

# Pre-emptive analgesia with continuous fascia iliaca compartment block reduces postoperative delirium in elderly patients with hip fracture

## *A randomized controlled trial*

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### ABSTRACT

**الأهداف:** لتقييم ما إذا كان تسكين الألم الوقائي هو وسيلة فعالة للحد من الهذيان بعد العملية الجراحية (PD) في المرضى كبار السن الذين يعانون من كسر الورك.

**الطريقة:** أجريت تجربة سريرية عشوائية مزدوجة التعمية. تم تقسيم 90 مريض من كبار السن المقرر إجراء عملية جراحية لكسر الورك في مستشفى هونغ هوى، جامعة شيان جياوتونغ خلال الفترة من مارس 2018م حتى يناير 2019م إلى مجموعتين. لدى وصوله إلى قسم الطوارئ، تلقت المجموعة التجريبية (العدد=44) أشعة فوق الصوتية الموجهة لحاجز اللقافة الحرقفية المستمرة (FICB) لتسكين الألم ما قبل الجراحة، بينما تلقت مجموعة التحكم (العدد=46) FICB المستمر الوهمي. تلقت جميع المرضى تخدير العمود الفقري وتسكين فوق الجافية المسيطر عليها بعد العملية الجراحية (PCEA). قارنا التغيير في درجات الألم قبل الجراحة وبعد العملية الجراحية، وحدوث PD، واستعمال المواد الأفيونية بين المجموعتين.

**النتائج:** لم يستوفوا 5 مرضى شروط المشاركة؛ لذلك، اشتملت الدراسة على 85 مريضاً. المرضى في المجموعة التجريبية كان لديهم ألم أقل قبل الجراحة ( $p < 0.05$ ). بين المجموعتين، لم يتم العثور على اختلافات كبيرة لدرجات الألم بعد العملية الجراحية. كانت نسبة حدوث PD أقل في المجموعة التجريبية 13.9% مقابل 35.7% ( $p = 0.018$ ). بالإضافة إلى ذلك، لوحظ قبل الجراحة انخفاض في استهلاك الفنتانيل في المجموعة التجريبية ( $0.08 \pm 0.21$  مقابل  $0.28 \pm 0.13$ ;  $p = 0.037$ ).

**الخاتمة:** أن التسكين الوقائي مع FICB المستمر تعد تقنية فعالة للحد من PD في المرضى كبار السن مع كسر الورك.

**Objectives:** To evaluate whether pre-emptive analgesia is an effective technique to reduce postoperative delirium (PD) in geriatric patients with hip fracture.

**Methods:** This is a double-blind randomized clinical trial. Ninety elderly patients scheduled for hipfracture

surgery at HongHui Hospital, Xi'an Jiaotong University, Xi'an, China between March 2018 and January 2019 were divided into 2 groups. On arrival at the emergency department, the experimental group (n=44) received ultrasound-guided continuous fascia iliaca compartment block (FICB) for preoperative analgesia, while the control group (n=46) received generic continuous FICB. All patients received spinal anaesthesia and postoperative patient controlled epidural analgesia (PCEA). We compared the change in preoperative and postoperative pain scores, the incidence of PD, and the consumption of opioid between the 2 groups.

**Results:** Five patients did not meet the participation requirements; therefore, 85 patients were included in the study. Patients in the experimental group experienced less preoperative pain ( $p < 0.05$ ). Between the 2 groups, no significant differences were found for postoperative pain scores. The incidence of PD was lower in the experimental group (13.9% versus 35.7%,  $p = 0.018$ ). In addition, before the surgery, a drop in consumption of fentanyl was noted in the experimental group ( $0.08 \pm 0.21$  versus  $0.28 \pm 0.13$ ,  $p = 0.037$ ).

**Conclusion:** Pre-emptive analgesia with continuous FICB is an effective technique to reduce PD in geriatric patients with hip fracture.

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**H**ip fracture is common in the elderly. The number of patients undergoing hip fracture surgery is increasing.<sup>1</sup> Postoperative delirium (PD) is a common surgical complication and the incidence has been reported to be as high as 40% after hip fracture surgery.<sup>2</sup> Postoperative delirium results in increased mortality and morbidity.<sup>3</sup> Therefore, it is necessary to explore methods to reduce PD. Severe pain is frequently observed in patients with hip fracture.<sup>4</sup> In elderly patients, time to surgery is often prolonged due to poor health and preoperative examination and treatment.<sup>5</sup> Thus, patients often suffer longer with preoperative pain. Whether effective preoperative analgesia can reduce the occurrence of PD is unknown.

Fascia iliaca compartment block (FICB) is an alternative method of preoperative analgesia for elderly patients with hip fracture.<sup>6</sup> Therefore, we conducted the study to investigate whether pre-emptive analgesia with FICB is an effective technique to reduce PD in geriatric patients with hip fracture.

**Methods.** The study protocol was approved by the Institutional Review Board of HongHui Hospital. The trial was designed in accordance with the principles of the Declaration of Helsinki and registered at the Chinese Clinical Trial Registry (ChiCTR1800014917). Ninety elderly patients scheduled for hip fracture surgery were enrolled in the study. Inclusion criteria included age 60-80 years and American Society of Anesthesiologists (ASA) physical status II or III. Patients with serious cardiovascular, respiratory, and endocrine diseases (ASA IV); known allergies to local anesthetics; and taking sedatives and analgesics within the last week before hip fracture were excluded from the study. Patients with Mini-Mental State examination (MMSE) scores <27, sleep disorders, and psychiatric illnesses were also excluded.

Using a sealed envelope technique, patients were randomized into the experimental group or control group. On arrival at the emergency department, the experimental group received ultrasound-guided continuous FICB for preoperative analgesia. Continuous FICB was performed under ultrasound guidance by the same anesthesiologist. A total of 30 ml (0.45%)

ropivacaine solution was infused. Then an electronic pump was connected to the catheter with 200 ml (0.9%) sodium chloride (NaCl) at a concentration of 0.25% ropivacaine and a speed of 6 ml/h. The control group received generic continuous FICB using 0.9% sodium chloride. On the ward, when patients suffered from severe pain (visual analogue scale [VAS]  $\geq 5$ ), fentanyl 0.05 mg intramuscular was given each time by the surgeon. The surgeon was blinded to the study.

The VAS was used to assess the pain (0=no pain, 10=worst pain). Pain assessment was repeated at admission (T1), 2 hours after preoperative analgesia (T2), 4 hours after preoperative analgesia (T3), 6 am on the day of surgery (T4), and upon entering the operation room (T5). The consumption of fentanyl was also recorded.

After completion of the preoperative preparation, patients were scheduled for hip fracture surgery. All patients received intravertebral anesthesia, and the level of anesthesia was maintained at  $T_{10}$ . Patients received patient controlled epidural analgesia (PCEA) within 48 hours. Age, height, weight, surgical procedure, blood loss, infusion quantity, and surgical time were recorded in our anesthesia chart.

Postoperative delirium was assessed one hour after the surgery and then twice daily (8 to 10am and 6 to 8pm). At the same time, the intensity of postoperative pain was evaluated using the VAS or Wong-Baker FACE Pain Rating Scale<sup>7</sup> (WBS; WBS was used to assess the pain in the patients who became delirious). The diagnostic criteria for PD are as follows: a) acute onset of mental changes and fluctuating course; b) inattention; c) disorganized thinking; and d) altered levels of consciousness. If a patient had the characteristics of a and b, c, or d, the patient was diagnosed with PD.<sup>8</sup>

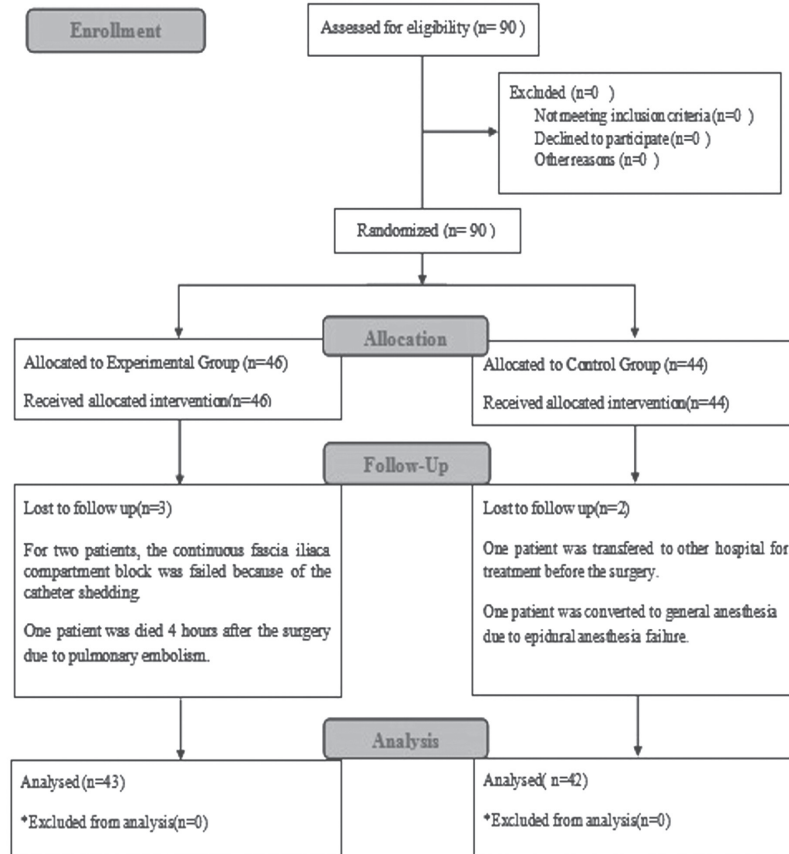
Data are shown as the mean $\pm$ SD, number of patients or n (%). The data was performed using the Statistical Package for Social Sciences for Windows version 19.0 (IBM Corp, Armonk, NY, USA). The demographic characteristics and clinical data were compared using student's t-test or the  $\chi^2$  test. The time from admission to surgery, pain scores, and fentanyl consumption were analyzed using the Mann-Whitney U test. The incidence of nausea and vomiting, pruritus, and delirium were analyzed using the  $\chi^2$  test. A *p*-value of <0.05 was considered statistically significant.

**Disclosure.** Authors have no conflict of interests, and the work was not supported or funded by any drug company.

**Results.** We recruited a total of 90 patients, and 5 did not meet the participation requirements (Figure 1); therefore, 85 patients were included in the study.

No significant differences were found for age, height, weight, ASA physical status, time from admission to surgery, fracture type, surgical procedures, duration of surgery, infusion quantity, and volume of bleeding between the 2 groups (Table 1).

Patients in the experimental group had lower VAS scores compared with the control group, except upon admission ( $p<0.05$ ) (Table 2), and no significant differences were found for postoperative pain scores between the 2 groups (Table 3).



**Figure 1** - The flowchart of the design and the protocol of the study.

**Table 1** - Demographic characteristics and clinical data in both groups.

Demographic characteristics	Experimental group (n=43)	Control group (n=42)	P-value
Gender (M/F)	23/20	23/19	0.906
Age (years)	72.30±3.78	72.52±4.26	0.800
Height (cm)	165.50±6.53	166.10±7.46	0.713
Weight (kg)	63.93±4.51	62.10±11.11	0.324
ASA (II/III)	28/15	29/13	0.816
Time from admission to surgery (hours)	29.49±4.58	29.81±3.78	0.725
Fracture type (I/T/S)	18/20/5	18/19/5	0.731
Surgical procedures (hemiarthroplasty/THR)	11/32	9/33	0.651
Blood loss (ml)	355.80±42.55	354.80±37.95	0.904
Infusion quantity (ml)	1890.70±249.60	1909.50±245.80	0.727
Duration of surgical time (min)	94.65±3.84	94.52±3.63	0.875

ASA - American Society of Anesthesiologists, I - intracapsular, S - subtrochanteric, T - trochanteric, THR - total hipjoint replacement

The incidence of PD was significantly lower in the experimental group (13.9% versus 35.7%,  $p=0.018$ ) (Table 4).

The consumption of fentanyl in the experimental group was significantly less than that in the control group before the surgery ( $0.08\pm 0.21$  versus  $0.28\pm 0.13$ ,

$p=0.037$ ). Before the surgery, there were 5 patients with nausea and vomiting and 4 patients with pruritus in the control group, while there were 2 patients with nausea and vomiting in the experimental group ( $p=0.025$ ) (Table 5).

**Discussion.** This first outcome of this study is that early continuous FICB significantly attenuated preoperative pain in geriatric patients with hip fracture. Patients with hip fracture often experience severe pain. Opioids remain the most commonly used analgesia. In our study, pain was relieved quickly after fentanyl was administered to the patients. However, the clinical use of opioid drugs still faces many obstacles, such as side effects and analgesic tolerance.<sup>9-10</sup>

Fascia iliaca compartment block could provide effective preoperative analgesia for the elderly with hip fracture, and its efficacy has been reported to be 90%.<sup>11</sup> In our study, there were only 2 failures of the FICB, with a total efficiency of 95%. The use of ultrasonography to guide the FICB increases the reliability of blockade.

Fascia iliaca compartment block is superior to traditional analgesia, such as intramuscular opioids or oral nonsteroidal anti-inflammatory drugs.<sup>12,13</sup> In our study, on arrival at the emergency department, patients who received continuous FICB experienced less pain before the surgery, and we found that pre-emptive analgesia with continuous FICB reduced the consumption of fentanyl. Patients who received the FICB before surgery experienced fewer opioid-related symptoms such as nausea, vomiting and pruritus. Therefore, compared with traditional analgesia, continuous FICB was a more effective method to provide preoperative analgesia for the elderly with hip fracture.

The second outcome of this study is that patients who received FICB for preemptive analgesia experienced less PD. The causes of PD are multifactorial, and studies have found that intense postoperative pain is an important precipitating factor and adequate postoperative pain control in patients who have undergone hip fracture

**Table 2** - The intensity of preoperative pain in 2 groups.

Time	Experimental group (n=43)	Control group (n=42)	P-value
T1	7.81±0.79	8.07±0.64	0.104
T2	2.74±0.73	4.19±0.40	<0.0001
T3	2.23±0.43	3.67±0.34	<0.0001
T4	2.26±0.44	3.51±0.38	<0.0001
T5	2.12±0.32	3.47±0.30	<0.0001

Data are presented as mean±SD. T1 - admission, T2 - 2-hours after preoperative analgesia, T3 - 4-hours after preoperative analgesia, T4 - 6am on the day of surgery, T5 - upon entering the operation room

**Table 3** - The intensity of postoperative pain after surgery.

Day	Time	Experimental group n=43	Control group n=42	P-value
1-hour after surgery	-	0.74±0.29	0.80±0.42	0.637
First day	6 to 8 p.m	1.15±0.21	1.19±0.40	0.642
Second day	8 to 10 a.m	1.16±0.37	1.21±0.47	0.113
	6 to 8 p.m	0.84±0.37	0.88±0.33	0.568
Third day	8 to 10 a.m	0.88±0.54	0.88±0.40	0.978
	6 to 8 p.m	0.79±0.51	0.86±0.47	0.537

**Table 4** - Comparison of the incidence of postoperative delirium between groups.

Day	Experimental group (n=43)	Control group (n=42)	P-value
1-hour after surgery	2	4	0.028
First day	3	7	0.038
Second day	1	3	0.042
Third day	0	1	0.489
Total (% of analyzed cases)	6 (13.9)	15 (35.7)	0.018

**Table 5** - Comparison of total consumption of fentanyl and adverse events between groups.

Consumption of fentanyl and adverse events	Experimental group (n=43)	Control group (n=42)	P-value
Fentanyl consumption dose (preoperative, mg)	0.08±0.21	0.28±0.13	0.037
Fentanyl consumption dose (postoperative, mg)	0.10±0.24	0.09±0.31	0.082
Preoperative nausea and vomiting	2 (4.65)	5 (11.90)	0.025
Preoperative pruritus	1 (2.32)	4 (9.52)	0.045

Values are presented as numbers and percentage (%).

surgery allows faster rehabilitation and reduces the rate of PD.<sup>14,15</sup> However, the influence of preoperative pain on PD is unknown. In our study, no significant difference in gender, age, height, weight, ASA physical status, time from admission to surgery, fracture type, surgical procedures, duration of surgery, infusion quantity, and volume of bleeding during the operation between the 2 groups. Postoperative delirium was associated with these factors.<sup>14</sup> To eliminate the influence of postoperative pain on PD, both groups received PCEA after the surgery in our study; no significant differences were found for postoperative pain scores. The only difference is that patients who received FICB for preemptive analgesia experienced less preoperative pain. Therefore, we can conclude that PD may be associated with preoperative pain, and preoperative pain is also a risk factor for the development of PD.

The reasons for the influence of preemptive analgesia with continuous FICB on PD may be related to relief of preoperative pain and the reduction in the “rescue” opioid requirements. Severe pain can cause activation and release of proinflammatory cytokines.<sup>16</sup> Excessive release of proinflammatory cytokines can promote the development of delirium.<sup>17,18</sup> Pre-emptive analgesia with continuous FICB may reduce the release of proinflammatory cytokines, which prevents the occurrence of PD. In addition, opioids can also stimulate the production of proinflammatory cytokines.<sup>19</sup> Preoperative analgesia with lesser amounts of opioid drugs may be an important factor for reduced levels of proinflammatory cytokines and reduced PD in patients managed with early continuous FICB.

**Study limitations.** First, this study possibly did not identify all the predictive factors of PD in the 2 groups, such as preoperative anxiety and preoperative fasting time. Second, the intensity of postoperative pain was assessed using the WBS in the patients who became delirious. However, the pain severity ratings on the WBS was highly correlated with those on a VAS.<sup>20</sup> Third, plasma cytokines were not measured concomitantly in this experiment, so further studies will be necessary to evaluate the systemic inflammatory response.

In conclusion, the results demonstrated that preoperative pain was also a risk factor for the development of PD, and pain management is critical in patients with hip fractures. Preemptive analgesia with continuous FICB is an effective technique to reduce preoperative pain, opioid requirements and PD in geriatric patients with hip fracture.

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