

# Additional femoral nerve block analgesia does not reduce the chronic pain after total knee arthroplasty

## A retrospective study in patients with knee osteoarthritis

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### Abstract

Femoral nerve block analgesia was deemed to the gold standard for acute pain management after total knee arthroplasty (TKA). But effect on chronic pain management is not investigated fully. We conducted a retrospective study to explore the effect of single-injection femoral nerve block on postsurgical chronic pain.

All medical records of patients undertaking TKA between January, 2013 and June, 2014 were reviewed via the Docare anesthesia database. Patients who administrated with the self-controlled intravenous analgesia were assigned to group P. Patients who received a single-injection femoral nerve block combined with patient self-controlled intravenous analgesia were assigned to group N+P. The visual analog scale (VAS) score before surgery, the first postoperative day (POD 1), POD 2, 3 months, 6 months, and 12 months after surgery were extracted from medical records. Pain score was compared over these 2 groups to investigate treatment outcomes.

In all, 470 patients met the selection criteria for group P and 266 patients met the selection criteria for group N+P. Compared with group P, the VAS score decreased significantly in group N+P at POD 1 ( $P < .001$ ), and the same was observed at POD 2 ( $P < .001$ ); the moderate to severe pain incidence rate decreased significantly in group N+P at POD 1 ( $P < .01$ ) and POD 2 (motion,  $P < .001$ ). The rescued anesthesia rate reduced significantly in group N+P in POD 1 ( $P = .001$ ), whereas no difference was found in POD 2 ( $P = .864$ ). No difference was found at 3, 6, and 12 months after surgery (all  $P > .05$ ).

The single-injection femoral nerve block could relieve the acute postsurgical pain in a short period of time. But no evidence was found that it could reduce the chronic pain between 3 and 12 months after TKA.

**Abbreviations:** BIS = bispectral, POD = postoperative day, TKA = total knee arthroplasty, VAS = visual analog scale.

**Keywords:** arthroplasty, chronic pain, femoral nerve, knee, ultrasonography

### 1. Introduction

Total knee arthroplasty (TKA) is a common orthopedic surgery,<sup>[1]</sup> which is performed for the end-stage knee osteoarthritis patients. The aim of TKA is reduce the knee joint associated pain, reverse joint function partly, and thus restore quality of life.<sup>[2-4]</sup> Unfortunately, some studies reported that the incidence of moderate to severe chronic pain was relatively high 3 to 5 years after TKA, ranging from 12.7% to 19%.<sup>[5-7]</sup> Severe chronic pain hinders knee joint function rehabilitation to a

certain extent. It was reported that preoperative pain sensitization,<sup>[8]</sup> revision TKA surgery,<sup>[5]</sup> psychological factors,<sup>[9,10]</sup> and increased number of comorbidities<sup>[11]</sup> could lead to more chronic postsurgical pain in general. Studies also showed that the acute postsurgical pain intensity was related to the development of chronic pain,<sup>[12,13]</sup> including TKA operation.<sup>[14]</sup>

At present, the conventional analgesia approaches after TKA include intravenous patient-controlled opioid-based analgesia, epidural patient-controlled local anesthetic based analgesia, and femoral nerve block along with intravenous patient-controlled opioid-based analgesia. Recently, femoral nerve block analgesia was deemed to a useful technique for pain management after TKA,<sup>[15-17]</sup> with comparable analgesic efficacy as epidural analgesia and less side effects.<sup>[17,18]</sup>

Study has shown that femoral nerve block analgesia may have limited impact on the chronic postsurgical pain after TKA,<sup>[19]</sup> whereas a conflicting result was found in a recent study.<sup>[20]</sup> Most previous studies only had short follow-up phase; therefore, impact of femoral nerve block on chronic pain incidence after TKA is unknown. In this retrospective study, we planned to compare the visual analog scale (VAS) by the patients who received a single-injection femoral nerve block analgesia right after the surgery to those who did not after TKA. The follow-up phase in our study was up to 12 months postoperatively. We hypothesized that patients received femoral nerve block would report less degree of pain than the patients without femoral nerve block, and we expected the pain-releasing effect would last to 12 months.

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The authors have no conflicts of interest.

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## 2. Methods

Methods of our research were approved by the Ethical Review Board Committee at the Second Affiliated Hospital of Zhejiang University. We reviewed the all medical records of patients undertaking TKA between January, 2013 and June, 2014 via the Docare anesthesia database. The requirement for written informed consent was waived by the Ethical Review Board Committee. Inclusion criteria was patients over 18 years and younger than 85 years who received selective unilateral TKA under general anesthesia with or without a single-injection femoral nerve block for postsurgical analgesia. Exclusion criteria were patients received bilateral knee replacement or other surgery at the same time, intrathecal anesthesia, and severe infection after TKA and chronic pain other than knee.

### 2.1. Clinical routine procedure

On the morning of surgery day, celecoxib 200 mg was always given by oral for preemptive analgesia. The patients were monitored with electrocardiogram, invasive arterial blood pressure, heart rate, and SpO<sub>2</sub> routinely after they entered the operation. General anesthesia was induced by midazolam 0.04 to 0.08 mg/kg, etomidate 0.2 to 0.3 mg/kg or propofol 1 to 2 mg/kg, sufentanil 0.4 to 1.0 μg/kg, rocuronium 0.6 to 1.0 mg/kg, and maintained with continuous intravenous infusion of propofol 4 to 7 mg/kg/h, remifentanyl 6 to 10 μg/kg/h and inhalation of 1% to 2% sevoflurane. After tracheal cannula, mechanical ventilation was performed. Sufentanil or rocuronium was added at the discretion of the anesthesiologist during surgery. Anesthetic depth was monitored with bispectral (BIS) to maintain a BIS index between 35 and 50. The TKA procedure was performed under tourniquet with the pressure of 45 kPa.

For those patient who did not receive nerve block (group P), the patients were given the self-controlled intravenous analgesia via a CADD-Legacy ambulatory infusion pump (Deltec Inc, St Paul, MN) with the basal rate of sufentanil 2 to 2.5 μg/h, a patient-controlled bolus dose of sufentanil 0.5 to 1.5 μg, and a lockout of 15 minutes. In the nerve block group (group N+P), a single-injection femoral nerve block was performed combined with patient self-controlled intravenous analgesia (the same as group P). The femoral nerve block was guided by SonoSite S-nerve ultrasound with a linear 6 to 13-MHz probe (SonoSite, Bothell, WA) with 0.25% ropivacaine (AstraZeneca AB, Sodertalje, Sweden) 25 to 30 mL.

### 2.2. Clinical routine outcome measurements

When the patient come to the hospital, VAS (score 0–10; 0=no pain; 10=worst pain imaginable) was explained to patients in detail, and pain assessment was performed before surgery on resting and motion (after 50m of walking). After surgery, pain was assessed twice daily on resting and mobilization routinely with VAS by the same nurse of acute pain service group at afternoon (4–5 PM) of surgery day and first day morning (9–10 AM) of post operation (first postoperative day [POD 1]). The assessment lasted 2 days after surgery. The VAS score recorded in the morning was used for analysis in present study. Additional parecoxib 40 mg (maximal dose 80 mg/d), tramadol 100 mg (maximal dose 200 mg/d), or flurbiprofen 100 mg (maximal dose 200 mg/d) was used if VAS scores ≥4 or patients required intensively.

After the patient-controlled intravenous analgesia pump was removed, oral celecoxib 200 mg or tramadol 100 to 200 mg every

12 hours was performed for analgesia till 3 to 5 days after the patient discharged from hospital. In our hospital, all patients undertaking anesthesia entered the Docare Anesthesia Database. Orthopedics patients were all required to follow up every 3 months, and VAS scores were recorded on resting state and motion upto 12 months after operation. If a patient failed to visit the surgeon's office on the scheduled date, a telephone investigation was performed within 2 weeks for assessing the VAS score. We defined the postsurgical pain according to International Association of Study on Pain.<sup>[21]</sup> where VAS score ≥4 was considered as moderate to severe pain.

Demographic information including patients' American Society of Anesthesiology physical status, sex, age, body mass index, level of education, comorbidity of chronic disease (hypertension, diabetes, etc), preoperative pain duration, and surgery with moderate to severe acute postsurgical pain history were extracted from medical records. Patient surgical information such as anesthesia duration, surgery duration, and sufentanil and remifentanyl dose used during surgery was also extracted from medical records.

### 2.3. Statistical analysis

In the present study, the primary outcome was the incidence rate of chronic pain after TKA with different postoperative analgesia pattern, and the secondary outcome was the relationship between the degree of preoperative pain and the chronic pain incidence. The incidence of moderate to severe chronic pain was about 19%, whereas the incidence of moderate to severe chronic pain was about 10% in patient with a single-injection femoral nerve block for postoperative analgesia.

A minimum sample size of 237 was required to achieve the desired statistical power level of 0.80 at a probability level of .05.

Data were presented as mean ± SD for quantitative data and frequencies for categorical variables as appropriate. After testing for normal distribution by Kolmogorov-Smirnov test, the Mann-Whitney *U* test or independent-sample *t* test was used to analyze quantitative data. The chi-square test was employed to analyze categorical variables. Spearman rank-correlation analysis was performed to determine the correlation between the degree of preoperative pain and chronic pain. Data were analyzed by using SPSS software version 18.0 (SPSS Inc., Chicago, IL), and figures were drafted by Prism 5.0 (GraphPad Software Inc., La Jolla, CA). Significance was determined at a *P* value less than .05.

## 3. Results

In all, 736 patients meeting the selection criteria were reviewed (group P=470; group N+P=266). No statistically significant difference was found between these 2 groups on baseline parameters (*P* > .05) (Table 1). There were 26 (5.5%) patients lost to follow-up in group P and 16 (6.0%) patients in group N+P in 12 months' follow-up (Fig. 1).

Compared with group P, the VAS score decreased significantly in group N+P at POD 1 (resting 2.28 ± 0.85 vs 2.65 ± 0.96, *P* < .001; and motion 3.20 ± 0.95 vs 4.13 ± 1.03; *P* < .001); and the same was observed at POD 2 (resting 1.60 ± 0.76 vs 1.87 ± 0.78, *P* < .001; and motion, 3.08 ± 0.96 vs 3.56 ± 0.82, *P* < .001). No difference was found at all other time points (all *P* > .05) (Fig. 2).

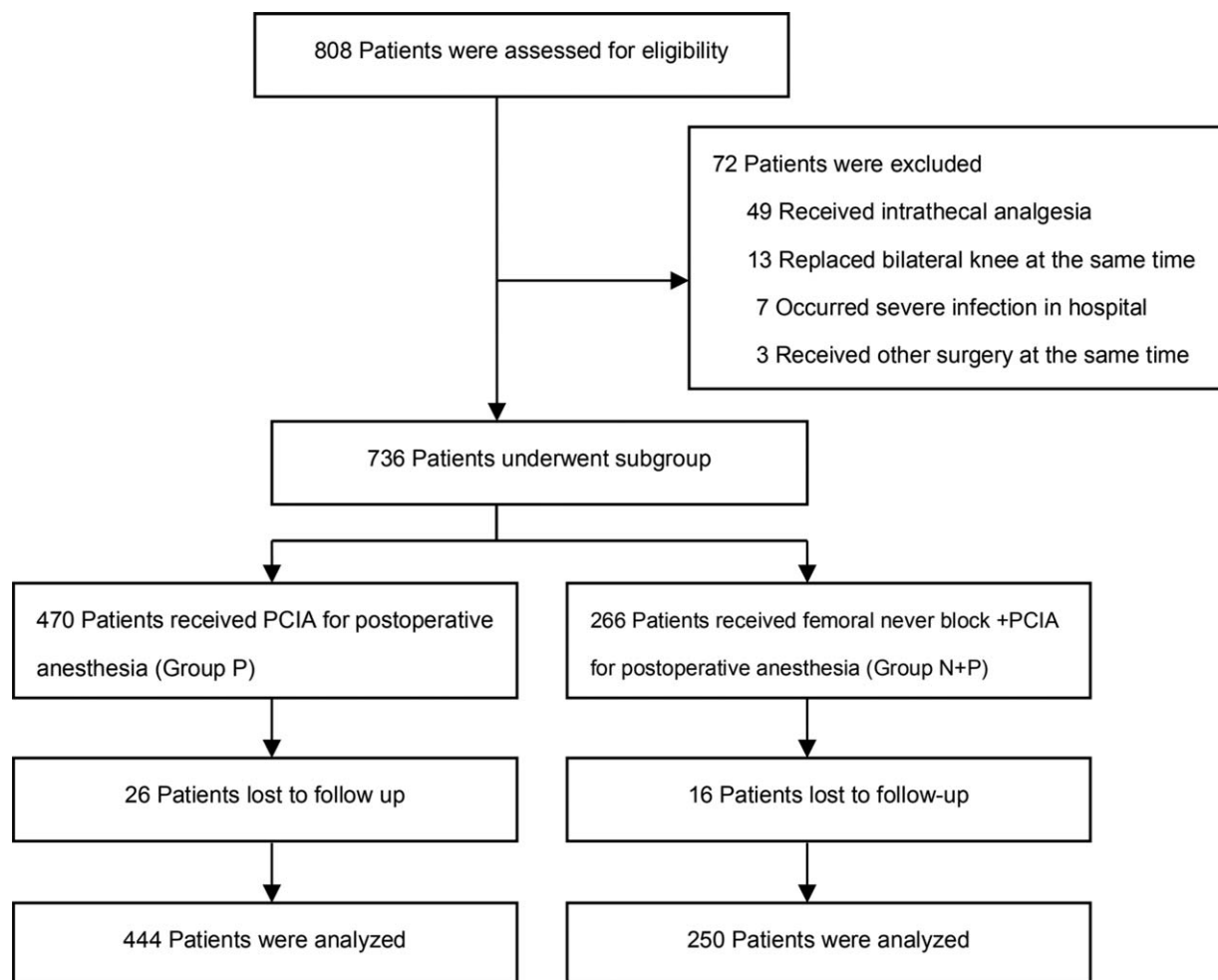
Compared with group P, the moderate to severe pain incidence rate decreased significantly in the group N+P at POD 1 (resting 9.77% vs 20.43%, *P* < .001; motion 36.09% vs 74.47%,

**Table 1**

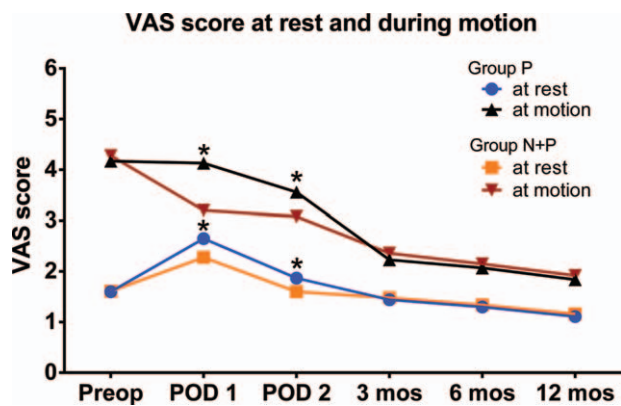
**Patients' demographic information.**

	Group P (n=470)	Group N+P (n=266)	P
ASA physical status (I/II/III)	17/424/29	7/246/13	.579
Age, y (mean ± SD)	66.6 ± 8.5	66.9 ± 8.5	.611
Sex, male/female	142/328	71/195	.312
Weight, kg (mean ± SD)	64.7 ± 11.7	65.0 ± 11.4	.720
Body mass index (mean ± SD)	25.5 ± 4.2	25.7 ± 3.9	.672
Major surgery history	130 (27.66%)	69 (25.94%)	.614
Preoperative pain duration (mean ± SD, y)	7.91 ± 6.71	8.39 ± 7.74	.372
Anesthesia duration (mean ± SD, min)	110.8 ± 21.9	113.8 ± 22.4	.078
Surgery duration (mean ± SD, min)	79.3 ± 19.8	80.0 ± 23.4	.680
Sufentanil dose during surgery (mean ± SD, µg)	44.0 ± 6.7	44.1 ± 6.6	.862
Remifentanyl dose during surgery (mean ± SD, mg)	0.55 ± 0.23	0.53 ± 0.18	.416
Level of education			
Illiteracy	107 (22.77%)	67 (25.19%)	
Primary to junior middle school	305 (64.89%)	169 (63.53%)	
Senior school and above	58 (12.34%)	30 (11.28%)	.730
Comorbidity of chronic disease			
Hypertension	199 (42.34%)	117 (43.98%)	.665
Diabetes	45 (9.07%)	32 (12.03%)	.296
Other	24 (5.11%)	9 (3.38%)	.278

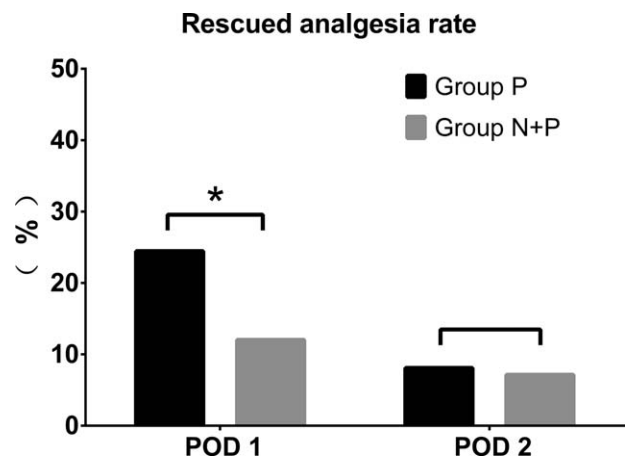
ASA=American Society of Anesthesiology, SD=standard deviation.



**Figure 1.** Flow chart showing patient enrollment, grouping, and analysis.



**Figure 2.** The VAS score of knee osteoarthritis patient at rest and during motion at different moment. Data was presented as mean±SD. Compared with group P, the VAS score decreased significantly in the group N+P at POD 1 and POD 2 (all  $^*P < .001$ ). No difference was found at all other time points (all  $P > .05$ ). POD 1=the first day of post operation, POD 2=the second day of post operation, VAS=visual analog scale.



**Figure 4.** The rescued anesthesia rate in POD 1 and POD 2. Compared with group P, the rescued analgesia rate reduced significantly in group N+P in POD 1 (24.26% vs 12.03%;  $^*P = .001$ ), whereas no difference was found in POD 2 (8.09% vs 7.14%;  $P = .864$ ). POD 1=the first day of post operation, POD 2=the second day of post operation.

$P = .003$ ) and POD 2 (motion 32.3% vs 54.47%,  $P < .001$ ). No difference was found at all other time points (all  $P > .05$ ). In group P, the incidence of moderate to severe chronic pain was 12.6% and 16.7% in rest and motion separately at 3 months, postoperatively, whereas in group N+P, the rate was 11.6% and 14.0%. At 6 months postoperatively, the rate dropped to 9.5% and 14.2% in group P, and 10.8% and 13.2% in group N+P. At 12 months postoperatively, this rate decreased to 5.2% and 9.9% in group P, and 5.6% and 10.0% in group N+P (Fig. 3).

Compared with group P, the rescued anesthesia rate reduced significantly in group N+P in POD 1 (12.03% vs 24.26%;  $P = .001$ ), whereas no difference was found in POD 2 (7.14% vs 8.09%;  $P = .864$ ) (Fig. 4).

**3.1. Secondary analysis**

In the secondary analysis, no significant correlation was found between the degree of preoperative pain and chronic pain at 3, 6, and 12 months after operation, and the correlation coefficient

was 0.043, 0.047, and 0.023 at rest, respectively; the correlation coefficient was 0.044, 0.050, and 0.037 during motion, respectively (all  $P > .05$ ).

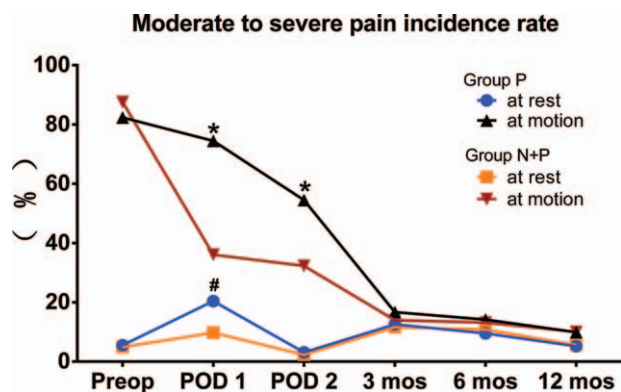
**4. Discussion**

Our research hypotheses were partially supported. Nerve block provided significant acute pain release to patient after joint surgery; however, such an effect did not last to 3, 6, and 12 months after TKA. The level of preoperative pain had little correlation with the degree of chronic pain at 3, 6, and 12 months after operation.

Our results support the findings of other studies that femoral nerve block could provide effective postsurgical analgesia for TKA,<sup>[17,18]</sup> even with a single injection.<sup>[18]</sup> In patients with single-injection femoral nerve block, the average VAS scores, the number of patients with moderate to severe pain, and the number of patients who needed rescue analgesia all reduced in 1 to 2 days after TKA. In the present study, it should be mentioned that the difference of the average VAS scores at POD 1 and POD 2 was small between with and without single-injection femoral nerve block, which was because the rescue analgesia was performed if VAS scores were  $\geq 4$  or patients required.

In present study, the chronic pain was observed from 3 to 12 months after TKA. The incidence of moderate to severe pain after TKA with an additional femoral nerve block was 11.6% at 3 months, and decreased to 5.6% gradually at 12 months at rest. The incidence of moderate to severe chronic pain in patients with patient-controlled intravenous analgesia was 12.6% at 3 months, and decreased to 5.2% at 12 months at rest. The moderate to severe chronic pain incidence had a slight difference with previous studies.<sup>[5-7]</sup> It can be explained by the different time<sup>[5]</sup> and different pain evaluation form<sup>[7]</sup> on which studies performed the follow-up after surgery.

Studies by other authors suggested that acute postsurgical pain was a predictor of chronic pain,<sup>[11-13]</sup> and regional analgesic techniques could decrease the chronic pain level and the incident rate if we come to a good strategy of managing pain in the early phase.<sup>[22-27]</sup> In this study, outcomes showed that the chronic pain incidence was not reduced between 3 and 12 months after TKA



**Figure 3.** The moderate and severe pain incidence rate of knee osteoarthritis patient at rest and during motion at different moment. Data was presented as percentage. Compared with group P, the moderate to severe pain incidence rate decreased significantly in the group N+P at POD 1 (rest,  $^*P < .001$ ; motion,  $^{\#}P = .003$ ) and POD 2 (motion,  $^*P < .001$ ). No difference was found at all other time points (all  $P > .05$ ). POD 1=the first day of post operation, POD 2=the second day of post operation.



with an additional femoral nerve block for analgesia. Most patients experienced chronic pain of knee joint because of osteoarthritis before surgery. Only when the painful osteoarthritis cannot be managed in primary care, TKA is performed. Recent studies demonstrated that preoperative chronic pain intensity emerged as a significant persistent pain predictor after TKA.<sup>[6,8,28–32]</sup> Persistent poorly controlled pain might trigger central sensitization, with a stepwise permanent modification of spinal pain pathways,<sup>[33]</sup> which could cause higher acute postsurgical pain because of hyperalgesia<sup>[32]</sup> and lead to postsurgical chronic pain.<sup>[34]</sup> A single injection might not reverse augmented central pain processing changes. Thus, the incidence of chronic pain might not be reduced.

In the secondary analysis, our study shown that there was no significant correlation between the degree of preoperative pain and chronic pain at 3, 6, and 12 months after operation. Some previous studies outcomes indicated that preoperative pain may contribute to chronic postsurgical pain,<sup>[28,30]</sup> but it was not the unique variable that could cause postsurgical chronic pain.

In the present study, only single-injection femoral nerve block was performed. Whether prolonged femoral nerve block would be beneficial for chronic pain or not existed conflict. Recently, study proved that compared with intravenous patient-controlled analgesia, continuous femoral nerve block revealed advantage in reducing incidence of chronic postsurgical pain at 3 and 6 months after TKA.<sup>[20]</sup> But Ilfeld et al<sup>[19,35]</sup> indicated that no evidence was found that extending an overnight continuous femoral nerve block to 4 days could relieve subsequent chronic pain between 7 days and 12 month after TKA, but the sample size was small. A well-designed large sample size, prospective, random, and controlled study should be performed to confirm these findings in the future.

There were some limitations in the present study. First, patients' psychological and physiologic factors were not included and analyzed in present study. These factors have been reported with the influence on patient's pain sensitivity.<sup>[9–11]</sup> Second, only information about pain was collected and analyzed, and we should include other measures, such as the degree of joint stiffness and functional disability, to give a better assessment on the outcome after surgery.

## 5. Conclusions

In summary, from the retrospective investigation, we observed that an additional single-injection femoral block provided a better controlled acute postsurgical analgesia, but it did not lead to a lower incidence of chronic pain between 3 and 12 months after TKA.

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## Author contributions

**Conceptualization:** Lina Yu, Min Yan.

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**Project administration:** Min Yan.

**Supervision:** Lina Yu, Min Yan.

**Writing – original draft:** Yuanyuan Yao, Qinghe Zhou.

**Writing – review & editing:** Yuanyuan Yao.

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