery, the dose should be appropriately and rationally reduced. Clinical studies have also shown that subanesthetic doses of ketamine can exert good analgesic effects in clinical practice, while the use of low-dose ketamine can significantly reduce psychiatric adverse effects after surgical recovery.^[17] Therefore, a subanesthetic dose of 0.2 mg/kg of esketamine was selected for this study.

addition, PNB technology has more In advantages as a way of intraoperative anesthesia and postoperative analgesia.^[18] The PENG is a new nerve block method proposed by Girón-Arango et al.^[5] Studies have shown that PENG has more advantages than traditional local analgesia methods; it is a fascial plane block and does not have direct contact with any nerve and, therefore, it is not accompanied by the risk of mechanical nerve injury. Furthermore, PENG innervates the sensory nerve coverage of the buttock more widely and completely and can more effectively relieve local analgesia.[19] Other advantages include that it is simple to use and has clear landmarks under ultrasound anatomy. Using this method, ultrasound-guided diffusion of local anesthetics can be observed, accidental intravascular injections can be easily avoided, the incidence of intraneural injections can be greatly reduced and the incidence of complications associated with epidural or lumbar plexus block can be reduced.^[20,21]

In this study, a subanesthetic esketamine dose combined with PENG was used for THA in elderly patients. The results showed that the onset time and duration of anesthesia in Group A were significantly shorter than those in Groups B and C, indicating that the onset time of anesthesia in PENG was shorter and the effect of block anesthesia was better. Furthermore, the postoperative recovery time and postoperative extubation time of patients in Group A were lower than those in the control Groups B and C (p<0.001), which may be as esketamine was used in anesthesia induction and maintenance to make hemodynamics more stable.^[22] The hip PENG can clearly display blood vessels, nerves and other tissues under ultrasound guidance. This allows Jt Dis Relat Surg

physicians to master the needle insertion angle and prevent the injury of peripheral nerves,^[23] and combined with the use of a subanesthetic esketamine dose, they can effectively achieve the needed analgesic and sedative effects. This is ultimately beneficial to maintain the hemodynamic stability of the patient. Moreover, the results of this study showed that the changes of MAP and HR at each time point in Group A were more stable than those in the control Groups B and C. They also indicated that a subanesthetic esketamine dose combined with PENG was beneficial to maintain the stability of intraoperative vital signs in patients. In elderly patients undergoing THA, stable postoperative hemodynamics and stable postoperative vital signs associated with subanesthetic esketamine combined with peripheral hip capsule nerve block contributed to the reduction of postoperative extubation time.

The results of this study showed that the VAS scores at 2, 6, and 12 h after the operation in Group A were significantly lower than those in the control Groups B and C (p<0.001). During the operation, a subanesthetic dose of esketamine combined with a nerve block around the hip joint capsule was used. The better nerve anesthesia effect caused by the nerve block around the hip joint capsule reduced the postoperative pain of the patients. Furthermore, injected subanesthetic doses of esketamine induce increased dopamine secretion in the central ventral striatum and caudate nucleus, causing the excitation of limbic structures, which led to good moods in patients. A good mood can reduce the reaction to pain after surgery. The RSS scores at 0.5, 2, 6, and 12 h after the operation in Group A were significantly higher than those in the control Groups B and C (p<0.001), indicating that the subanesthetic dose of esketamine combined with the use of PENG achieved a good sedative effect. This sedative effect was better than that of sufentanil, propofol and rocuronium drugs, which were used in the control groups. Compared to the incidence rate of postoperative adverse reactions, the incidence rate of postoperative delirium, nausea and vomiting, drowsiness and skin itching in the Group A was lower than that in the control groups. The difference in the incidence rate of nausea and vomiting had a statistical significance (60% vs. 52.5% vs. 25.0%, p<0.001), indicating that the subanesthetic esketamine dose combined with PENG method can effectively reduce the postoperative analgesia in elderly patients undergoing THA. Furthermore, this achieved satisfactory analgesic effects with fewer adverse reactions, which made patients more comfortable.

Nonetheless, there are some limitations to this study. First, as the sample size was small, it was not possible to further control potential confounders. Second, as a randomized-controlled study, it lacks a long postoperative follow-up. In addition, the recording time of the VAS score and RSS score was only 24 h, and the long-term postoperative score was not observed, which was not conducive to the evaluation of the prognosis. In future research, a more rigorous, multi-center, prospective studies to be designed are needed to further explore the postoperative analgesic effect of a subanesthetic dose of esketamine combined with peripheral hip nerve block in elderly patients undergoing THA.

In conclusion, the subanesthetic dose of esketamine combined with PNB of the hip joint capsule has a good postoperative analgesic effect in elderly patients undergoing THA, which may effectively shorten the postoperative recovery time and postoperative extubation time of patients, maintain the stability of vital signs during the operation, and reduce the occurrence of postoperative adverse reactions.

Ethics Committee Approval: The study protocol was approved by the IRB of the Hospital of Traditional Chinese Medicine in Changzhou (date: 24.11.2021, no: 2021-LL-09 [L]). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

- Akkaya M, Buday Z, Akcaalan S, Linke P, Gehrke T, Citak M. In-hospital complications following total knee and hip arthroplasty in patients with human immunodeficiency virus. Jt Dis Relat Surg 2022;33:3-8. doi: 10.52312/ jdrs.2022.550.
- Nakasuji M, Suh SH, Nomura M, Nakamura M, Imanaka N, Tanaka M, et al. Hypotension from spinal anesthesia in patients aged greater than 80 years is due to a decrease in systemic vascular resistance. J Clin Anesth 2012;24:201-6. doi: 10.1016/j.jclinane.2011.07.014.
- 3. Basques BA, Toy JO, Bohl DD, Golinvaux NS, Grauer JN. General compared with spinal anesthesia for total hip

arthroplasty. J Bone Joint Surg [Am] 2015;97:455-61. doi: 10.2106/JBJS.N.00662.

- Cheng L, Zheng S, Chen C, Zhao R, Wang G. Application of hip sac peripheral nerve block in hip arthroplasty. Chinese Journal of Medicine Application of hip sac peripheral nerve block in hip arthroplasty. Chinese Journal of Medicine 2021;56:578-580. doi: 10.3969/j.issn.1671-3141.2021.89.182
- Girón-Arango L, Peng PWH, Chin KJ, Brull R, Perlas A. Pericapsular nerve group (PENG) block for hip fracture. Reg Anesth Pain Med 2018;43:859-63. doi: 10.1097/ AAP.000000000000847.
- Society of Anesthesiology, Shanghai Medical Association, Society of General Surgery, Shanghai Medical Association. Shanghai expert consensus on perioperative analgesia managment in general surgery patients (2020 edition). Chinese Journal of Practical Surgery 2021;41:31-7. doi: 10.19538/j.cjps.issn1005-2208.2021.01.04
- Zanos P, Gould TD. Mechanisms of ketamine action as an antidepressant. Mol Psychiatry 2018;23:801-11. doi: 10.1038/ mp.2017.255.
- Brinck ECV, Maisniemi K, Kankare J, Tielinen L, Tarkkila P, Kontinen VK. Analgesic effect of intraoperative intravenous S-ketamine in opioid-naïve patients after major lumbar fusion surgery is temporary and not dose-dependent: A randomized, double-blind, placebo-controlled clinical trial. Anesth Analg 2021;132:69-79. doi: 10.1213/ ANE.000000000004729.
- Brinck EC, Tiippana E, Heesen M, Bell RF, Straube S, Moore RA, et al. Perioperative intravenous ketamine for acute postoperative pain in adults. Cochrane Database Syst Rev 2018;12:CD012033. doi: 10.1002/14651858. CD012033.pub4.
- Sung YT, Wu JS. The Visual Analogue Scale for Rating, Ranking and Paired-Comparison (VAS-RRP): A new technique for psychological measurement. Behav Res Methods 2018;50:1694-715. doi: 10.3758/s13428-018-1041-8.
- Rasheed AM, Amirah MF, Abdallah M, P J P, Issa M, Alharthy A. Ramsay Sedation Scale and Richmond Agitation Sedation Scale: A cross-sectional study. Dimens Crit Care Nurs 2019;38:90-5. doi: 10.1097/DCC.00000000000346.
- Reine S, Xi Y, Archer H, Chhabra A, Huo M, Wells J. Effects of depression, anxiety, and pain catastrophizing on total hip arthroplasty patient activity level. J Arthroplasty 2023;38:1110-4. doi: 10.1016/j.arth.2022.12.026.
- Kopitkó C, Czermann R, Orosz M, Hangody G, Kiss D, Szabó Z, et al. A randomized comparative evaluation of local infiltration analgesia, extended nerve blocks, and conventional analgesia in pain management after total knee arthroplasty. Jt Dis Relat Surg 2021;32:290-8. doi: 10.52312/ jdrs.2021.68.
- Daly EJ, Singh JB, Fedgchin M, Cooper K, Lim P, Shelton RC, et al. Efficacy and safety of intranasal esketamine adjunctive to oral antidepressant therapy in treatment-resistant depression: A randomized clinical trial. JAMA Psychiatry 2018;75:139-48. doi: 10.1001/jamapsychiatry.2017.3739.
- Stoker AD, Rosenfeld DM, Buras MR, Alvord JM, Gorlin AW. Evaluation of clinical factors associated with adverse drug events in patients receiving sub-anesthetic ketamine infusions. J Pain Res 2019;12:3413-21. doi: 10.2147/JPR. S217005.
- 16. Carstensen M, Møller AM. Adding ketamine to morphine for intravenous patient-controlled analgesia for acute

postoperative pain: A qualitative review of randomized trials. Br J Anaesth 2010;104:401-6. doi: 10.1093/bja/aeq041.

- 17. Zanos P, Moaddel R, Morris PJ, Riggs LM, Highland JN, Georgiou P, et al. Ketamine and ketamine metabolite pharmacology: Insights into therapeutic mechanisms. Pharmacol Rev 2018;70:621-60. doi: 10.1124/pr.117.015198.
- Tetsunaga T, Sato T, Shiota N, Tetsunaga T, Yoshida M, Okazaki Y, et al. Comparison of continuous epidural analgesia, patient-controlled analgesia with morphine, and continuous three-in-one femoral nerve block on postoperative outcomes after total hip arthroplasty. Clin Orthop Surg 2015;7:164-70. doi: 10.4055/cios.2015.7.2.164.
- Orozco S, Muñoz D, Jaramillo S, Herrera AM. Pediatric use of pericapsular nerve group (PENG) block for hip surgical procedures. J Clin Anesth 2019;57:143-4. doi: 10.1016/j. jclinane.2019.04.010.

- Ahiskalioglu A, Aydin ME, Ahiskalioglu EO, Tuncer K, Celik M. Pericapsular nerve group (PENG) block for surgical anesthesia of medial thigh. J Clin Anesth 2020;59:42-3. doi: 10.1016/j.jclinane.2019.06.021.
- Singh S. Total hip arthroplasty under continuous pericapsular nerve group block (cPENG) in a high risk patient. J Clin Anesth 2021;68:110096. doi: 10.1016/j. jclinane.2020.110096.
- 22. Atik OŞ. Which articles do the editors prefer to publish? Jt Dis Relat Surg 2022;33:1-2. doi: 10.52312/jdrs.2022.57903.
- Ilfeld BM, Gelfand H, Dhanjal S, Hackworth R, Plunkett A, Turan A, et al. Ultrasound-guided percutaneous peripheral nerve stimulation: A pragmatic effectiveness trial of a nonpharmacologic alternative for the treatment of postoperative pain. Pain Med 2020;21(Suppl 2):S53-61. doi: 10.1093/pm/pnaa332.