

# Effects of Intrathecal Bupivacaine and Bupivacaine Plus Fentanyl in Elderly Patients Undergoing Total Hip Arthroplasty

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## ABSTRACT

**Objective:** To determine and compare the clinical efficacy of spinal anesthesia with bupivacaine combined with fentanyl and bupivacaine alone in geriatric patients scheduled for total hip arthroplasty (THA).

**Study Design:** Experimental study.

**Place and Duration of Study:** Department of Anesthesiology, Renmin Hospital of Wuhan University, Wuhan, Hubei, China, from April 2016 to April 2017.

**Methodology:** Sixty-five geriatric patients were randomised into two groups. Group B was anaesthetised with 0.5% bupivacaine 10 mg and Group F with 0.5% bupivacaine 7.5 mg plus fentanyl 20 µg. Hemodynamic stability, effect and satisfaction of anesthesia, time to the first postoperative analgesic requirement, adverse effects, and incidence of postoperative indwelling catheter were compared.

**Results:** There was no significant difference in time to reach maximum sensory block level, maximum sensory block level, maximum motor block, duration of motor block, quality of anesthesia, adverse effects or the incidence of postoperative indwelling catheter between the two groups. However, Group F required less dosage of ephedrine for stable hemodynamics and longer time to use the primary postoperative analgesic in comparison to Group B ( $p < 0.05$ ).

**Conclusion:** Adding 20 µg fentanyl to a lower dose of 7.5 mg bupivacaine can provide safe and effective spinal anesthesia for THA in geriatric patients.

**Key Words:** *Elderly, Total hip arthroplasty, Spinal anesthesia, Bupivacaine, Fentanyl.*

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## INTRODUCTION

Spinal anesthesia is a common anesthetic technique in total hip arthroplasty (THA). However, most patients who plan to have THA tend to be elderly, with cardiac, pulmonary or other diseases.<sup>1,2</sup> Anesthesia has a large risk for complications, such as ischemia secondary to the hypotension, whereas THA must be performed urgently. The authors sought to identify a reliable spinal block by using a single-shot, low-dose technique for these patients with few side effects.

The objective of this study was to compare the effect and satisfaction of anesthesia, hemodynamic stability and side-effects in elderly patients scheduled for THA, who were grouped to receive spinal anesthesia either with bupivacaine 10 mg or bupivacaine 7.5 mg plus fentanyl 20 µg.

## METHODOLOGY

This study was approved by the Hospital Ethics Committee of Renmin Hospital of Wuhan University,

China. Patients classified as American Society of Anesthesiologists I-III undergoing elective THA signed informed consent, from April 2016 to April 2017. Exclusion criteria were age less than 65 years old, misunderstanding of oral information about the study, other severe systemic diseases, relative or absolute contraindications of spinal block, failure of block, or massive bleeding during the operation, surgery duration more than 90 minutes.

Patients were categorised into two study groups using a random number table method, which was prepared by an objective statistician, as follows: Group B were administered spinal anesthesia with 0.5% bupivacaine 10 mg and Group F with 0.5% bupivacaine 7.5 mg plus fentanyl 20 µg. If spinal anesthesia did not satisfy the surgery, we utilised general anesthesia for remedial measure, and these patients were excluded from the study.

The patients did not receive any sedation, analgesia or fluid infusion before arriving in the operating room. Five-lead electrocardiography, oxygen saturation, and non-invasive blood pressure monitoring were used. Before inducing spinal block, a 20-gauge intravenous cannula was inserted and compound sodium lactate solution 15 ml/kg/h was infused for approximately 30 minutes. An anesthesiologist, who was unaware of the clinical nature

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of the study, monitored and conducted the case. At the midline of L3-4 interspace in lateral position, lumbar puncture was performed. After observing the free flow of clear CSF, the scheduled drug was diluted to 3 mL with CSF and administered over 20-25 seconds with cephalad orientation. The patients were then immediately restored to supine position.

Pinprick testing was used to establish maximum sensory block level, and the time from subarachnoid injection drugs to reach highest level of sensory block was recorded. To judge maximum motor block scale, the modified Bromage score was used. The same team of orthopedic surgeons performed all operations after the anesthetist confirming adequate analgesia.

Heart rate (HR) and mean arterial pressure (MAP) were recorded at six time points (T0, baseline; T1, 5 minutes after spinal injection; T2, 15 minutes after spinal injection; T3, 30 minutes after spinal injection; T4, 45 minutes after spinal injection; T5, out of the post-anesthesia care unit). Hypotension was defined as a systolic arterial pressure below 90 mm Hg or 20% below MAP baseline. If patients met either criterion, they were given ephedrine 3-10 mg intravenously, and the total dosage of ephedrine was recorded.

The quality of anesthesia during the operation was analysed as follows: 1 No discomfort or pain; 2 Mild pain or discomfort, whereas no requirement for additional analgesics; 3 Pain that needed analgesics; 4 Severe pain that needed analgesics. After the surgery, patients were taken to the post-anesthesia recovery room, hemodynamic parameters and the degree of analgesia were recorded until they were transferred to the surgical

ward. During the operation and recovery, adverse effects, such as nausea, vomiting, shivering and pruritus were recorded.

Patients were transferred back to the surgical ward without indwelling catheters and early ambulation; and independent urination was encouraged. Indwelling catheters were inserted when the postoperative bladder filled with urine (>400 mL diagnosed by ultrasound) and could not be properly discharged. In case of visual analogue scale for postoperative pain was at least 4 (0=no pain, 10=worst possible pain), intravenous flurbiprofen (50 mg) was administered. The first time to give flurbiprofen is the time required for the first postoperative analgesia. The incidence of indwelling catheters and the time required for the first postoperative analgesia were recorded by an uninformed post-operative staff 24 hours after surgery.

Statistical analysis was performed using GraphPad Prism. Categorical variables were represented as count (%); mean ± standard deviation (SD) represented quantitative variables. Normality analysis was performed using Shapiro-Wilk normality test or Kolmogorov-Smirnov test with Dallal-Wilkinson-Lillie for p-value in GraphPad Prism software (p>0.10 indicate that the data was Gaussian distribution). The unpaired t-test, Mann-Whitney test, Fisher's exact test and Chi-square test were used for statistical analysis. Considered statistically significant were those p-values that were less than 0.05.

## RESULTS

In each group (Figure 1), there were 30 patients. Patients' characteristics were similar between the two groups

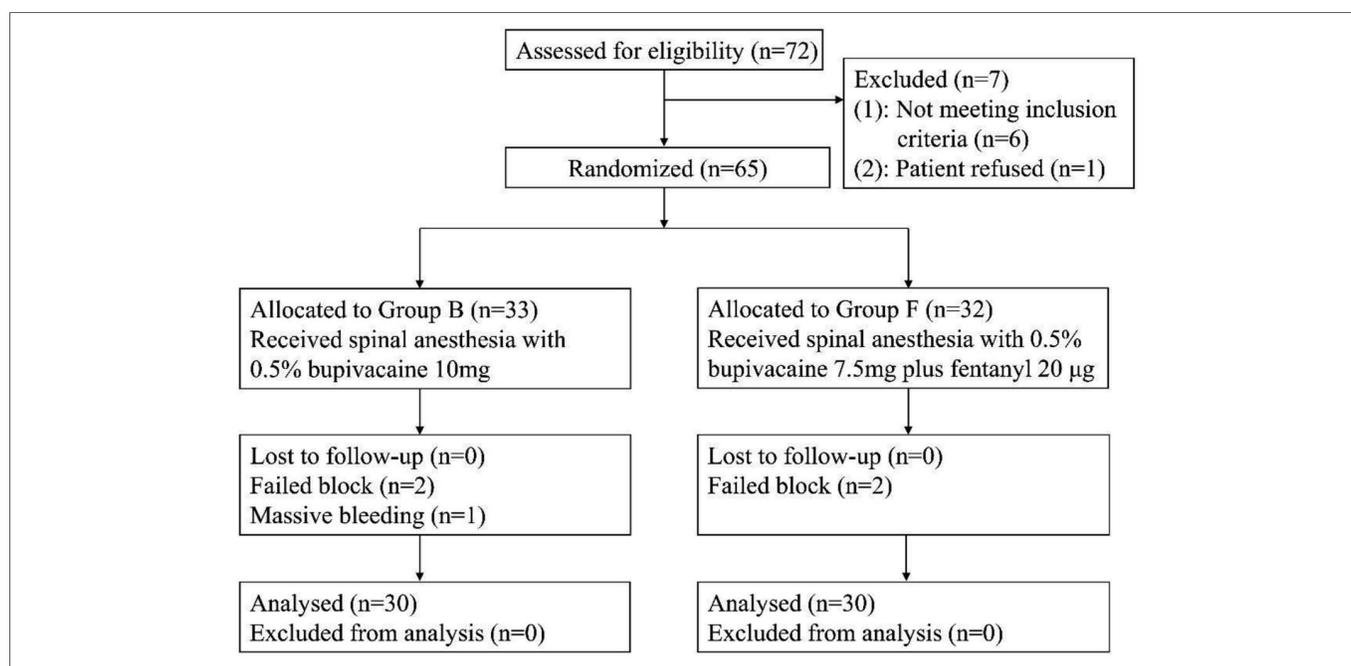
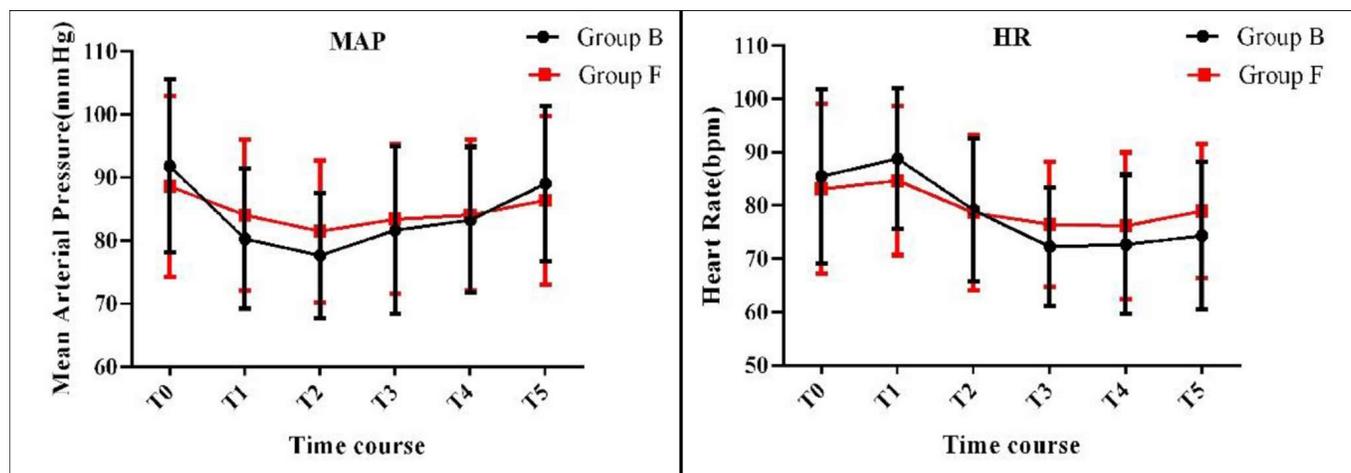


Figure 1: Flow diagram of patient recruitment.



**Figure 2:** Hemodynamic variables at each recording time point. Values are shown as mean ±SD. T0, baseline; T1, 5 min after spinal injection; T2, 15 min after spinal injection; T3, 30 min after spinal injection; T4, 45 min after spinal injection; T5, out of the post-anesthesia care unit.

**Table I:** Similar baseline characteristics in both groups.

	Group B (n=30)	Group F (n=30)	p-value
Age (years)	74.0 ±6.0	75.2 ±5.8	0.464
Gender			
Male	27 (90%)	28 (93.3%)	1.000
Female	3 (10%)	2 (6.7%)	
Weight (kg)	58.4 ±9.3	61.1 ±9.6	0.343
Height (cm)	167.0 ±7.9	168.1 ±8.5	0.646
ASA			
ASA I	3 (10%)	4 (13.3%)	0.811
ASA II	18 (60%)	19 (63.3%)	
ASA III	9 (30%)	7 (23.3%)	
Duration of operation (min)	50.9 ±8.7	49.0 ±8.0	0.429

Data are shown as mean ± SD or number of patients, SD=Standard deviation; ASA=American Society of Anesthesiologists.

(Table I). There was no difference in MAP and HR at the corresponding time points between the two groups (Figure 2); however, Group F needed significantly less ephedrine than Group B (Table II).

There was no significant difference in the time to reach the highest level of sensory block, maximum sensory block level, maximum motor block, or quality of anesthesia between the two groups (Table II). Time to the first postoperative analgesic requirement in Group F was longer than that in Group B. No difference was identified in adverse effects or the incidence of indwelling catheter postoperatively between the two groups (Table III).

### DISCUSSION

In this study, administration of bupivacaine plus fentanyl spinal anesthetic (7.5 mg bupivacaine plus 20 µg fentanyl) for THA in elderly patients provided more effective anesthesia, required a lower dose of ephedrine for stable hemodynamics, and increased postoperative analgesic efficacy without increasing the incidence of adverse effects and postoperative indwelling catheters.

**Table II:** Characteristics of spinal anesthesia.

	Group B (n=30)	Group F (n=30)	p-value
Time to reach maximum sensory block level (min)	12.3 ±3.4	13.6 ±4.0	0.184
Maximum sensory block level			
T4	2 (6.7%)	1 (3.3%)	0.752
T6	8 (26.7%)	6 (20%)	
T8	16 (53.3%)	20 (66.7%)	
T10	4 (13.3%)	3 (10%)	
Maximum motor block			
Modified Bromage scale 1	26 (86.7%)	24 (80%)	0.588
Modified Bromage scale 2	3 (10%)	5 (16.7%)	
Modified Bromage scale 3	1 (3.3%)	1 (3.3%)	
Modified Bromage scale 4	0 (0%)	0 (0%)	
Duration of motor block (min)	183.7 ±31.5	193.0 ±30.0	0.200
Time to the first analgesic requirement (h)	6.3 ±2.0	7.8 ±2.5	0.030*
Quality of anesthesia			
Quality of anesthesia 1	27(90%)	26 (86.7%)	0.839
Quality of anesthesia 2	2 (6.7%)	2 (6.7%)	
Quality of anesthesia 3	1 (3.3%)	2 (6.7%)	
Quality of anesthesia 4	0 (0%)	0 (0%)	
Total ephedrine (mg)	11.8 ±7.8	6.5 ±5.3	0.005*

Values are shown as mean ± SD or number of patients. Modified Bromage scale: 1, complete motor block; 2, medium block: difficulty raising legs; 3, minimal block: difficulty moving feet; 4, no block. Quality of anesthesia was rated as follows: 1, no discomfort or pain; 2, mild pain or discomfort; no need for additional analgesics; 3, pain that required analgesics; 4, severe pain that required analgesics. \*Indicates a significant difference at p<0.05.

**Table III:** Adverse effects and indwelling catheter postoperatively.

	Group B (n=30)	Group F (n=30)	p-value
Nausea	2 (6.7%)	4 (13.3%)	0.389
Vomiting	1 (3.3%)	2 (6.7%)	0.554
Pruritus	0 (0%)	1 (3.3%)	0.313
Shivering	2 (6.7%)	1 (3.3%)	0.554
Indwelling catheter	5 (16.0%)	6 (20.0%)	0.739

Values indicate the number of patients and percentage.

Elderly patients undergoing THA often have concurrent serious diseases, such as lung disease, coronary disease and brain ischemia disease. Spinal anesthesia

can be used to low rates of perioperative adverse effects.<sup>3-5</sup> However, unstable hemodynamics following spinal anesthesia is well known, and can be problematic for these patients. To maintain stable hemodynamics and reduce the potential complications due to hypotension during spinal anesthesia, general clinical practice is to decrease the dosage of local anesthetic, increase fluid infusion and use various adrenergic agonists; however, this approach increases the unacceptable anaesthetic failure rate and perioperative risks in elder patients.<sup>6-8</sup> Moreover, it was demonstrated that both colloidal fluid and lactated Ringer's solution were safe for elderly patients undergoing total hip arthroplasty under spinal anesthesia.<sup>9</sup> In this study, strategies aimed to maintain stable hemodynamics with compound sodium lactate solution preloading and with ephedrine were used.

Local anesthetics and opioids administered together intrathecally have a potent synergistic analgesic effect and can be potentially beneficial in critical patients.<sup>10-12</sup> A few research reported that administration of low-dose bupivacaine with fentanyl could provide adequate anesthesia and recovery in patients scheduled for cesarean delivery or transurethral prostatectomy.<sup>13,14</sup> Fentanyl is a lipid soluble synthetic opioid and has a small molecular weight and high potency. Intrathecal fentanyl can enhance sensory blockade without changing the degree of sympathetic blockade.<sup>15</sup> To the best of authors' knowledge, there was no published report on the administration of bupivacaine (7.5 mg) plus fentanyl (20 µg) in elderly patients undergoing THA.

In this study, both groups received the same quality of anesthesia; however, administration of bupivacaine with fentanyl required less ephedrine to maintain stable hemodynamics compared with single bupivacaine. Several studies demonstrated that the combination of intrathecal bupivacaine with fentanyl is effective in reducing impact on hemodynamics,<sup>16,17</sup> which is consistent with our findings. However, their drug formula was a mini-dose, with bupivacaine (4 mg) plus fentanyl (20 µg or 25 µg).<sup>16,17</sup> These differences in doses may be due to the drug injection speed and drug density. In our study, using a combination of intrathecal bupivacaine plus fentanyl significantly increased time to first post-operative analgesic requirement. Farzi *et al.* and Gauchan *et al.* also showed that adjuvant fentanyl administration could significantly increase duration of analgesia compared with bupivacaine only.<sup>18,19</sup>

In our study, the incidence of adverse effects did not show any significant difference between the two groups. Lee *et al.* reported that the incidence of nausea and pruritus increased, while the incidence of shivering decreased after administering intrathecal fentanyl.<sup>20</sup> These different results in adverse effects could have resulted from using different dosages of drug, the distinct

types of surgery performed, and the variable ages of patients in the two studies.

Reducing indwelling catheter placements could help avoid related secondary urinary tract infection,<sup>21</sup> especially in elderly patients.<sup>22</sup> The authors previously showed that the incidence of postoperative indwelling catheter following administration of 3 mL 0.25% bupivacaine and 3 mL 0.375% bupivacaine for spinal anesthesia were 13.3% and 23.3%, respectively.<sup>23</sup> Moreover, additional fentanyl administration with intrathecal bupivacaine did not significantly increase the incidence of postoperative indwelling catheters. However, Fernandez *et al.* reported postoperative urinary retention only in 9% of male and 3% of female patients who underwent spinal anesthesia and intrathecal fentanyl.<sup>24</sup> This difference was likely due to the greater age and smaller sample size in this study.

## CONCLUSION

Administration of 20 µg fentanyl to intrathecal 7.5 mg bupivacaine can provide safe and effective spinal anesthesia with no major adverse effects in elderly patients undergoing total hip arthroplasty.

This trial was registered at the Chinese Trial Registry. Registration number: ChiCTR-IOR-16007781. <http://www.chictr.org.cn/showproj.aspx?proj=13084>.

## ETHICAL APPROVAL:

This study has been approved by the Hospital Ethics Committee of Renmin Hospital of Wuhan University prior to commencement of this research.

## PATIENTS' CONSENT:

All patients signed informed consent for this study.

## CONFLICT OF INTEREST:

Authors declared no conflict of interest.

## AUTHORS' CONTRIBUTION:

Wang H, Peng X: Made substantial contributions to the conception or design of the idea or the acquisition; drafted the work; revised it critically for important intellectual content. Zhan L: Analysed data, helped in writing the manuscript. Xiao Y: Participated in the design and coordination of the paper.

Zhao B: Participated in the design; final approval of the version to be published; agreement to be accountable for all aspects of the work.

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