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ORIGINAL RESEARCH

Comparative study of dexmedetomidine and esketamine in elderly patients undergoing percutaneous vertebroplasty

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Abstract

Background: The study aims to compare the effectiveness of intravenous dexmedetomidine and intravenous esketamine on sedation and analgesia in elderly patients undergoing percutaneous vertebroplasty (PVP). **Methods**: We conducted a retrospective analysis of clinical data from 60 elderly patients with osteoporotic fractures who underwent percutaneous vertebroplasty at our institution. For comparision, the patients were divided into two groups: the dexmedetomidine group and the esketamine group. Each group comprised 30 patients. **Results**: The Ramsay scores at T2 and T3 for patients in the esketamine group (3.73 ± 0.74, 4.20 ± 0.60) were significantly higher than those in the dexmedetomidine group (3.30 ± 0.65, 3.80 ± 0.76) ($p < 0.05$). Conversely, the visual analog scale (VAS) scores at T3 and T4 for patients in the esketamine group (3.77 ± 0.73, 2.97 ± 0.49) were lower than those for the dexmedetomidine group (4.40 ± 0.77, 3.50 ± 0.51) ($p < 0.05$). There was no statistically significant difference in blood oxygen saturation (SpO_2) between the two groups at all time points ($p > 0.05$). Additionally, the mean arterial pressure (MAP) and heart rate (HR) of patients in the esketamine group were higher than those in the dexmedetomidine group at T2 and T3 ($p < 0.05$). Furthermore, there was no significant difference in intraoperative bleeding between the two groups ($p > 0.05$), while patients in the esketamine group experienced shorter hospitalization times and earlier ambulation compared to those in the dexmedetomidine group. Moreover, there was no significant difference in the incidence of adverse reactions or overall satisfaction between the two groups ($p > 0.05$). **Conclusions**: Both dexmedetomidine and esketamine, when combined with local anesthesia, demonstrated positive outcomes in PVP for elderly patients. However, esketamine combined with local anesthesia offered superior analgesia and enhanced hemodynamic stability in patients, but also leading to a deeper degree of sedation.

Keywords

Dexmedetomidine; Esketamine; Percutaneous vertebroplasty; Sedation; Analgesia

1. Introduction

Percutaneous vertebroplasty (PVP) is a highly effective treatment for osteoporotic vertebral compression fractures in elderly patients, offering the advantages of minimal trauma and expedited recovery [1]. While traditional general anesthesia methods can achieve satisfactory levels of analgesia and sedation, they carry risks such as respiratory depression, postoperative cognitive dysfunction and other adverse reactions. In addition, elderly patients often present with a variety of underlying diseases, which can make them less tolerant and responsive to anesthetic drugs [2]. Propofol, a short-acting intravenous anesthetic, can provide good sedation. However, it also poses risks of respiratory and circulatory depression and has a short duration of action, requiring continuous intravenous infusion and careful anesthetic management. Therefore, it is important to explore safer and more effective anesthesia options.

Dexmedetomidine is a highly selective α2-adrenergic receptor agonist that produces multiple effects such as analgesia, sedation and anxiolysis, as well as mild inhibition of the respiratory and circulatory systems. This makes it suitable for anesthesia management in elderly patients [3]. Esketamine, a N-methyl-D-aspartate (NMDA) receptor antagonist, is known for its rapid onset of action, strong analgesic and sedative effects, rapid awakening and mild respiratory depression [4]. Administering a subanesthetic dose of esketamine can effectively relieve pain and reduce perioperative stress in elderly patients undergoing total hip arthroplasty, demonstrating its significant clinical value [5]. However, there is currently no comprehensive information regarding the comparative effects

of dexmedetomidine and esketamine on sedation and analgesia during PVP.

This study aimed to investigate the effects of dexmedetomidine and esketamine, each combined with local anesthesia, on sedation and analgesia during PVP in elderly patients. Our goal is to provide valuable insights into the optimization of anesthesia regimens suitable for elderly patients with PVP.

2. Materials and methods

2.1 Patients

The study conducted a retrospective analysis of clinical data from sixty elderly patients diagnosed with osteoporotic fractures who underwent PVP from June 2022 to December 2022 at Nanjing BenQ Medical Center, an affiliated hospital of Nanjing Medical University. According to the treatment protocol, they were divided into two groups: the dexmedetomidine group and the esketamine group.

The patients included in this study met the diagnostic criteria for osteoporotic fractures [6] and were non-emergency cases who underwent PVP surgery. All patients had a disease duration of less than 12 months, age $\geq$60 years old and had a body mass index (BMI) ranging from 18 to 24.5 kg/m^2. In addition, the patients had an American Society of Anesthesiologists (ASA) physical status classification of I or II. Exclusion criteria: (1) coagulation disorders; (2) pathological fractures caused by myeloma or vertebral metastases; (3) receiving other analgesic and sedative treatments 1 week prior to enrollment; (4) concurrent conditions such as osteomyelitis, osteoarthritis, tuberculosis or other osteoarthritic disorders; (5) allergic to anesthesia drugs; (6) cardiovascular diseases such as myocardial infarction, angina pectoris and other cardiovascular disorders within the last 6 months.

2.2 Calculation of sample size

The calculation of sample size in this study was mainly based on statistical principles. The significance level α was set at 0.05, the test efficacy $1-\beta$ was 0.9, and the ratio of sample size between the two groups was 1:1. After calculating that the sample size of each group needs at least 25 cases, considering that there may be a dropout rate of about 20%, the final total number of samples included is 60 cases, 30 cases in each group.

2.3 Surgical programs

The patients fasted for 6 h and abstained from drinking for 2 h preoperatively. Venous access was opened in the operating room. Mean arterial pressure (MAP), heart rate (HR), oxygen saturation (SpO_2), and electroencephalogram and bispectral index (BIS) were routinely monitored. BIS was set between 40 and 60. The patients inhaled oxygen at a rate of 2 L/min through a nasal cannula. Prior to the start of surgery, patients in the dexmedetomidine group received intravenous infusion of dexmedetomidine 0.5 μg/kg (done within 10 min). Subsequently, 5 μg of sufentanil was injected intravenously, and dexmedetomidine 0.5 μg/(kg·h) was continuously infused until 5 min before the end of surgery. During this procedure, local infiltration anesthesia was administered using 40 mL of 1.0% lidocaine. Patients in the esketamine group received an intravenous infusion of esketamine 0.5 μg/kg (over 10 min). Subsequently, 5 μg of sufentanil was injected intravenously and esketamine 0.1 mg/(kg·h) was continuously infused until 5 min before the end of the operation. Local anesthesia was administered as in the dexmedetomidine group. Perioperative anesthesia management was performed by the same anesthesiologist in both groups.

The patient's MAP and HR were maintained within $\pm$25% of the basaline values during the procedure. If a patient's pain score exceeded 4, an additional analgesic, sufentanil, could be administered at a dosage of 0.5 μg/kg.

Patients were given intraoperative anesthesia mainly according to the order of patients' admission and registration, using an alternating assignment to distribute the two groups as evenly as possible in the time dimension and to reduce the confounding effect due to the time factor. If a patient had a history of allergy to either esketamine or dexmedetomidine, the corresponding drug could not be used. Physicians had some experience with both esketamine and dexmedetomidine and had no apparent routine preference. The dispensing protocols regarding esketamine and dexmedetomidine remained consistent and unchanged throughout the study period. No patient factors influenced clinical decision-making during this period, ensuring the reliability of the study.

The nature of the PVP surgery and contemporaneous care measures did not differ among all patients.

2.4 Indicators

The primary outcomes of the study were assessed as follows: (1) The visual analog scale (VAS) [7] was used to assess the pain level before the start of surgery (T0), at the time of anesthetic injection (T1), when the puncture needle reached the vertebral body (T2), at the time of cement infusion (T3), at the immediate aftermath of surgery (T4), and at 24 h postoperatively (T5). The total score on the VAS ranged from 0 to 10, with higher scores indicating more significant pain. (2) The Ramsay sedation score [8] was used to assess the degree of sedation in patients at T1, T2 and T3. The scoring criteria were: a patient who demonstrated restlessness and anxiety, attempted to sit up or expressed obvious uneasiness through speech received a score of 1 point; a patient who was in a quiet state and was able to understand and cooperate with the health care provider's instructions scored 2; a patient who was drowsy but responded quickly to instructions, scored 3; a patient who was in a light sleep but could be quickly awakened by a tap on the eyebrow or a loud call, scored 4; a patient who was asleep and unresponsive to calls, scored 5; and a patient who was in a deep sleep and was unresponsive to calls, scored 6. A score of 1 indicated inadequate sedation, 2 to 4 indicated proper sedation, and 5 to 6 indicated excessive sedation.

The secondary outcomes were assessed as follows: (1) The amount of intraoperative bleeding, the cumulative intraoperative dose of additional analgesics, the length of hospitalization, and the time to get out of bed were recorded. (2) MAP, HR and SpO_2 were recorded at T0, T1, T2, T3 and T4. (3) The adverse reactions of patients after surgery, such as dizziness, hypotension, respiratory depression and bradycardia, were recorded.

(4) Patients' postoperative satisfaction was also evaluated, focusing on their willingness to continue with this anesthetic regimen for future operations or, conversely, their dissatisfaction and reluctance to use this anesthetic method again.

2.5 Statistical analysis

The data of this study were analyzed statistically using SPSS 26.0 (IBM Corp., SPSS Statistics, Armonk, NY, USA). Categorical data were compared using chi square test (χ^2) test or Fisher's exact probability method. Continuous data that conformed to a normal distribution were expressed as mean $\pm$ standard deviation and compared using the *t*-test. Measures not normally distributed were described as M (Q1, Q3) and compared using the Mann-Whitney U test. Repeated-measures data were compared using repeated-measures analysis of variance (ANOVA) and least significant difference (LSD)-*t* test. $p < 0.05$ was considered statistically significant.

3. Results

3.1 Comparison of general information and perioperative indicators

There was no statistically significant difference in the distribution of gender, age, body mass index, comorbid underlying diseases, and ASA physical status classification between the two groups ($p > 0.05$, Table 1). In addition, there was no significant difference in intraoperative bleeding and the cumulative dose of additional intraoperative analgesic drugs between the two groups ($p > 0.05$, Table 2). However, in the esketamine group, the length of hospitalization and the time to get out of bed were significantly shorter than those in the dexmedetomidine group ($p < 0.05$, Table 2).

3.2 Comparison of hemodynamic parameters

The MAP and HR at T2 and T3 of patients in the esketamine group were significantly higher than those in the dexmedetomidine group ($p < 0.05$, Fig. 1 and Table 3). The difference in SpO_2 between the two groups at all time points was not statistically significant ($p > 0.05$, Fig. 1 and Table 3).

3.3 Comparison of VAS scores at different time points in the perioperative period

The difference between the VAS scores at T1 and T2 in the two groups was not statistically significant ($p > 0.05$, Fig. 2 and Table 4). The VAS scores at T3 and T4 of patients in the esketamine group (3.77 ± 0.73, 2.97 ± 0.49) were lower than those of the dexmedetomidine group (4.40 ± 0.7, 3.50 ± 0.51) ($p < 0.05$, Fig. 2 and Table 4).

3.4 Comparison of Ramsay scores

The Ramsay scores at T2 and T3 of patients in the esketamine group (3.73 ± 0.74, 4.20 ± 0.60) were significantly higher than those in the dexmedetomidine group (3.30 ± 0.65, 3.80 ± 0.76) ($p < 0.05$, Fig. 3 and Table 5).

3.5 Comparison of postoperative adverse effects and satisfaction

There were 2 cases of hypotension, 1 case of bradycardia, and 1 case of nausea and vomiting in the dexmedetomidine group. There was 1 case of tachycardia and 1 case of respiratory depression in the esketamine group. The difference in the incidence of adverse reactions and satisfaction between the two groups was not statistically significant ($p > 0.05$, Table 6).

4. Discussion

With the continued trend of an aging population, the incidence of osteoporotic vertebral compression fractures in the elderly is rising annually. PVP has emerged as a clinically effective and minimally invasive treatment widely utilized in elderly patients [9]. However, elderly patients often face challenges such cardiopulmonary insufficiency and their overall physical condition tends to be poor, which can heighten the risk of adverse reactions to general anesthesia including respiratory abnormalities and gastrointestinal reactions. These factors

TABLE 1. General information and perioperative indicators of patients in dexmedetomidine group and esketamine group.

Group	Dexmedetomidine group (n = 30)	Esketamine group (n = 30)	t/χ^2	*p*
Male	16	18	0.271	0.602
Age (yr)	71.97 ± 6.16	73.23 ± 7.11	0.734	0.466
BMI (kg/m^2)	23.09 ± 1.09	22.83 ± 1.37	0.813	0.419
Comorbidities				
Hypertension	7	9	0.341	0.559
Diabetes mellitus	11	8	0.693	0.405
Respiratory diseases	8	10	0.317	0.573
ASA physical status classification				
I	9	10	0.077	0.781
II	21	20		

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

TABLE 2. Perioperative indicators of patients in dexmedetomidine group and esketamine group.

Group	Dexmedetomidine group (n = 30)	Esketamine group (n = 30)	*t*	*p*
Surgical time (min)	40.27 ± 4.54	39.37 ± 4.84	0.738	0.464
Additional dose of analgesic (μg)	276.93 ± 1.30	286.43 ± 5.90	0.824	0.413
Intraoperative bleeding (mL)	13.80 ± 2.58	12.97 ± 2.17	1.348	0.183
Hospitalization time (d)	7 (6, 7)	6 (5, 6)	2.945	0.003
Time to get out of bed (h)	43.23 ± 6.23	38.70 ± 5.40	3.009	0.004

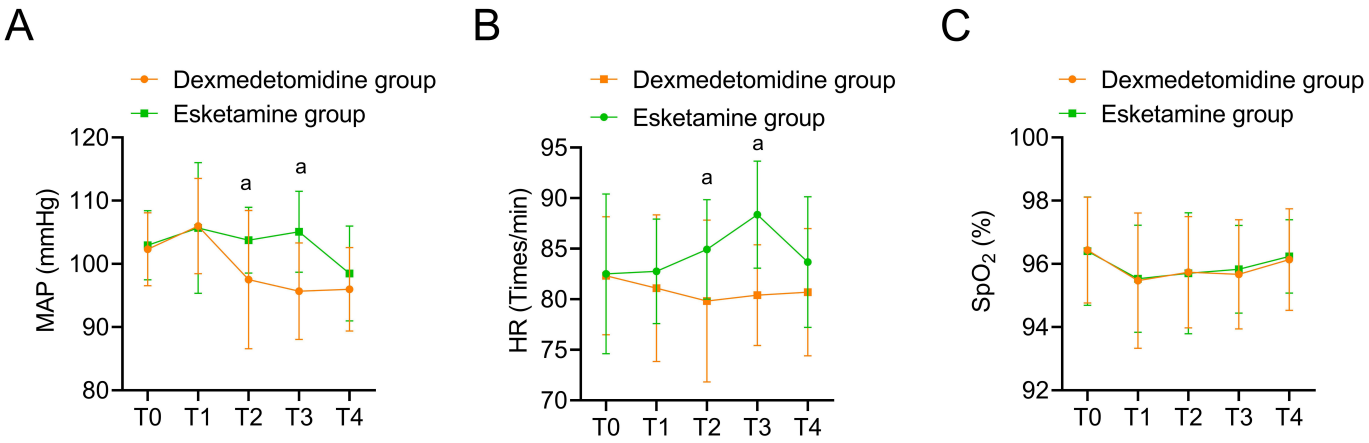

FIGURE 1. Comparison of hemodynamic parameters. (A) MAP. (B) HR. (C) SpO_2. Compared with dexmedetomidine group, $^{a}p < 0.05$. MAP, Mean arterial pressure; HR, heart rate; SpO_2, oxygen saturation.

TABLE 3. Comparison of changes in perioperative hemodynamic parameters between the two groups.

Group	Time	MAP (mmHg)	HR (min)	SpO_2 (%)
Dexmedetomidine group (n = 30)				
	T0	102.33 ± 5.77	82.50 ± 7.90	96.43 ± 1.67
	T1	105.97 ± 7.56	82.77 ± 5.17	95.47 ± 2.15
	T2	97.50 ± 10.96	79.83 ± 8.01	95.73 ± 1.76
	T3	95.67 ± 7.66	80.40 ± 4.99	95.67 ± 1.73
	T4	95.97 ± 6.61	83.67 ± 6.47	96.13 ± 1.61
Esketamine group (n = 30)				
	T0	102.93 ± 5.50	82.33 ± 5.85	96.40 ± 1.71
	T1	105.67 ± 10.35	81.10 ± 7.25	95.53 ± 1.70
	T2	103.73 ± 5.22^{a}	84.93 ± 4.91^{a}	95.70 ± 1.91
	T3	105.10 ± 6.41^{a}	88.37 ± 5.30^{a}	95.83 ± 1.39
	T4	98.47 ± 7.51	80.70 ± 6.29	96.23 ± 1.17

Note: Compared with Dexmedetomidine group, $^{a}p < 0.05$. MAP, Mean arterial pressure; HR, heart rate; SpO_2, oxygen saturation.

can adversely affect the perioperative safety and postoperative recovery [10]. Therefore, it is important to adopt effective sedation and analgesia management during surgery.

As a α2 adrenergic receptor agonist, dexmedetomidine exerts its analgesic and sedative effects primarily through action on α2 receptors in the nucleus accumbens [11]. This leads to a reduction in sympathetic tone by inhibiting central nervous system activity, which not only alleviates patient anxiety but also facilitates the safe conduct of surgery. Additionally, dexmedetomidine inhibits the transmission of pain signals to the brain, effectively minimizing patient discomfort [12, 13].

Esketamine, the dextro isomer of ketamine, exhibits a greater affinity for NMDA receptors compared to ketamine. It possesses twice the anesthetic and analgesic potency of

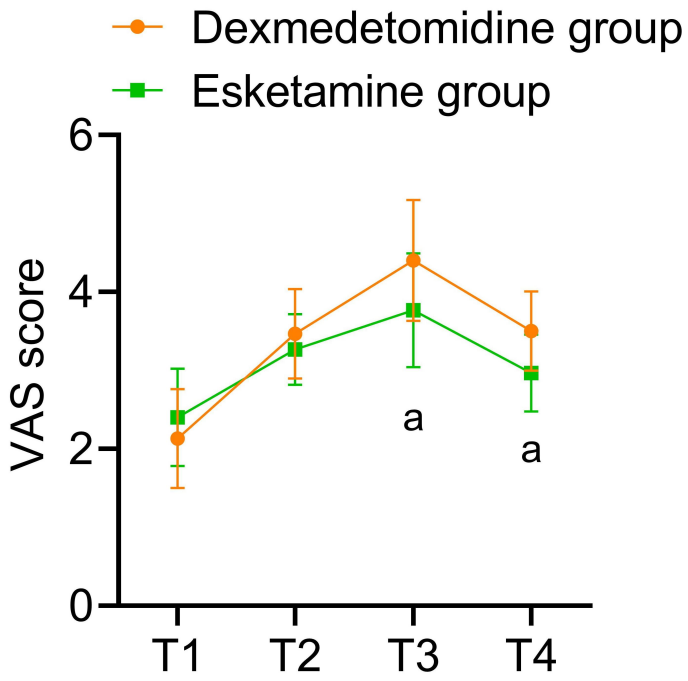

FIGURE 2. Comparison of VAS scores at different time points in the perioperative period. Compared with dexmedetomidine group, $^{a}p < 0.05$. VAS, visual analog scale.

TABLE 4. Comparison of VAS scores at different time points in the perioperative period between the two groups of patients.

Group	T1	T2	T3	T4
Dexmedetomidine group (n = 30)	2.13 ± 0.63	3.47 ± 0.57	4.40 ± 0.77	3.50 ± 0.51
Esketamine group (n = 30)	2.40 ± 0.62	3.27 ± 0.45	3.77 ± 0.73^{b}	2.97 ± 0.49
t	1.673	1.508	3.252	4.105
p	0.100	0.137	0.002	<0.001

Note: Compared with dexmedetomidine group, $^{b}p < 0.05$.

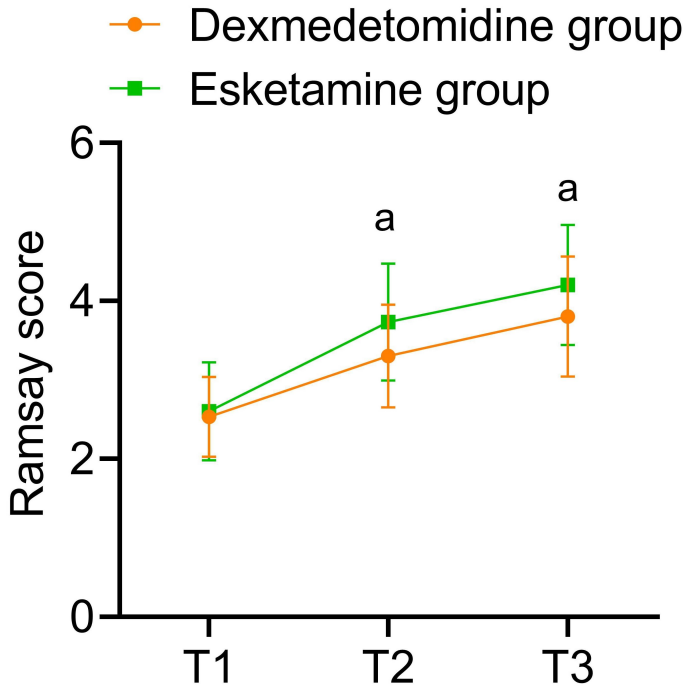

FIGURE 3. Comparison of Ramsay scores. Compared with dexmedetomidine group, $^{a}p < 0.05$.

TABLE 5. Comparison of Ramsay scores between the two groups of patients.

Group	T1	T2	T3
Dexmedetomidine group (n = 30)	2.53 ± 0.51	3.30 ± 0.65	3.80 ± 0.76
Esketamine group (n = 30)	2.60 ± 0.62	3.73 ± 0.74[c]	4.20 ± 0.60[c]
t	0.478	2.391	2.263
p	0.635	0.020	0.027

Note: Compared with dexmedetomidine group, [c]$p < 0.05$.

TABLE 6. Comparison of postoperative adverse effects and satisfaction between the two groups.

Group	Dexmedetomidine group (n = 30)	Esketamine group (n = 30)	χ^2	*p*
Adverse reactions	4 (13.33)	2 (6.67)	0.185	0.667
Satisfaction	27 (90.00)	28 (93.33)	0.218	0.640

ketamine while presenting fewer adverse effects [14], making it uniquely advantageous for anesthetic management in elderly patients. The analgesic mechanism of esketamine primarily involves the blockade NMDA receptors and interaction with u-opioid receptors [15].

Despite their differing mechanisms of action, the two drugs are expected to yield comparable outcomes regarding analgesia and sedation during surgery, especially when considering the body's stress response and the synergistic effects of the drugs. The results of this study demonstrated that the VAS scores at T3 and T4 for patients in the esketamine group were lower than those in the dexmedetomidine group. Furthermore, the Ramsay sedation scores at T2 and T3 were higher in the esketamine group than those in the dexmedetomidine group, suggesting that the combination of esketamine with local anesthesia using lidocaine may provide superior analgesia.

The analgesic effect of esketamine extend beyond the spinal cord level, delivering enhanced pain relief through a range of mechanism. These include the activation of opioid receptors, inhibition of motor nerves, and flipping central sensitization for comprehensive pain management [16]. In PVP, esketamine can effectively reduce the pain stimulation caused by surgical operations, lowering the patient's pain level from intense to mild or even achieving a pain-free state [17]. This significant analgesic effect not only enhances patient comfort but also alleviates the tension and anxiety caused by pain, facilitating better cooperation during surgical procedures. However, the sedative effects of esketamine may pose a risk of bias. Wang *et al.* [18] reported that the intravenous injection of esketamine to patients undergoing cesarean sections before delivery resulted in effective analgesia and helped relieve pain during uterine traction. Nonetheless, the strong sedative effect can lead to drowsiness in patients, which is an important consideration in its use. This may be related to the pharmacological effects of esketamine, which acts on multiple receptor systems, including opioid and monoaminergic receptors, thereby enhancing its analgesic and sedative effects [19]. Given that severe sedation can impair a patient's respiratory and circulatory function, as well as increase surgical risks, it is important to monitor the patient's level of sedation during clinical application. If necessary, the dosage of the drug can be appropriately lowered or wake-up techniques can be administered.

The results of this study revealed that patients in the esketamine group experienced shorter hospital stays and quicker recovery times to get out of bed compared to those in the dexmedetomidine group. Furthermore, the MAP and HR at T2 and T3 were higher in the esketamine group than those in the dexmedetomidine group, indicating that the combination of esketamine with lidocaine local anesthesia is more conducive to the stabilization of intraoperative hemodynamic parameters and postoperative recovery of patients. Compared with traditional anesthetics, esketamine has a higher NMDA receptor affinity, enabling effective anesthesia with a lower dosage and a reduced time to wake up. This may lead to more advantageous postoperative recovery for patients [20]. In addition, esketamine enhances the effects of the central inhibitory neurotransmitter gamma-aminobutyric acid (GABA), aiding in the maintenance of hemodynamic stability in intraoperative patients [21]. Wang *et al.* [22] found that the administration of esketamine in hysteroscopic anesthesia had a minimal effect on intraoperative parameters such as MAP and HR, while significantly decreasing postoperative recovery times in comparison to patients who did not receive esketamine. The results of the present study are consistent with these findings, suggesting that esketamine may be better able to ensure less stable intraoperative fluctuations in hemodynamic parameters and facilitate postoperative recovery.

Furthermore, the study's findings indicate that there was no statistically significant difference in the incidence of adverse reactions or levels of patient satisfaction between the two groups. This suggests that the combination of dexmedetomidine and esketamine with lidocaine local anesthesia during PVP surgery for elderly patients is safe and effective, and it is unlikely to result in significant adverse reactions while achieving high levels of patient satisfaction. Esketamine and dexmedetomidine present notable advantages concerning their routes of administration, particularly through transmucosal delivery methods such as intranasal or sublingual application. This offers significant therapeutic benefits and reduced incidence of adverse effects, especially in the pretreatment of elderly patients.

In this study, the dosage of dexmedetomidine and esketamine was selected with reference to a large number of published clinical studies as well as drug inserts. It was ensured

that they provided good sedation while maintaining relative hemodynamic stability and a low incidence of adverse effects. Although they have different mechanisms of action, both have been shown to play an important role in anesthesia for PVP in several clinical studies. In the design stage of the study, through a comprehensive analysis of previous similar studies, we believe that at the doses set in this study, the two drugs are comparable in terms of analgesia and sedation, and can meet the needs of the study to compare the effects of different anesthesia regimens.

However, this study has several limitations. Firstly, as a retrospective analysis, the sample selection may be subject to bias. In addition, the limited sample size highlights the need for future large-scale, multicenter studies. Such studies would allow for the inclusion of a broader range of patients with diverse characteristics, thereby enhancing the representativeness and generalizability of the findings. This would enable a more accurate assessment of drug effects across different contexts, mitigate selection bias stemming from regional factors, and provide stronger evidence for clinical practice. Furthermore, future research should explore new avenues, such as combining esketamine with lower doses of other anesthetics to optimize sedation levels while minimizing risk.

5. Conclusions

In conclusion, both dexmedetomidine and esketamine when combined with lidocaine local anesthesia, offer sedation and analgesia during PVP in elderly patients. However, there are notable differences in VAS scores, Ramsay scores and hemodynamic parameters between the two anesthetic regimens at different time points. In clinical practice, it is essential to select an appropriate anesthetic regimen tailored to the patient's specific conditions, considering a range of factors, to enhance both the safety of the operation and the comfort of the patient.

AVAILABILITY OF DATA AND MATERIALS

The authors declare that all data supporting the findings of this study are available within the paper and any raw data can be obtained from the corresponding author upon request.

AUTHOR CONTRIBUTIONS

AL—designed the study and carried them out. AL, XW—interpreted the data. AL, XW, LL—supervised the data collection; analyzed the data; prepared the manuscript for publication and reviewed the draft of the manuscript. All authors have read and approved the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the Ethics Committee of Nanjing BenQ Medical Center, The Affiliated BenQ Hospital of Nanjing Medical University (Approval no. 2022-KL011). Written informed consent was obtained from a legally authorized representative for anonymized patient information to be published in this article.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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