

Multimodal Cocktail Periarticular Injection vs Femoral Nerve Block After Total Knee Arthroplasty: A Simultaneous Bilateral Randomized Study

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Abstract

Background Pain control after total knee arthroplasty (TKA) is important for early postoperative experience and knee rehabilitation. However, there is no consensus on the Pain management after TKA. Whether early analgesic effect and patient satisfaction can reach or even exceed the femoral nerve block has been controversial. The aim of our study was to compare the early analgesia effect with multimodal cocktail periarticular injection (MCPI) and Femoral nerve block (FNB) during simultaneous knee arthroplasty.

Methods Our study was a prospective randomized, double-blind controlled trial. From December 2018 to August 2019, 85 patients (170 knees) who underwent bilateral total knee arthroplasty at our institution were randomly treated with MICP and FNB. Randomization was done via a computerized randomization list. The visual analogue scores for pain, bilateral knee range of motion (ROM), postoperative adverse events, and patients satisfaction were assessed preoperatively and two weeks postoperatively. This trial is registered at ClinicalTrials.gov, number ChiCTR1800020003.

Results A total of 85 patients (170 knees) were enrolled for bilateral TKA. Finally, 80 (160 knees) patients were included for analysis and comparison. The operation time of the MCPI group was significantly lower than the FNB group (66.5 ± 8.7 min compared with 72.8 ± 9.5 min, $P < 0.05$). postoperative 2nd–3rd and 5th days, the MCPI group in VAS for pain at rest and Straight elevated leg were significantly lower than FNB group ($P < 0.05$). The knee flexion of MCPI group was statistically greater than FNB group on the postoperative 3rd, and 5th days ($P < 0.05$).

Conclusions MCPI analgesia is better than FNB after total knee arthroplasty, which can shorten the operation time, and evidently prolong the Postoperative effective analgesia duration. Higher patient satisfaction is beneficial to early postoperative recovery.

Trial registration: Chinese Clinical Trials Registry, ChiCTR1800020003,11/12/2018

1.introduction

Knee osteoarthritis (KOA) is a clinically common chronic degenerative disease, causing chronic pain, knee dysfunction and mood disorders. However, Total knee arthroplasty (TKA) can improve the quality of life, reduce pain and restore function in patients with end-stage disease, which is recognized as a reliable treatment method[1-3]. Intraoperative osteotomy and balancing of soft tissue can lead to early postoperative pain, irritability and other unpleasant feelings. In addition, Fear of patients caused by a long incision on the knee joint, as well as adverse events such as nausea and vomiting caused by drugs, may aggravate patients depression, decrease the satisfaction of the operation, and further affect the functional recovery after TKA[4-6]. Therefore, excellent pain control after TKA is of great significance for postoperative surgical satisfaction and early recovery[7, 8].

Postoperative pain management has been a hot topic for decades. There are a variety of pain management in the clinic. Oral drugs, continuous epidural anesthesia, peripheral nerve block, controlled analgesia, cold compress therapy and preventive analgesia are commonly used in clinical practice [7]. However, this has not yet reached a consensus[9]. Although these analgesic methods have been proven to be effective in relieving pain, adverse events is increased such as nausea and vomiting, respiratory depression, urine retention and other symptoms also occur, and the incidence of venous thromboembolism[10, 11]. Femoral nerve block (FNB) is one of the commonly used postoperative analgesic methods in total hip arthroplasty (THA) and TKA, which can reduce postoperative pain and opioid use. However, it has also been proved that there are some problems, such as causing quadriceps weakness and increasing the probability of postoperative fall [8, 12-14]. Some scholars reported that the incidence of periprosthetic fractures after primary joint arthroplasty was 0.3% ~4.0%. Falling is an important risk factor and 75% of periprosthetic fractures are caused by falls[15, 16].

Multimodal cocktail periarticular injection (MCPI) is a new popular method to reduce postoperative pain. Previous studies showed that the use of MCPI is not higher than FNB in pain control and opioid consumption reduction, and range of motion (ROM) of knee is better than FNB group. Compared to FNB, it not only reduces pain and consumption of opioids, but also reduce the risk of falls [13, 17-19]. Other scholars reported that the effect of MCPI on pain control after TKA was not good.

Previous studies mostly compared pain management after unilateral knee arthroplasty, which are biased. The influence of MCPI on recovery, range of motion, and patient satisfaction following TKA is still largely unknown, particularly in comparison to FNB. In view of this, we designed simultaneous bilateral TKA for the same patient, with MCPI on one side and FNB on the other side, and finally compared and analyzed its postoperative effect of pain relief. The visual analogue scores (VAS) for pain, bilateral knee ROM, postoperative adverse events, and patient's satisfaction were assessed preoperatively and two weeks postoperatively. We hypothesized that the MCPI group would show better early analgesia, higher patient satisfaction and better knee motion.

2.patients And Methods

2.1Study design and participants

A single-center, randomized controlled trial was compared MCPI or FNB in postoperative analgesia in simultaneous bilateral total knee arthroplasty. The study was organized by Department of Orthopedic Surgery in our institution from December 2018 to August 2019. Our study was in compliance with the medical institution regulations and conforms to the ethical standards of the national research council and the Helsinki declaration of 1964. Our study was approved by our institutional review board. Informed consent was obtained from all patients. This trial is registered at ClinicalTrials.gov, number ChiCTR1800020003. A CONSORT Flow Diagram is provided in Figure1.

Inclusion criteria: (1) The patient was diagnosed as osteoarthritis of the knee, with poor conservative treatment effect. Suitable for TKA, (2) Both knees have similar levels of degenerative changes and Varus/

valgus deformity. (3) Simultaneously bilateral TKA.

Exclusion criteria: (1) Revision total knee arthroplasty or staged bilateral TKA, (2) Previously allergic or intolerant to a drug in an analgesic scheme, (3) Rely on opioids to relieve pain, (4) Liver and kidney dysfunction, (5) Knee joint infection or suspected infection. Additionally, patients with a history of cardiac disease, deep vein thrombosis, or surgery of the knee joint were excluded.

2.2 Randomization and masking

Basing on the above selection and exclusion criteria, we prospectively investigated the clinical data of 85 patients who received primary TKA from December 2018 to August 2019. The number was on the expected enrolment and drop-out of patients in our region. A computerized randomization list was created by a statistician in a random order using a concealed block size of 4. The list was used to randomly assign knees to either the MCPI or FNB group. Allocations were sealed in consecutively numbered opaque envelopes. Once the patient agrees to be included in the trial, the next sealed envelope is opened by an independent investigator to randomly assign an analgesic method. Patients and clinical data collectors were blinded to the group assignment. The data center based at the Department of Orthopedic Surgery was responsible for treatment allocation, central monitoring, and statistical analyses under the supervision of the statistician in charge.

2.3 Procedures

All patients received general anesthesia. The surgical procedures were performed by the Senior surgeon. Pneumatic tourniquets were used in the surgery. Routine disinfection was performed and towels were applied. A knee median incision was made, extending to the inner side near the patellar region. Intraoperative bilateral knee joints use the same arthroplasty technique and prosthesis type (Zimmer Posterior Stabilized prosthesis). All patients underwent patellar Patella resurfacing. The incision was closed and drainage was placed When the knee was bent at 45°. The tourniquet was released. After the one side was completed, the other side was performed.

MCPI group: Contents of MCPI: 1% ropivacaine (447 mg), flurbiprofen (100 mg), epinephrine (1 mg), dexamethasone (5 mg), 0.9% saline. This was formulated into a 100 ml solution. Before closing the incision, 1/3 cocktail was injected into the posterior capsule periosteum of the femur and tibia and bilateral collateral ligament areas, and 1/3 was injected into the subcutaneous tissue of the incision. The remaining 1/3 of the cocktail was injected through the drainage tube after closing the incision. The tube was rinsed with 50 ml of saline and clamped for 6 hours.

FNB group: Contents of FNB: ropivacaine (5mg/ml, 20ml). Femoral nerve block was performed by ropivacaine (5mg/ml, 20ml) under the guidance of color doppler ultrasound by the same anesthesiologist after the incision was closed (Table 2).

2.4 Postoperative treatment

All patients used the same nutritional interventions, antibiotics, thromboprophylaxis, and the same care and rehabilitation exercise regimen. The quadriceps isometric contraction and knee flexion exercise were performed on postoperative 1st day. The drainage tube was removed 24 hours after surgery. Regular dressing changes are performed by the same physician (Y.Z). After extubating, the patients were instructed to exercise with the CPM machine, and the patients were informed of the relevant precautions after surgery. Intraoperative and postoperative comprehensive patient clinical manifestations and blood routine examination results determine blood transfusion. Blood transfusions are given if the patient has significant anemia symptoms or hemoglobin is below 70 g/L. All patients underwent subcutaneous injection of low molecular weight heparin (4100 IU/d) on postoperative first day in accordance with the Guidelines for Prevention of Venous Thromboembolism in Major Orthopedic Surgery. Oral rivaroxaban (5 mg/d) was continued after discharge to prevent deep vein thrombosis of the lower extremities. The shortest time for anticoagulation is five weeks. X-ray examination of the knee was performed after surgery. The patients underwent routine color Doppler ultrasonogram of the lower extremities on postoperative 7th day. The suture was removed about 14 days after surgery.

Our primary outcome was to compare the difference of postoperative analgesia and patient satisfaction within 2 weeks of surgery. Operative time, intraoperative blood loss, postoperative drainage, incision length, postoperative complications and adverse events were recorded in the two groups. Postoperative pain level was evaluated by the patient on VAS. The patients were told that the left end of assessment form represented no pain and the right end represented the most extreme pain. Postoperative VAS for pain (during rest and straight elevated leg, once every 6 hours within 3 days after surgery), knee active flexion (ROM, measured by measuring instrument within 2 weeks after surgery).

2.5 Statistical analysis

Data were processed with SPSS 23.0 statistical software and expressed as mean values±standard deviation ($x\pm s$). Data among groups were compared with paired t tests. The chi-squared test or Fisher's exact test was used to determine the statistical significance of differences in the categorical variables. The differences were considered statistically significant at $P<0.05$.

3. Results

A total of 85 patients (170 TKAs) enrolled in the study received bilateral TKA, and eligible patients will be included in the analysis. One patient declined to participate and two patients had incorrect postoperative analgesia. The data of two patients were lost. This condition resulted in 160 knees in 80 patients for analysis (Figure 1). The surgeon (XYC) completed 56 operations in 80 cases of bilateral total knee arthroplasty, and another surgeon (GCC) completed 24 operations. There were 25 males and 55 females aged 65.0 ± 8.3 years on years (Table 1). Four patients developed superficial infection at the incision and recovered after regular dressing change. Five patients were found to have venous thrombosis by lower limb color Doppler ultrasound after surgery, transferred to the interventional department to place the vena cava filter and improved. Three patients felled down after surgery, and no obvious abnormalities were

found after imaging examination. Ten patients developed symptoms of nausea and vomiting after surgery, and improved after symptomatic treatment such as antiemetic. Satisfaction of all patients with postoperative pain relief was good. 65% patients were more satisfied with the MCPI side knee, which were significantly higher than 15% of FNB group ($P < 0.001$, Table 3). And the remaining 20% did not feel bilateral differences. The details of the study population are presented in Table 3.

No statistically significant differences were observed in Patient Baseline Clinical Characteristics including implant type, preoperative VAS at rest and Straight elevated leg (SEL), preoperative flexion and extension, length of incision, Intraoperative blood loss, postoperative drainage ($P > 0.05$, Table 3).

The operation time of MCPI group was lower than that of FNB group, and the difference was statistically significant (66.5 ± 8.7 min compared with 72.8 ± 9.5 min, $P < 0.05$, Table 3). The curve of VAS at rest were all lower in the MCPI group than in the FNB group, but the difference was statistically significant on the 2nd, 3rd and 5th day ($P < 0.05$, Figure 2A,2B). In the curve of VAS on SEL, the MCPI group was slightly lower than the FNB group within 2 weeks after surgery. The difference was statistically significant on the 2nd and 3rd day. For knee flexion, the MCPI group was significantly higher than the FNB group on postoperatively the 3rd, and 5th days ($P < 0.05$, Figure 3).

4. discussion

Total knee arthroplasty is recognized as one of the effective methods for the treatment of advanced knee osteoarthritis. As the number of elderly people increase, the number of TKAs will increase accordingly. It is reported that more than 600,000 people in the United States undergo TKA surgery each year[17]. Due to intraoperative mechanical soft tissue destruction and femoral and tibial osteotomy, the pain after TKA is more severe than other orthopedic surgery. 50% of patients with TKA have moderate or severe pain after surgery. Effective pain management can improve patient satisfaction and promote early activities. Earlier physical therapy can reduce cardiopulmonary complications, promote recovery, improve quality of life, and reduce the likelihood of chronic pain syndrome[20, 21]. Therefore, pain management after TKA is important for early quality of life improvement and rehabilitation. Studies have shown that cocktail injection analgesia around the joint can produce good analgesic effects and fewer adverse events[18, 19, 22–25]. But some scholars reported that the effect of MCPI on pain control after TKA was not good. Previous studies have compared the effect of local injection analgesia on postoperative pain control in patients with unilateral knee arthroplasty. Pain thresholds may vary from patient to patient, which does not adequately reflect postoperative pain relief and improved mobility. Therefore, our study compared different analgesic methods in the simultaneous bilateral knee arthroplasty in a prospective, double-blind, randomized controlled trial to confirm that cocktail analgesia is superior to FNB in early postoperative analgesia and knee function. And the patients own satisfaction is higher than FNB.

Currently, the commonly used analgesic methods in TKA include peripheral nerve block, epidural analgesia, analgesic drugs around the joints, and patient-controlled analgesia[26]. Commonly used drugs include NSAIDs, analgesics such as acetaminophen, local anesthetics such as ropivacaine and

bupivacaine, non-opioid central analgesics such as tramadol, and opioids such as morphine and fentanyl[27]. A single analgesic method was difficult to achieve the desired results, and there are a series of side effects. Therefore, multimodal analgesia has become a favorite method for surgeons. In our study, ropivacaine, flurbiprofen, epinephrine and dexamethasone were combined to achieve postoperative analgesic effect.

In our study, MCPI group and FNB group had different analgesic effects compared at rest and SEL within 72 hours after surgery. And there is an increasing trend in the 2nd and 3rd days (Fig. 2), which may be related to incomplete elimination of general anesthesia and subcutaneous removal of drainage tube on the first day after surgery. The results of Koh[13] are different from ours. They found no difference in the extent of pain during the first 48 hours, but there was a significant difference in the recovery of knee quadriceps muscle strength. Ng[28] used cocktails and cFNB in patients with bilateral knee arthroplasty, and found that the two analgesic methods had similar pain relief at rest and during exercise within 72 hours after surgery. The difference is not statistically significant. Their findings are the opposite of our study. The concentration of the drug is much higher than FNB, and the analgesic effect will continue. However, some studies have shown that FNB will increase the postoperative patients fall events[17]. Some scholars reported that the incidence of periprosthetic fractures after primary joint arthroplasty was 0.3% ~4.0%. Falling is an important risk factor, 75% of which is caused by falling. Barrington[29] showed a higher pain score in female and young patients by regression analysis in an analgesia study of one-knee TKA. Our study is to avoid this confounding factor by comparing the two-sided TKA in the same period, and the conclusion is more realistic and reliable.

In the knee ROM, the MCPI group showed better flexion activity on the 3rd, and 5th day than the FNB group. Better ROM may indirectly reflect the analgesic effect of MCPI group over the FNB group. Tsukada[30] also used postoperative knee ROM to indirectly evaluate the pain relief, and the results were similar to our study. In addition, the analgesic effect of MCPI and FNB can also be evaluated by the consumption of morphine. The results showed that postoperative morphine consumption in the MCPI group was significantly lower than that in the FNB group[22, 31, 32]. Wang[17] analyzed twelve articles in the meta-analysis to show that MCPI group was lower than FNB group in postoperative analgesia and opioid consumption, and the ROM was better.

In addition, the MCPI group had less operation time than the FNB group. The process of cocktail injection is convenient and simple. The solution is prepared by the nurse in proportion and then injected by the surgeon with a syringe. The whole process takes no more than 2 minutes. For the FNB group, the anesthesiologist used color Doppler to locate the femoral nerve. The drug is then injected through a puncture needle. The whole process takes about 5–8 minutes, much higher than cocktail injection. The operation time is a risk factor of postoperative infection, the risk for each additional 15 minutes increased by 9% [33].

Our study had several limitations. First, the number of patients is small and more data is needed for further research. Due to the domestic medical insurance policy and the hospital system requirements, it is

difficult to continue the simultaneous bilateral knee arthroplasty in our hospital. So, our study near to end. Second, Contents of analgesic cocktail include ropivacaine, dexamethasone, adrenaline and flurbiprofen are in our study, which may differ from other studies. So, the conclusion may be different. For example, morphine drugs are used in some studies to achieve better analgesic effects. morphine is a kind of restricted drug in China, and it is difficult to carry out our research. Therefore, the promotion of cocktail analgesics may be controversial. Third, our study only evaluates Chinese patients, so the demographic characteristics should be noted before extrapolating to other populations[29]. Fourth, our study was unable to assess postoperative hospital stays. Most unilateral TKA studies have shown that MCPI can reduce postoperative hospital stays[18, 22, 34]. But it's a simultaneous bilateral TKA study which is not possible to assess the difference in postoperative hospital stays. Meanwhile, the average postoperative hospital stays was about 7.36 days, which is the standard in our hospital. There is no doubt that our research is also valuable. Because the hospital stays is not a key factor in postoperative pain. Despite these limitations, the simultaneous bilateral TKA using MCPI and FNB provides valuable information for pain relief and functional recovery.

5.conclusion

MCPI analgesia is better than FNB after total knee arthroplasty, which can shorten the operation time, and evidently prolong the Postoperative effective analgesia duration. Higher patient satisfaction is beneficial to early postoperative recovery.

Abbreviations

TKA: Total Knee Arthroplasty;MCPI: Multimodal Cocktail Periarticular Injection; FNB: Femoral Nerve Block; VAS: Visual Analogue Scores; ROM: Knee Range of Motion; KOA: Knee Osteoarthritis; THA: Total Hip Arthroplasty

Declarations

Ethics approval and consent to participate

This study has been approved by the Ethic Committee of the Affiliated Hospital of Xuzhou Medical University (XXXX). All patients received informed consent and signed the informed consent.

Consent for publication

All co-authors read and approved the final manuscript.

Availability of data and materials

All data generated or analyzed during this study are included in this published article, and the supplementary file. We do not wish to share our patients' data because it involves patient's privacy.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Ye Z, SF did the study, analyzed the data, and wrote the manuscript. Yu Z, JNS, WC, XYC, SF was involved in the design, data management, and analysis of the study. All authors read and approved the final manuscript.

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Tables

Table 1 Baseline patient demographics and postoperative complications

	Patients
Male/ Female	25/55
Age (Years)	65.0±8.3
BMI[kg/m ²]	24.1±4.0
ASA I / II / III	0/15/65
DVT	5
Infection	4
nerve palsy	2
Fall	3
PONV and dizziness	10

DVT: deep vein thrombosis, PONV: postoperative nausea and vomiting

ASA: American Society of Anesthesiologists.

Table 2 Contents of analgesic MCPI and FNB

	Dose	Amounts
MCPI:		
Ropivacaine mesylate (mg)	89.4	5
<u>flurbiprofen axetil</u> (mg)	50	2
<u>epinephrine</u> (mg)	1	1
<u>hexadecadrol</u> (mg)	5	1
FNB: Ropivacaine mesylate (mg)	89.4	1

Table 3 Patient Baseline Clinical Characteristics

	MCPI	FNB	t or cl	P
Preoperative Varus Deformity	9.2±2.2	8.9±2.5	0.992	0.324
Preoperative max. flexion (°)	117.5±7.0	117.3±6.1	0.393	0.695
Preoperative max. extension (°)	2.8±2.5	3.1±2.6	-0.551	0.583
Preoperative VAS Rest	6.65±0.6	6.64±0.5	0.152	0.880
Preoperative VAS SEL	6.9±0.8	6.7±0.9	1.606	0.112
Operative time(min)	66.5±8.7	72.8±9.5	-4.427	0.001
Length of incision(cm)	19.8±2.0	20.0±1.6	-0.899	0.371
<u>Intraoperative blood loss</u> (ml)	116.0±5.5	114.9±6.3	0.963	0.339
Postoperative drainage(ml)	129.0±31.3	125.6±28.1	0.838	0.405
Patient satisfaction	65% (52)	15% (12)	0.334	0.001
Postoperative hospital stays(days)	7.36±1.5	7.36±1.5	-	-

SEL: Straight elevated leg; VAS: Visual analog scale score

Figures

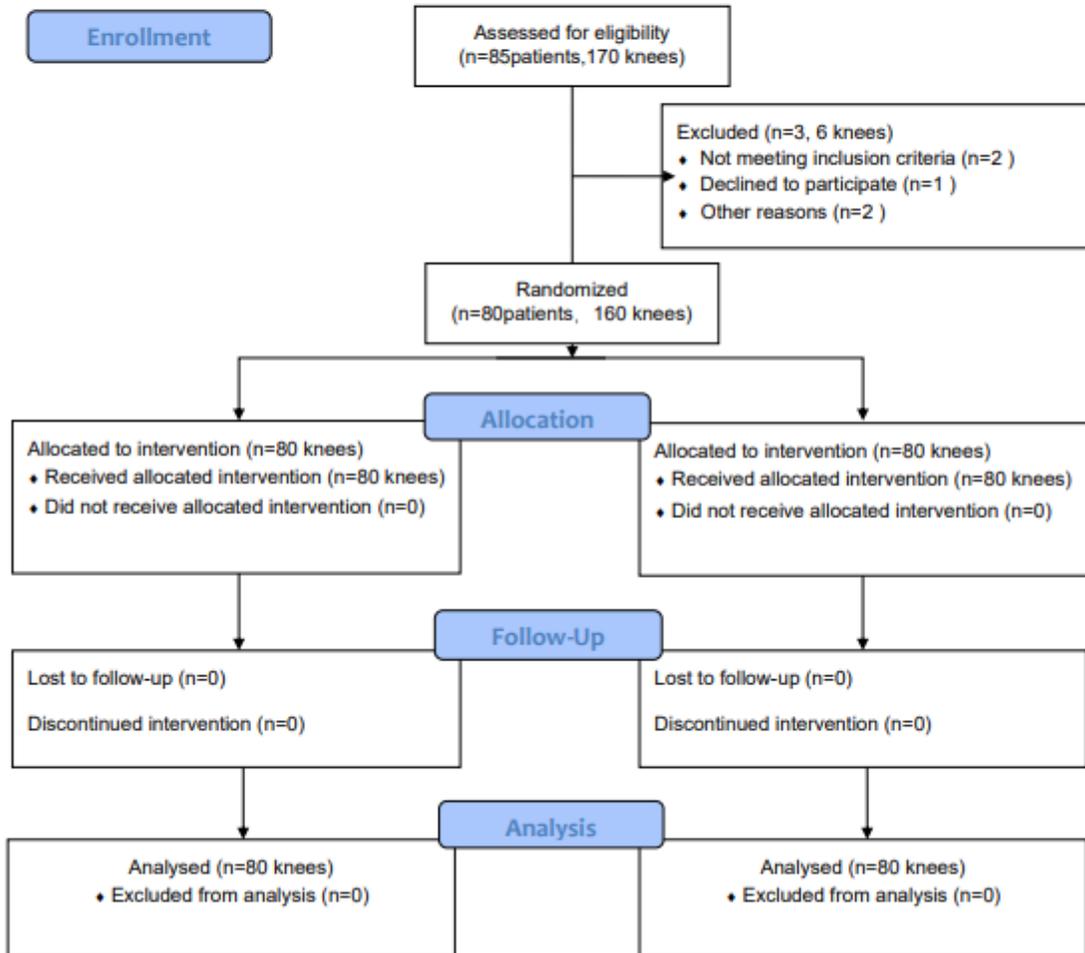


Figure 1

Flow diagram.

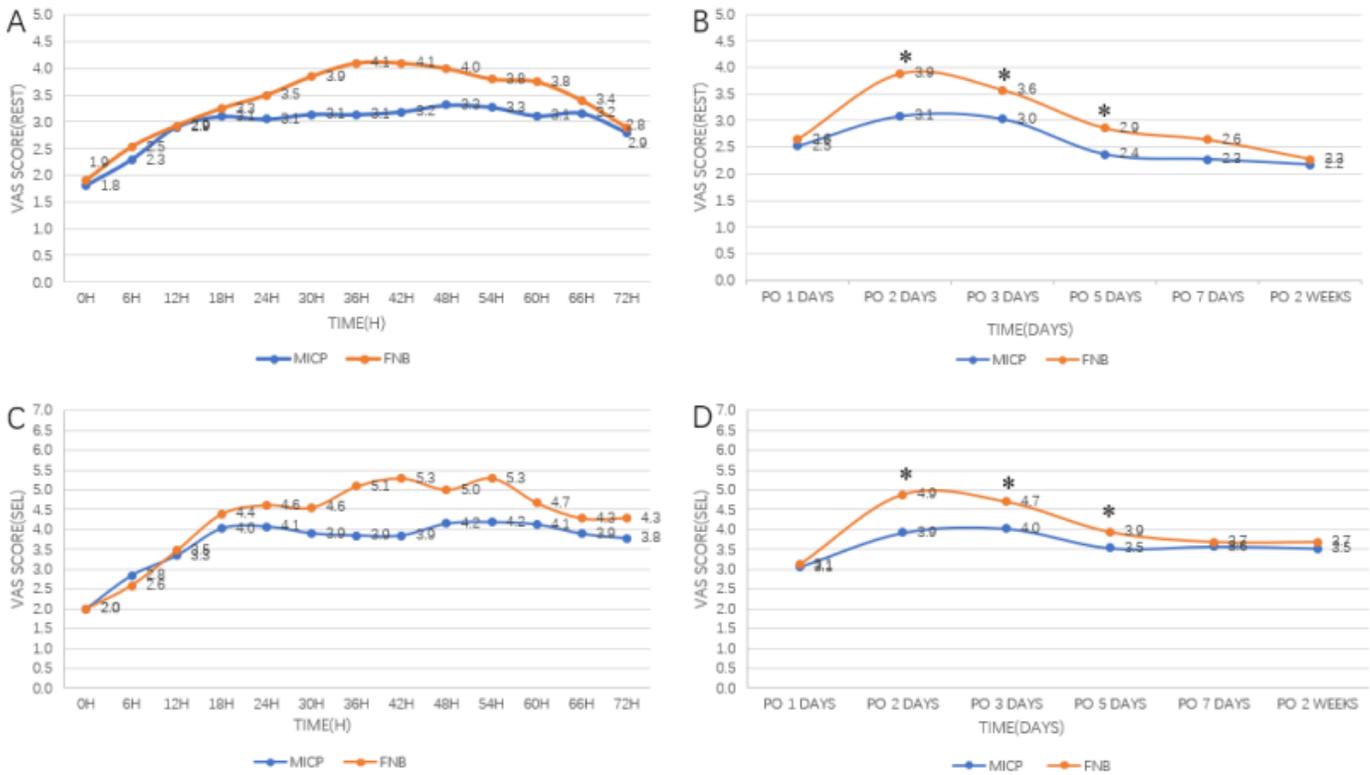


Figure 2

Postoperative pain score in simultaneous bilateral knee arthroplasty. A: Mean visual analog pain scores for MCPI (multimodal cocktail periarticular injection) or FNB (femoral nerve block) during rest Within 3 days after surgery. B: Mean visual analog pain scores for MCPI or FNB during rest Within 2 weeks after surgery. C: Mean visual analog pain scores for MCPI or FNB during SEL Within 3 days after surgery. D: Mean visual analog pain scores for MCPI or FNB during SEL Within 2 weeks after surgery. VAS: Visual analog scale, SEL: Straight elevated leg. *: P<0.05.

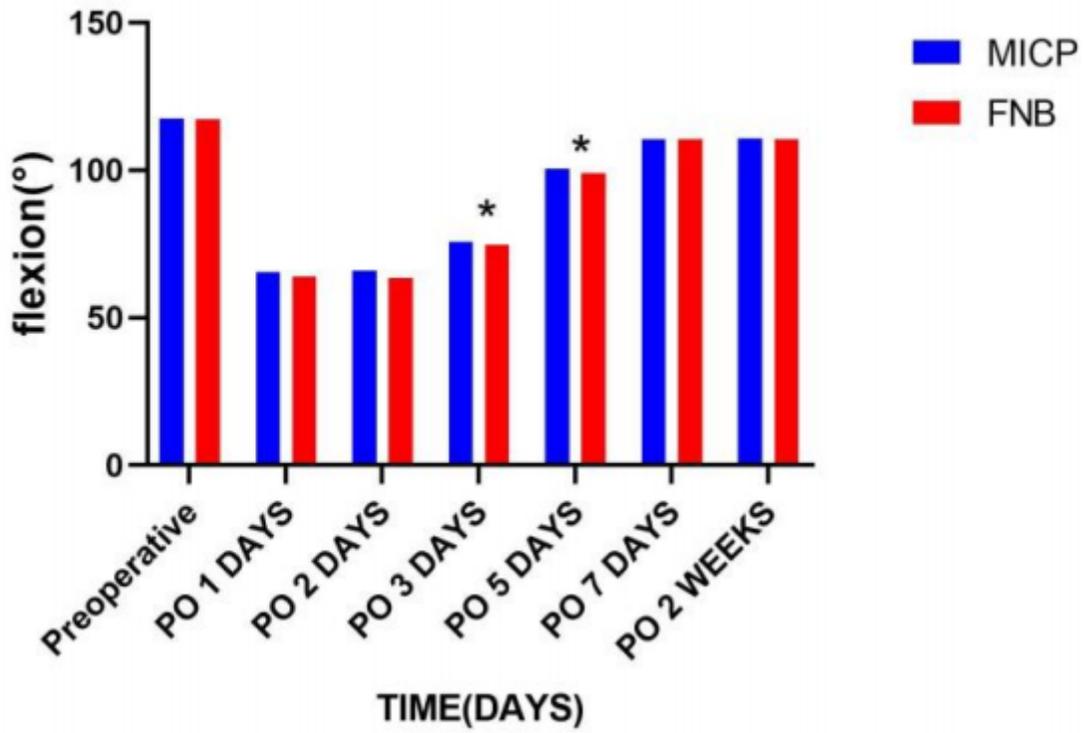


Figure 3

Knee flexion after simultaneous bilateral total knee arthroplasty. *: P<0.05.