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Article

To study the ED50 value of ropivacaine for unilateral spinal anesthesia in elderly patients with different heights undergoing total knee arthroplasty

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Abstract: Objective: To investigate the median effective dose (ED50) of ropivacaine for unilateral spinal anesthesia in total knee arthroplasty (TKA) in elderly patients with different heights. **Methods:** Sixty ASA ii-iii patients, aged ≥ 60 yr, BMI 20.0–29.9 kg/m^2, undergoing total knee arthroplasty under unilateral spinal anesthesia, were enrolled in this study. The patients were divided into three groups according to their height. The height of the patients was 151–155 cm, which was recorded as S group. Group M (height 156–160 cm); Group H (height 161–165 cm), puncture was performed in the L3-4 space, and 0.25% ropivacaine was used (such as 1% ropivacaine hydrochloride 1 mL, plus sterile water for injection 3 mL). According to the results of the preliminary experiment and the principle of the sequential method, the first patient in group S was given a dose of 0.25% ropivacaine of 6.0 mg, the first patient in group M was given a dose of 7.0 mg, and the first patient in group H was given a dose of 8.5 mg. If the dose of local anesthetic used in the previous patient met the criteria for efficacy, the dose of local anesthetic was reduced by 0.5 mg for the next patient. Otherwise, it was upregulated by 0.5 mg. The study was completed when 7 inflection points were obtained. The median effective dose (ED50) of ropivacaine was estimated by means of the turning point method, and then Probit regression analysis was used to calculate the more precise ED50, ED95 and 95% confidence interval (CI) of ropivacaine. CI) was calculated. Vital signs, level of sensory block and motor block were recorded at each time point after administration. **Results:** ED50 of group S, group M and group H was 6.04 mg, 7.11 mg and 7.96 mg, respectively. Probit regression analysis showed that ED50 and ED95 in group S were 6.02 mg (95% CI: 5.29–6.74 mg) and 6.24 mg (95% CI: 5.52–6.97 mg), and ED50 and ED95 in group M were 7.05 mg (95%CI: 5.29–6.74 mg) and 7.05 mg (95% CI: 5.52–6.97 mg), respectively. The ED50 and ED95 of group H were 7.97 mg (95%CI: 7.26–8.68 mg) and 8.18 mg (95% CI: 7.47–8.90 mg), respectively ($P < 0.05$). No adverse reactions such as hypotension and bradycardia occurred in all patients during the operation. There was no significant difference in the level of sensory block on the affected side among the three groups ($P > 0.05$). **Conclusions:** The ED50 of hypogravity ropivacaine for unilateral spinal anesthesia in total knee arthroplasty increases with the increase of body height. The median effective dose of ropivacaine for unilateral spinal anesthesia in elderly patients with different body height groups is 6.02 mg, 7.05 mg and the 95% effective drug doses were 6.24 mg, 7.24 mg and 8.18 mg, respectively.

Keywords: unilateral spinal anesthesia; total knee replacement; ropivacaine; height; medial effective dose

ED50 is a fundamental concept in pharmacokinetics and pharmacodynamics, which refers to the dose of a drug that produces 50% of the maximum effect in a quantitative response or elicits a positive response in 50% of subjects in a qualitative response study [1]. Currently, pharmacodynamic research on ED50 has been

extensively applied in various anesthetic modalities, including intravenous anesthesia, neuraxial anesthesia, and inhalation anesthesia.

Clinical observations have shown that height is an important factor affecting the plane of spinal anesthesia. In actual practice, anesthesiologists will appropriately adjust the subarachnoid dose according to the patient's height. However, studies have shown that it is meaningless to adjust the subarachnoid dose according to differences in patient height [2]. Up to now, whether the patient's height affects the height of the subarachnoid block plane remains controversial. The knee joint is the joint with the highest incidence rate in the whole body. Knee osteoarthritis is more common in the elderly. The prevalence rate in people over 60 years old is about 50%, and it is as high as 80% in people over 75 years old [3]. Total knee arthroplasty (TKA) is currently one of the most effective methods for treating osteoarthritis in middle-aged and elderly patients, and it is becoming more and more common among elderly patients.

Unilateral spinal anesthesia is a regional anesthesia technique that achieves the anesthetic effect of blocking the sensory and motor nerves of the limbs on the surgical side while not blocking the limbs on the non-surgical side by injecting an appropriate amount of lightweight local anesthetic into the patient's lumbar intervertebral space. It is especially suitable for elderly patients with large hemodynamic fluctuations. Unilateral spinal anesthesia is one of the specific applications of the current precision anesthesia concept in clinical practice, and the implementation of unilateral spinal anesthesia that meets surgical needs based on height is more in line with the concept of precision anesthesia to minimize drug doses, maximize surgical effects, and minimize patient physiological interference. However, there is currently no recommended dose of ropivacaine for unilateral spinal anesthesia in total knee replacement surgery for elderly patients of different heights, and the goal of precision medication cannot be achieved.

This study aimed to explore the effect of height on the plane of subarachnoid block, as well as the median effective dose (ED50) of ropivacaine for unilateral spinal anesthesia in total knee replacement surgery in elderly patients of different heights. The results showed that the ED50 of ropivacaine was 6.02 mg in patients with a height of 151–155 cm, 7.05 mg in those with a height of 156–160 cm, and 7.97 mg in those with a height of 161–165 cm. The findings aim to provide a reference for the safe and effective dose of ropivacaine used in clinical practice. During surgery, none of the patients experienced severe hemodynamic fluctuations, such as hypotension or bradycardia. There were no statistically significant differences among the three groups in terms of sensory block level or motor block characteristics ($P > 0.05$).

1. Materials and methods

1.1. General information

This study was approved by the hospital's scientific research and clinical trial ethics committee, and all subjects or their families voluntarily signed informed consent. A total of 60 elderly patients aged 60 to 80 years who underwent unilateral total knee replacement surgery in our hospital from June 2024 to September 2024 were selected. They had no severe cardiopulmonary disease, ASA II to III grade, BMI 20.0 to 29.9 kg/m^2, and no contraindications to spinal anesthesia before surgery. Exclusion criteria:

Abnormal muscle strength on the affected side, BMI greater than 29.9 kg/m^2, repeated attempts still failed to puncture, accompanied by severe damage to other important organ functions, hearing impairment, language barriers, inability to communicate, and refusal of spinal anesthesia. The patients were divided into three groups according to their height: height 151 to 155 cm, recorded as group S; height 156 to 160 cm, recorded as group M; height 161 to 165 cm, recorded as group H.

1.2. Anesthesia method

Patients were routinely fasted for 8 h and 4 h before surgery, and no preoperative medication was given. After the patient entered the room, intravenous access was established, and 300–500 mL of sodium lactate Ringer's injection was intravenously infused before anesthesia. The monitor was connected to continuously monitor the invasive radial artery blood pressure, heart rate, electrocardiogram and pulse oxygen saturation. All patients were placed in a lateral position with the affected limb on top. The L3-4 interspace was punctured by combined spinal-epidural nerve block (CSEA). The spinal anesthesia needle was opened toward the affected side. After clear cerebrospinal fluid flowed out, a test dose of 0.25% ropivacaine was given within 30 s (for example, 1 mL of 1% ropivacaine hydrochloride, add 3 mL of sterile water for injection). According to the results of the preliminary experiment and the principle of the sequential method, the first patient in group S was given 6.0 mg of 0.25% ropivacaine, the first patient in group M was given 7.0 mg of 0.25% ropivacaine, and the first patient in group H was given 8.5 mg of 0.25% ropivacaine. If the dose of local anesthetic used by the previous patient met the effective standard, the dose of local anesthetic for the next patient was adjusted down by 0.5 mg; otherwise, it was adjusted up by 0.5 mg. The study was terminated after 7 inflection points were obtained. After completion, the spinal anesthesia needle was withdrawn, and the epidural catheter was routinely inserted and fixed in case the anesthetic effect was insufficient and additional medication was required. After the operation was completed, the patient was kept lying on his side for 15 min, and the patient was assisted to take the supine position after the anesthesia plane was fixed on one side. All puncture operations were performed by the same anesthesiologist, and all surgical steps were completed by the same clinical working group and the same surgeon.

1.3. Observation indicators

The patient's vital signs and sensory block level were recorded at 3, 6, 9, 15, and 20 min after subarachnoid administration. Sensory block onset time, time to achieve maximum sensory block level stabilization, and time to sensory block regression were recorded at 2-minute intervals. According to the Hollmen scoring scale, the level of disappearance of acupuncture pain was the sensory block level. The modified Bromage scoring method was used to determine the motor nerve block at 15 and 20 min and 1 and 2 h after administration. Additionally, motor block onset time and motor block recovery time were documented. The visual analogue scale (VAS) was used to evaluate the patient's intraoperative pain status and record it accordingly. At the end of the operation, the patient's vital signs and the time from administration to the end of the operation were recorded. The side effects of perioperative lightweight unilateral

spinal anesthesia, such as hypotension (SBP decrease > 30% of the baseline value or SBP < 90 mmHg), bradycardia (HR < 50 beats/min), respiratory depression, nausea, vomiting, postdural puncture headache, urinary retention, and bleeding at the puncture site, as well as the number of cases of vasoactive drugs used were recorded. 24 h after the operation, patients were followed up to evaluate sensory and motor recovery and to identify any abnormal conditions.

1.4. Intraoperative management

Crystalloid and colloid fluids were routinely supplemented during the operation. If the patient's SBP dropped by more than 30% of the baseline value or SBP was less than 90 mmHg after anesthesia, dopamine or methoxamine was given intravenously; if HR was less than 50 times/min, atropine 0.3 to 0.5 mg was given intravenously. If the patient experienced pain or tourniquet reaction during the operation, and the block plane was not enough to complete the operation, 0.5% ropivacaine was added as needed through the epidural catheter to maintain the anesthesia plane. After the operation, the patient was admitted to the PACU and the analgesic pump (PCA) with a unified formula was connected intravenously for postoperative analgesia. The patient's sensory and motor recovery was followed up 24 h after the operation.

1.5. Effectiveness criteria

(1) The sensory block plane reaches at least T12 level 20 min after subarachnoid block anesthesia. (2) The Bromage score of the motor block of the affected lower limb reaches 2 points or above 20 min after subarachnoid block anesthesia. (3) No additional local anesthetic is added to the epidural space ≥ 120 min after subarachnoid block anesthesia. If the above three criteria are met, it is judged as effective; otherwise, it is judged as ineffective.

1.6. Statistical methods

All data were analyzed using SPSS 26.0 and GraphPad Prism 10. Sequential data were first estimated by the turning point mean method for ropivacaine ED50 in elderly patients of different height groups undergoing unilateral spinal anesthesia for total knee replacement. Probit regression analysis was then used to calculate a more accurate ED50, ED95 and its 95% confidence interval (CI). The quantitative data of this trial were first subjected to the Shapiro-Wilk test. If they were in accordance with the normal distribution, they were expressed as mean ± standard deviation ($x \pm s$). Inter-group comparisons were performed using analysis of variance, and intra-group comparisons were performed using paired *t*-tests. If they were not in accordance with the normal distribution, they were expressed as medians (quartiles), and inter-group comparisons were performed using Kruskal-Wallis rank sum tests. Enumeration data were expressed as percentages (%), and inter-group comparisons were performed using chi-square tests or Fisher's exact probability methods. $P < 0.05$ was considered statistically significant.

2. Results

2.1. General information

A total of 60 elderly patients who met the criteria were enrolled in this trial, of which 1 patient in each of the M and H groups was excluded from the study due to multiple puncture failures and was converted to general anesthesia (see **Table 1**). Finally, 19 patients in the S group, 19 patients in the M group, and 20 patients in the H group were included. All patients successfully completed the operation. There was no statistically significant difference in age, BMI, and ASA grade among the three groups ($P > 0.05$), and there were significant statistical differences in height, weight, and gender among the different groups ($P < 0.01$).

Table 1. Comparison of general information of patients in three groups.

index	Group S	Group M	Group H	*P*-value
Age (years)	67.6 ± 4.2	69.6 ± 5.4	71.8 ± 6.7	0.068
Height (cm)	1.53 ± 0.01	1.58 ± 0.01	1.63 ± 0.01	0.000
Weight (kg)	64.4 ± 3.7	68.6 ± 3.7	69.1 ± 6.9	0.02
BMI (kg/m^2)	27.5 ± 1.6	27.5 ± 1.6	26.0 ± 2.6	0.112
men and women	0/19	5/14	9/11	0.002
ASA (II/III)	15/4	14/5	16/4	0.926

Note: ASA is the American Society of Anesthesiologists.

2.2. ED50

The results of the sequential test are shown in **Figure 1**. Each group obtained 7 turning points, which met the requirements of the sequential method for sample size calculation. This study first used the turning point mean method to preliminarily estimate the ED50 of group S to be 6.04 mg, group M to be 7.11 mg, and group H to be 7.96 mg. Then, probit regression analysis was performed on the sequential data of the three groups using SPSS software, and the results showed that the ED50 and ED95 of group S were 6.02 mg (95% CI: 5.29–6.74 mg) and 6.24 mg (95% CI: 5.52–6.97 mg), the ED50 and ED95 of group M were 7.05 mg (95% CI: 6.35–7.75 mg) and 7.24 mg (95% CI: 6.54–7.94 mg) , and the ED50 and ED95 of group H were 7.97 mg (95% CI: 7.26–8.68 mg) and 8.18 mg (95% CI: 7.47–8.90 mg) ($P < 0.05$). There was a certain difference between the two calculation results, and the final value obtained by probit regression was used as the standard.

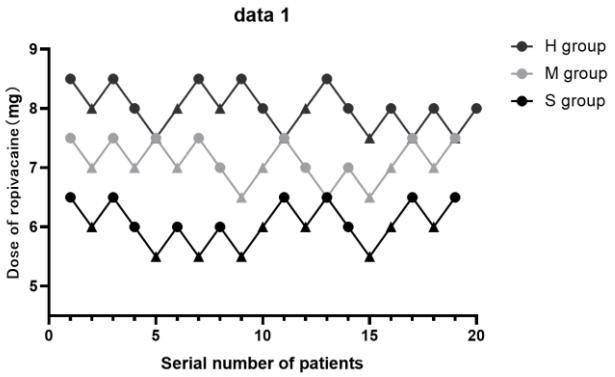

Figure 1. Sequential diagram of the response of patients in three groups to different doses of ropivacaine.

2.3. Hemodynamic changes

When comparing between the three groups, there was no significant difference in the mean arterial pressure (MAP) and heart rate (HR) after entering the room, and the mean arterial pressure and heart rate at 3 min, 6 min, 9 min, 15 min, 20 min after subarachnoid administration, and at the end of surgery ($P > 0.05$). Further intra-group comparison was carried out, and the various hemodynamic indicators after administration were compared with the baseline values. The detailed results are shown in the table below. All patients did not experience adverse reactions such as hypotension and bradycardia during the operation, so there was no need to use vasoactive drugs (see **Table 2**).

Table 2. Comparison of MAP and HR among three groups at different time points.

Group		Base Value	3 min	6 min	9 min	15 min	20 min	End of surgery
Group S	MAP	103.5 ± 10.0	99.9 ± 9.2※	100.4 ± 7.4※	99.8 ± 8.6※	98.9 ± 8.6※	97.0 ± 9.1※	96.4 ± 7.9※
	HR	78.2 ± 9.4	76.5 ± 9.8	77.1 ± 9.0	77.6 ± 9.4	77.3 ± 9.6	75.9 ± 9.5	69.1 ± 8.9※
Group M	MAP	98.9 ± 8.7	97.8 ± 9.8	97.2 ± 9.9	97.6 ± 9.5	96.2 ± 9.6	95.8 ± 7.9※	94.3 ± 7.9※
	HR	83.7 ± 7.8	82.3 ± 8.7※	81.6 ± 8.1※	81.4 ± 7.9※	79.8 ± 7.4※	79.6 ± 7.8※	72.8 ± 6.3※
Group H	MAP	99.0 ± 11.9	98.2 ± 10.2	98.8 ± 10.2	97.3 ± 10.6	96.0 ± 11.6	97.1 ± 10.9	92.2 ± 10.0※
	HR	79.1 ± 11.8	77.1 ± 10.4※	76.7 ± 11.3※	74.9 ± 10.3※	74.4 ± 9.3※	74.4 ± 9.4※	71.3 ± 9.3※
MAP P value		0.294	0.771	0.574	0.670	0.615	0.890	0.325
HR P value		0.193	0.139	0.218	0.095	0.166	0.183	0.392

Note: Compared with the baseline value after entering the room, ※ $P < 0.05$.

2.4. Sensory block on the affected side

There was no statistically significant difference in the sensory block plane on the affected side among the three groups of patients at different time points after subarachnoid administration ($P > 0.05$) (see **Table 3**). No statistically significant differences were observed among the three groups regarding the onset time of subarachnoid sensory block, the stabilization time of the maximum sensory block level, or the time to sensory block regression ($P > 0.05$) (see **Table 4**).

Table 3. Comparison of sensory block planes among the three groups at different time points after drug administration.

Group	3 min	6 min	9 min	15 min	20 min
Group S	12 (12, 12)	12 (10, 12)	10 (10, 12)	10 (10, 12)	10 (10, 12)
Group M	12 (10, 12)	12 (10, 12)	10 (10, 12)	10 (10, 12)	10 (10, 12)
Group H	12 (10, 12)	11 (10, 12)	10 (10, 12)	10 (10, 11.5)	10 (10, 11.5)
P-value	0.495	0.726	0.927	0.856	0.856

Table 4. Comparison of sensory block duration among the three groups.

Sensory Block	Group S	Group M	Group H	*P*-value
Onset times (s)	19.1 ± 1.4	18.8 ± 1.3	18.5 ± 1.1	0.348
Time to maximum level stabilization (min)	12.8 ± 1.3	13.4 ± 1.1	13.3 ± 1.6	0.391
Regression time (min)	74.0 ± 3.1	72.8 ± 3.9	74.2 ± 3.0	0.425

2.5. Comparison of motor block among the three groups.

There were no statistically significant differences in the onset time and recovery time of subarachnoid motor block among the three groups ($P > 0.05$) (see **Table 5**).

Table 5. Comparison of motor block among the three groups.

Motor Block	Group S	Group M	Group H	*P*-value
Onset time (min)	9.3 ± 1.5	9.4 ± 1.2	8.7 ± 1.2	0.147
Recovery time (min)	80.6 ± 3.4	81.2 ± 2.3	82.6 ± 2.6	0.075

2.6. Intraoperative situation

There were no significant differences in intraoperative VAS scores, time from drug administration to the end of surgery, blood loss, and fluid infusion volume among the three groups ($P > 0.05$) (see **Table 6**).

Table 6. Comparison of intraoperative conditions among the three groups of patients.

Group	VAS score	Time from injection to end of surgery	Amount of bleeding	Intraoperative fluid volume
Group S	0 (0, 2)	105.8 ± 9.5	100.5 ± 13.5	1000 ± 60
Group M	1 (0, 1)	107.6 ± 6.9	98.2 ± 7.3	989 ± 57
Group H	0 (0, 1)	109.0 ± 7.2	98.8 ± 11.0	988 ± 53
P-value	0.714	0.454	0.785	0.765

2.7. Comparison of perioperative adverse events among the three groups

There were no statistically significant differences in perioperative adverse events among the three groups ($P > 0.05$) (see **Table 7**). In Group M, two patients experienced puncture site bleeding, while three cases were reported in Group H; all were managed promptly. No cases of hypotension, bradycardia, respiratory depression, nausea, vomiting, postoperative headache, or urinary retention were observed in any group. No patients required vasopressor use, and no abnormalities were reported during the 24-hour postoperative follow-up.

Table 7. Comparison of perioperative adverse events among the three groups.

Perioperative Adverse Events	Group S	Group M	Group H	*P*-value
Hypotension	0	0	0	/
Bradycardia	0	0	0	/
Respiratory depression	0	0	0	/
Nausea and vomiting	0	0	0	/
Postoperative headache	0	0	0	/
Urinary retention	0	0	0	/
Puncture site bleeding	0	2	3	0.267

3. Discussion

3.1. Initial measurement setting

A previous sequential trial showed that the ED50 of 0.5% ropivacaine for subarachnoid block in middle-aged and elderly patients undergoing knee replacement surgery was 9.25 mg [4], so this trial used 10.0 mg of lightweight ropivacaine for a pilot test. The doses of ropivacaine that achieved sensory block at the T10 level in groups S, M, and H were 6.5 mg, 7.5 mg, and 8.5 mg, respectively. Therefore, the initial dose for the first patient in group S was set at 6.5 mg, group M at 7.5 mg, and group H at 8.5 mg. The trial was terminated after 7 turning points were obtained.

3.2. Advantages of unilateral spinal anesthesia in elderly patients

Subarachnoid block anesthesia is a common anesthesia method for total knee replacement surgery. Unilateral spinal anesthesia, as a special form of subarachnoid block, only affects the sensory, motor and sympathetic nerve functions of one side of the body. It has the advantages of a subarachnoid block but does not have the typical side effects of a bilateral block [5]. Esmaoglu et al. found that unilateral spinal anesthesia significantly reduces the incidence of hypotension by restricting sympathetic block to one side while preserving contralateral sympathetic reflexes [6]. The underlying mechanism is attributed to the anatomical distance of approximately 10–15 cm between the nerve roots of the thoracic and lumbar spinal segments, which facilitates the preferential spread of unilateral subarachnoid block [7]. Since unilateral spinal anesthesia has fewer physiological effects on the body, it provides a relatively safe and effective anesthesia method, which is particularly suitable for elderly patients. Studies have shown that the incidence of hypotension after unilateral spinal anesthesia in elderly patients undergoing hip replacement surgery is lower than that after conventional subarachnoid block [8]. The 2020 version of the Chinese Perioperative Anesthesia Management Guidelines for Knee Surgery in Elderly Patients clearly states that unilateral spinal anesthesia can be used for unilateral knee surgery with an estimated operation time of less than 2 h [3]. At present, 0.25% light specific gravity ropivacaine is often used in clinical practice for unilateral spinal anesthesia of patients [9]. In this study, 58 total knee replacement surgeries were performed, and the duration from subarachnoid injection to the end of surgery was less than 2 h, so 0.25% light specific gravity ropivacaine was used for unilateral spinal anesthesia. Although some patients had MAP or HR lower than the baseline value after administration, all patients did not experience severe hemodynamic fluctuations such as hypotension and bradycardia, and no vasoactive drugs were needed, indicating that unilateral subarachnoid blockade can help maintain hemodynamic stability in elderly patients during surgery and reduce the risk of cardiovascular complications. In this study, the MAP and HR of the three groups of patients at the end of surgery were significantly lower than the baseline level of each group, which may be because the tension and anxiety of the patients were relieved after the surgery.

Furthermore, ropivacaine exhibits a characteristic differential blockade, meaning that at low doses, it preferentially blocks sensory nerve fibers while exerting a lesser effect on motor nerve fibers. This property allows for faster postoperative mobilization, reducing the incidence of urinary retention, dizziness, and motor impairment, thereby promoting accelerated recovery and early discharge [10]. This aligns well with the principles and objectives of Enhanced Recovery After Surgery.

3.3. Effect of height on the subarachnoid block plane

The subarachnoid block plane is affected by multiple factors, and the effect of height on it is still controversial. Studies have shown that there is no significant difference in the dose requirement of ropivacaine for cesarean section under spinal anesthesia in pregnant women of different heights [11]. Some scholars have pointed out that in adults with a "normal height" range, the height of the patient does not affect the spinal block plane [12]. However, Pargger et al. believed that height has a significant effect on the spinal block plane [13]. Previous studies have demonstrated that adjusting the intrathecal drug dosage based on patients' height and weight can achieve relatively satisfactory blockade effects [14,15]. When predicting the sensory block level of spinal anesthesia, experts have suggested that sensory block height is negatively correlated with patient height [16].

In-depth research on the reasons why height affects the block plane found that it may be mainly related to the distribution of cerebrospinal fluid (CSF) and the diffusion of local anesthetics in the subarachnoid space. However, the distribution of cerebrospinal fluid and drug diffusion cannot be specifically measured during the perioperative period; clinicians usually use general characteristics of patients such as height, weight and BMI to predict the block plane because they are relatively easy to know. Further studies have shown that spinal length, amniotic fluid index and abdominal circumference are the key factors affecting the block plane [17], and the ED50 of isobaric ropivacaine increases with increasing spinal length [18]. Norris et al. showed that height factors accounted for 10.6% of the change in spinal length, and there was a certain statistical correlation between spinal length and height [19]. Therefore, in theory, the plane of the subarachnoid block is affected by the patient's height. In addition, studies have shown that administering anesthetic drugs based on the height algorithm during subarachnoid block can provide sufficient anesthetic effects and a low incidence of hypotension [20].

In this study, the ED50 of intrathecal injection of 0.25% lightweight ropivacaine was 6.02 mg in patients with a height of 151 to 155 cm, while the ED50 in the group of 161 to 165 cm increased to 7.97 mg, indicating that the ED50 of ropivacaine will increase with the increase of patient height. Clinical experience has confirmed that when we inject the same dose of local anesthetic in the same way into the L3-4 space of the subarachnoid space of patients with different heights, the anesthetic effect produced is different: the spinal block level of patients with taller height is usually lower, while the opposite is true for patients with shorter height. One reason is that the volume of cerebrospinal fluid in patients with different heights may be different, which will affect the distribution of local anesthetics in the subarachnoid space. Patients with taller height may have a larger volume of cerebrospinal fluid, resulting in a wider distribution of drugs, and a larger drug dose may be required to achieve the same block effect. Another reason is that patients with taller heights usually have longer spinal cords, which may affect the distribution of drugs in the spinal cavity and the height of the block plane. Our study further improves the understanding of the relationship between patient height and local anesthetic dose. A study has shown that for women undergoing cesarean section under spinal anesthesia, the ED50 of subarachnoid injection of ropivacaine increases with the patient's height [21], which is basically

consistent with the results of this study. In this study, patients were categorized into four groups based on height: 150–155 cm, 156–160 cm, 161–165 cm, and 166–170 cm.

3.4. Differences between unilateral spinal anesthesia and conventional spinal anesthesia

Research results have shown that the dose of hypobaric ropivacaine required for unilateral subarachnoid block in elderly patients undergoing hip replacement surgery is lower than that for conventional spinal anesthesia. The mechanism of this difference may be related to the fact that the spinal needle is injected toward the upper side of the patient. This operation method may promote the mixing of drug molecules with cerebrospinal fluid, resulting in a reduction in drug demand [22]. The hypobaric ropivacaine ED50 of patients in different height groups in this study was lower than the ED50 of subarachnoid block in knee replacement surgery in China. Studies have shown that for surgical procedures in the supine position, patients need to remain in the lateral position for 8 to 10 min after unilateral subarachnoid block to fix the anesthesia plane [23]. In this study, all patients remained in the lateral position for 15 min after puncture, and then the operator assisted in changing the body position to obtain a relatively stable block effect.

3.5. Calculation and clinical significance of ED50

Among the various statistical methods for calculating ED50, the turning point mean method is a simplified method for estimating ED50, which is obtained by taking the arithmetic mean of two adjacent positive/negative paired values in sequential tests and is widely used in early studies [24]. Probit regression uses probability transformation to calculate ED50 based on the different probabilities of each subject with a pre-set drug dose having a specific reaction during the test. In this study, the turning point mean method was first used to preliminarily calculate ED50. The ED50 estimation method, derived from fitting a dose-response curve, provides an accurate estimate along with a confidence interval.

In clinical practice, the ED50 of a drug plays a crucial role in evaluating drug efficacy, determining therapeutic doses, assessing safety, and optimizing drug administration. For anesthesiologists, selecting an appropriate drug dose is essential to minimizing adverse effects while maintaining therapeutic effectiveness [25]. Total knee arthroplasty has relatively low anesthesia level requirements but necessitates adequate intraoperative analgesia and sufficient muscle relaxation. Additionally, anesthesia for elderly patients presents unique challenges. Achieving both optimal surgical analgesia and perioperative stability requires precise dosing of anesthetic agents. To improve the accuracy of the calculation, probit regression analysis was further used for calculation, and the ED50 calculated by probit regression was finally used as a reference.

3.6. Intraoperative VAS score

The visual analogue scale (VAS) is a commonly used pain assessment tool. A score of 0 is considered to be pain-free, 1 to 3 points are considered mild pain, 4 to 6

points are considered moderate pain, and 7 to 10 points are considered severe pain. The higher the score, the higher the pain level [26]. The results of this study showed that the intraoperative VAS score of all patients was less than 3 points, which was a mild pain level, indicating that unilateral subarachnoid block can provide a good analgesic effect, and when the block plane is insufficient, local anesthetics can be immediately added through the epidural catheter to relieve the patient's pain and discomfort.

3.7. Research on the ED50 and 95% CI of ropivacaine for unilateral spinal anesthesia to guide clinical application

With the development and innovation of science and technology, personalized precision anesthesia will better meet the needs of elderly patients during perianesthetic management [27]. Adjusting the subarachnoid dose of unilateral spinal anesthesia according to the patient's height can be regarded as a precise regional anesthesia technique. This study relatively accurately determined the ED50 and 95% CI values of ropivacaine in various height groups, providing a basis for the use of ropivacaine solution in clinical elderly patients of different heights for unilateral spinal anesthesia, rather than empirical medication. In future clinical applications, the goal of precise drug administration can be achieved by adjusting the drug dose individually and reducing the impact on the patient's systemic physiology, thereby providing a safer, more comfortable and personalized anesthesia diagnosis and treatment process for elderly patients.

This study still has some shortcomings. First, there were significant differences in the weight of the three groups of patients in this study. Clinical observations have confirmed that weight is an important factor affecting the block plane. Although we clearly divided BMI in the inclusion criteria, we did not avoid the effect of weight on the dose of local anesthetics, which may have a certain impact on the results. Second, the time for epidural additional local anesthetics depends partly on the patient's tolerance to surgical stimulation and the surgeon's operating level, and there are individual differences. Third, the overall sample size of this study was too small, and all patients did not experience adverse reactions of subarachnoid block, such as hypotension and bradycardia, and more universal conclusions need to be drawn from further research.

4. Conclusion

In summary, the ED50 of lightweight ropivacaine for unilateral subarachnoid block during total knee replacement surgery increases with the increase of patient height. The median effective dose of ropivacaine for unilateral spinal anesthesia in elderly patients of different height groups was 6.02 mg, 7.05 mg, and 7.97 mg, respectively; the 95% effective drug dose was 6.24 mg, 7.24 mg, and 8.18 mg, respectively, which indicates a correlation between the intrathecal ropivacaine dose and patient height, providing valuable guidance for clinicians in optimizing precise drug administration.

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Ethical approval: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of Linyi People's Hospital (protocol code 202405-H-036 and date of approval 2024.05.22). Informed consent was obtained from all subjects involved in the study.

Conflict of interest: The authors declare no conflict of interest.

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