

Effects of multi-site infiltration analgesia on pain management and early rehabilitation compared with femoral nerve or adductor canal block for patients undergoing total knee arthroplasty: a prospective randomized controlled trial

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Abstract

Purpose The aim of this study was to combine intra-articular and peri-articular with wound infiltration analgesia (multi-site infiltration analgesia, MIA) for patients undergoing total knee arthroplasty (TKA) and compare its pain management and early rehabilitation effect with the commonly used nerve block including adductor canal block (FNB) and femoral nerve block (ACB).

Method We conducted a prospective randomized controlled trial and 77 patients were included for analysis. The patients were randomized over three groups. The first group (26 patients) received multi-site infiltration analgesia (MIA group), the second group (27 patients) received femoral nerve block (FNB group), and the third group (24 patients) received adductor canal block (ACB group).

Results MIA showed better pain control at rest during the first 12 hours ($p < 0.05$ respectively) and less opioid

consumption after operation than the other two groups ($p < 0.05$, respectively), but ACB and FNB revealed similar outcomes ($p > 0.05$). At the same time, there are no significant differences in pain score with activity, vital signs, and occurrence of complication ($p > 0.05$, respectively) among the three groups. When evaluated the early rehabilitation, MIA and ACB had similar outcomes on post-operative muscle strength ($p > 0.05$), but they showed better quadriceps strength when compared FNB ($p < 0.05$). Although the knee ROM of the patients with FNB showed better results ($p < 0.05$), their ambulation ability was inferior to those in MIA group ($p < 0.05$ and ACB group ($p < 0.05$) early after the operation, besides, MIA patients were superior to ACB patients ($p < 0.05$). Furthermore, MIA spent less time on operation and post-operative hospital stays when compared with FNB and ACB ($p < 0.05$, respectively), while the ACB and FNB were without significant difference ($p < 0.05$, respectively).

Conclusion ACB was not inferior to FNB on pain control, but it was better on early mobilization. However, MIA that combine intra-articular and peri-articular with wound infiltration analgesia after TKA was more effective on pain control at rest, with better efficacy on early rehabilitation and easier to perform when compared with these commonly used nerve block. We recommended our MIA for pain relief and fast rehabilitation after TKA.

Keywords Adductor canal block · Femoral nerve block · Infiltration analgesia · Total knee arthroplasty

Introduction

Osteoarthritis (OA), characterized by pain and joint dysfunction, is a disease that frequently occurs in middle-

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aged and old populations. OA of the knee is one of the most disabling diseases and a common reason for total knee arthroplasty (TKA). However, TKA often causes intense post-operative pain. According to previous studies, more than 60 % of patients suffer such pain, which influence their appetite, sleep, functional recovery, and even delay hospital stays [1–3]. The growing trend of quicker recovery following orthopedic procedures has stimulated the development of the techniques focused on improving post-operative pain management. However, it remains one of the major challenges for anesthesiologists. Although the methods used for controlling the pain are various and tremendous work has been done in this field, additional sufficient evidence supporting the effectiveness of these protocols is still needed, and the most appropriate program remains undetermined [4–6].

Femoral nerve block (FNB) is one of the most commonly used pain-relief methods, which has been proven to be effective on relieving the pain, reducing the usage of opioid painkiller, and shortening the hospital stays [7–11]. Moreover, FNB is regarded as the gold standard for post-operative analgesia after TKA by some surgeons [8, 9]. As we know, early exercise and mobilization is important to patients to decrease risk of complications such as pneumonia, deep venous thrombosis, dyspepsia, pulmonary embolism, and urinary retention, but FNB may lead to post-operative quadriceps weakness, which not only limits the patients' ambulation and early physical rehabilitation, but also increases the risk of falling [12–14]. These deficiencies make the rehabilitation results unsatisfactory [14, 15]. Adductor canal block (ACB) is the other analgesia for TKA and has been developed gradually in recent years. ACB attracted extensive attention due to its lower complication of reducing quadriceps strength and similar outcomes of opioid consumption, pain management, opioid adverse events, and ambulation ability when compared with FNB [16–20]. The adductor canal is a cavity surrounded by the sartorius muscle, medial femoral muscle, and the adductor muscles with saphenous nerve, medial femoral cutaneous nerve, cutaneous branches of obturator nerve, etc. [19, 21, 22]. However, some studies demonstrate that the ACB may influence the obturator nerve supply to the knee and weaken the adductor muscle, which is an unwanted outcome that could block the knee extensor or hip flexor [24, 25]. At the same time, some other reports present the opposite conclusion that ACB only develop complete sensory block but no motor block [21, 23, 26].

Local infiltration analgesia (LIA) has been used for pain management after TKA for ages and is regarded as an adjunct to femoral nerve block [27–29]. However, in recent years, many reports indicate that LIA can be comparable to the FNB on pain control and may even be

better in terms of complication occurrence, functional recovery, and hospital stays [5, 9, 30–32]. However, more effective works need to be carried out to prove the previous conclusions.

LIA can be performed in multiple sites, such as intra-articular analgesia [33, 34], peri-articular analgesia [20, 35, 36], and wound infiltration analgesia [37, 38]. Consequently, we combined intra-articular and periarticular with wound infiltration analgesia in this study and evaluated the pain management and early rehabilitation of this multi-site infiltration analgesia (MIA). As a single shot FNB may reduce the occurrence of the fall compared with continuous FNB and the placement of the catheter may cause infection [14, 18, 23, 39], we chose the single nerve block in this trial and tried to study whether ACB was not inferior to FNB and if MIA can be comparable to these commonly used nerve blocks.

Materials and methods

Patients

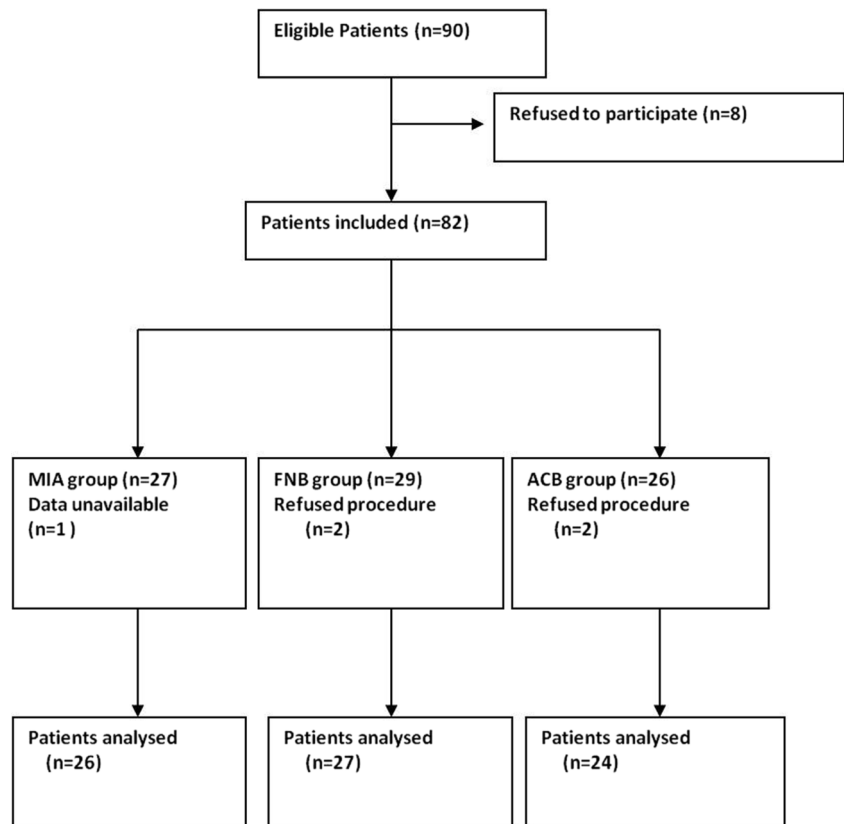
Ninety patients going for unilateral total knee replacement for osteoarthritis were eligible for this trial from October 2015 to May 2016. Inclusion criteria were patients ready for unilateral primary total knee arthroplasty for osteoarthritis with the age of 55 to 80 years old, BMI of 20–35 kg/m², and the risk grade of American Society of Anesthesiologists before operation was I–III. Those patients with a history of septic arthritis, rheumatic disease, excessive drinking and opioid consumption, patients who are allergic to medications used, with nerve affection of the legs and inability to understand the numeric rating scales (NRS), patients who have severe osteoarthritis with knee deformity, mental disorder, and ulcer in digest track were excluded.

Randomization and double-blind

Patients were randomized into three groups: multi-site infiltration analgesia (MIA group), single-shot femoral nerve block (FNB group), and single-shot adductor canal block (ACB group). A computerized random number generator was used. Numbers were stored in opaque sealed envelopes. The patient was asked to select one envelope on the morning of surgery. This trial was blind to the patients, surgery, and statisticians.

Analgesia and operation procedure

After the patients were in hospital, pain management methods were propagandized and NRS score measurement was taught. Starting three days before surgery, 200 mg

Fig. 1 Flow chart of patients selection

celecoxib was taken two times a day. The FNB group had FNB performed before operation using ultrasound-guidance with 20 ml 5 g/L ropivacaine and 0.1 mg adrenaline at the upper thigh. The ACB group was conducted at the middle and distal of the thigh of the patients with the same method and dosage of drug. The MIA group did not have nerve block. All nerve blocks were performed by the anesthesiologists from the same group.

All operations were performed using the same surgical technique, including a midline skin incision with medial parapatellar approach, and a measured resection technique was used in all cases. A tourniquet was applied to all the patients with a strategy of inflating before incision and deflating after compressing the lower limb with two elastic bandage under control at 100 mmHg above systolic pressure. Intramedullary guides were used for all femoral preparation, and extramedullary guides were used for tibial preparation. Autologous bone was used to fill the femoral medullary canal before implant cementation. All patients received a surgeon selected cemented posterior-stabilized prosthetic design and the patellar was properly prepared after resurfacing.

After the prosthesis was placed, the MIA group conducted the infiltration analgesia, which was injecting 30 ml 2.5 g/L ropivacaine and 0.1 mg adrenaline to the periarticular including joint capsule, medial and lateral

collateral ligament, the distal of quadriceps, ligamentum patellae, deep fascia, and popliteal fossa. After the arthrotomy was closed, 20 ml 2.5 g/L ropivacaine and 0.1 mg adrenaline was injected into the joint and 20 ml of the mix was taken for infiltration of the subcutaneous tissue at the time of wound closure. The nerve block groups were without these processes. Before closing the wound, a regular drainage tube was placed in all patients. The operations were completed by the same group of surgeons.

After the operation, all patients were sent back to the bedward without using the patient controlled intravenous analgesia, but the ice compress around the incision for 24 hours was selected. At the first post-operative day, the total volume of drainage was recorded and then the drainage tube was removed. Diclofenac sodium (50 mg/12 h) and oxycodone hydrochloride prolonged-release tablets (10 mg/12 h) were taken on schedule, and parecoxib was intramuscularly injected every 12 hours after operation until hospital discharge. If the patients could not tolerate the pain or the NRS score was higher than 6, 50 mg pethidine hydrochloride was used via intramuscular injection.

The dorsal and plantar flexion, quadriceps muscle strength exercise was initiated as soon as awake from anesthesia. All the patients began to walk under partial weight-bearing after reviewing x-ray of knee on post-operative day one. Daily

rehabilitation exercise, including quadriceps strength training, active range of motion (ROM) training, and walking training were performed under the supervision and assistance of a physiotherapist.

Outcome measurements

Primary outcomes included post-operative pain score at rest and with activity (knee flexion of 45°) using numerical rating score (NRS, in the scale of 0 to 10, where 0 = no pain and 10 = worst pain ever can tolerate) and the change of vital signs of the patients after operation including mean heart rate and mean arterial pressure measured at two hours, six hours, 12 hours, 24 hours, 36 hours, 48 hours, and 72 hours post-operatively. Besides, the total use of the opioid drug (pethidine hydrochloride in this study) and complication occurrence was recorded after operation.

Second outcomes: 1) Quadriceps strength and hip adductor strength were estimated at two hours, six hours, 12 hours, 24 hours, 36 hours, 48 hours, and 72 hours post operation using a manual muscle test with a standardized 0–5 motor-strength scale [40]. 2) Knee range of motion tested active flexion degree, TUG test measured the time it took a patient to get up from a chair, walk three metres, and return to the sitting position in the chair [41] and patients' daily ambulation distance at one day, two days, and three days after operation. 3) Post-operative hospital stays.

Other outcomes including total operative time, tourniquet time, incision drain, patient satisfaction [42] etc. were also analyzed.

Statistical analysis

The SPSS19.0 software (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis. The results were analyzed with one-way variance analysis, each group was compared with SNK-q test and LSD test, P-values of number and percent variables were calculated by chi-square and Fisher exact test, with $p < 0.05$ indicating statistical significance.

Results

Patients analyzed

Thirteen patients were excluded by various reasons and 77 patients who underwent unilateral total knee arthroplasty were assessed at last. The trial flow diagram is presented in Fig. 1. There was no statistically significant difference in demographic profile or in clinical characteristics (Table 1).

Table 1 Demographic characteristics of patients

Parameter	Multi-site infiltration analgesia (n = 26)	Femoral never block (n = 27)	Adductor canal block (n = 24)	P values among three groups
Age (years)	62.6 ± 7.3	61.4 ± 6.8	62.3 ± 6.5	P = 0.82
BMI (kg/m ²)	25.4 ± 3.8	26.6 ± 4.2	26.1 ± 5.0	P = 0.86
Gender (male/female)	14/12	13/14	11/13	*P = 0.84
Knee range of motion (°)	105.4 ± 9.8	102.7 ± 10.6	104.5 ± 10.3	P = 0.72
Quadriceps strength	4.5 ± 0.6	4.4 ± 0.8	4.5 ± 0.8	P = 0.90
Adductor muscle strength	4.8 ± 0.3	4.7 ± 0.3	4.6 ± 0.2	P = 0.81
NRS score at rest	2.3 ± 0.6	2.2 ± 0.5	2.2 ± 0.7	P = 0.90
NRS score with activity	3.1 ± 1.0	3.2 ± 1.1	3.0 ± 1.2	P = 0.83

NRS numeric rating scales, BMI body mass index. *Presented as number and percent, and P-values were calculated by chi-square and Fisher exact test

Primary outcomes

Primary outcomes concerned pain management. First, the MIA group showed better pain control at rest two hours, six hours, and 12 hours post-operation ($p < 0.05$), but ACB and FNB revealed a similar outcomes ($p > 0.05$). There were no statistically significant differences among the three groups in NRS pain scores at rest after 12 hours ($p > 0.05$, ANOVA) and with activity ($p > 0.05$, ANOVA) during the first 72 hours post-operatively (Fig. 2). Second, the mean heart rate and mean arterial pressure which may be influenced by pain also showed similar changes among the three groups after operation ($p > 0.05$, ANOVA, respectively) (Fig. 3). Third, the total postoperative opioid consumption was found to be less in MIA group compared with the other two groups ($P < 0.05$; ANOVA), but the FNB group and ACB group were similar (Table 2). There were two cases, three cases, and two cases in MIA group, FNB group, and ACB group respectively where gastrointestinal side effect ($p = 0.35$) happened, two patients had urinary retention in MIA group and FNB group respectively and three in ACB group ($p = 0.21$). Other complications such as wound problems, venous thrombus, pulmonary embolism, infection, etc. did not happen. Besides, the falling of the patients in FNB group did not occur.

Second outcomes

Second outcomes evaluated the early rehabilitation. When assessing the muscle strength, the quadriceps strength was weaker in the FNB group than the other two groups in the

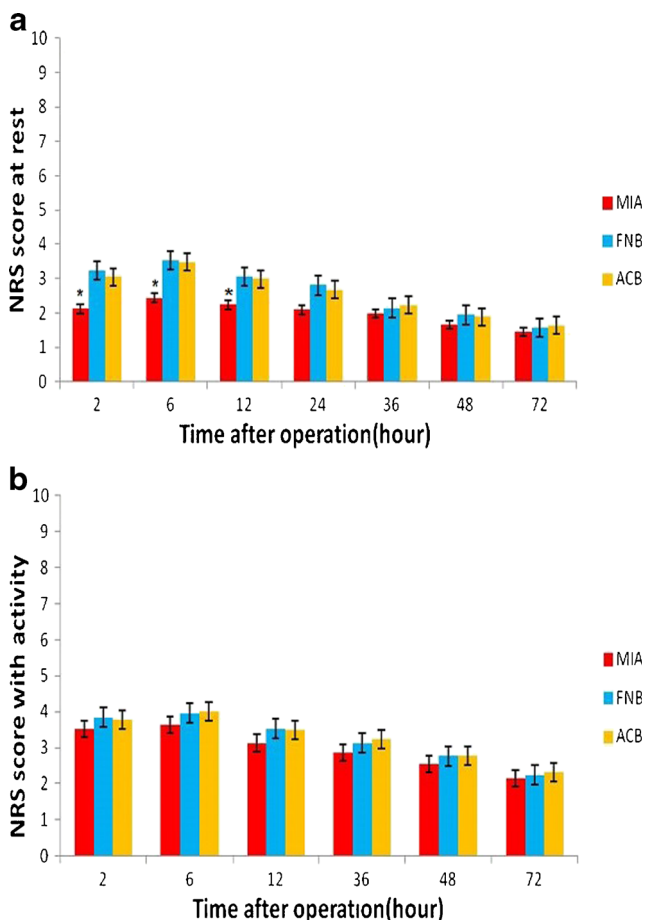


Fig. 2 NRS pain score of the three groups presented as mean and standard error. (a) The pain scores at rest (NRS). (b) The pain scores with activity (NRS). * means $p < 0.05$ when the MIA group was compared with the other two groups at the first 12 hours after operation

first 12 hours post operation ($p < 0.05$, ANOVA, respectively), while after 12 hours there was no significant difference ($p > 0.05$, ANOVA, respectively) (Fig. 4a). The hip adductor muscle strengths were similar among the groups according to Fig. 4b ($p > 0.05$, ANOVA, respectively). When analyzing the knee ROM, our results indicated that the ROM degree in the FNB group was better than the other two groups at the first day after operation ($p < 0.05$, ANOVA) but was similar at the second day and the third day ($p > 0.05$, ANOVA, respectively) (Fig. 5). Daily mobilization distance and TUG test were used to evaluate the capacity for activity, and the results showed that MIA group was better at the first day than the other two groups ($p < 0.05$) and superior to the FNB group ($p < 0.05$) while similar to the ACB group ($p > 0.05$) at the second day. At the third, the MIA group was without significant difference to the ACB group ($p > 0.05$), but revealed a better outcome of daily mobilization distance when compared with the FNB group ($p < 0.05$) (Fig. 6a and b). Moreover, the MIA group had less postoperative hospital stays compared with the other two groups ($p < 0.05$, respectively) (Table 2).

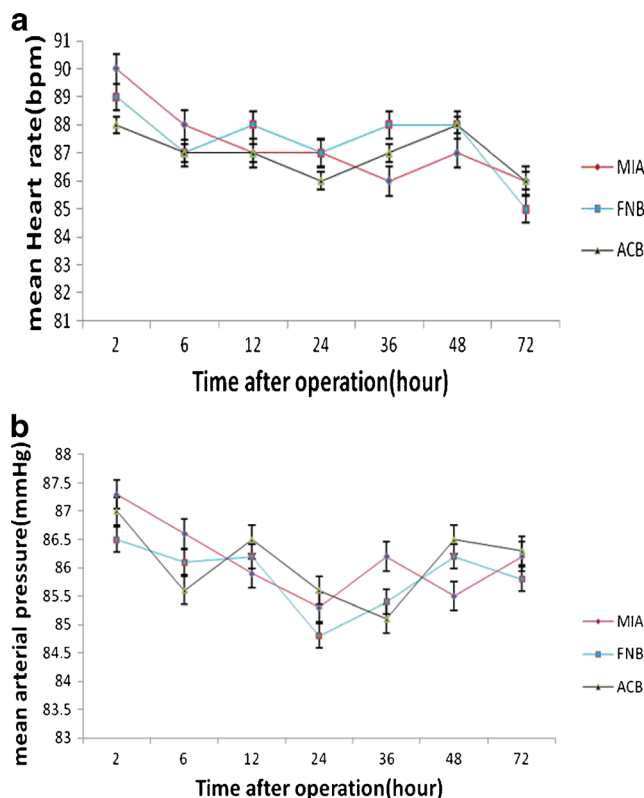


Fig. 3 Vital signs comparison among the three groups, presented as mean and standard error. (a) Mean arterial pressure and (b) Heart rate

Table 2 Other outcomes among the three groups

Parameter	Multi-site infiltration analgesia (n = 26)	Femoral nerve block (n = 27)	Adductor canal block (n = 24)	P values
Total operative time (min)	68.3 ± 7.5	76.6 ± 8.4	77.6 ± 8.2	* $p < 0.05$
Tourniquet time (min)	54.6 ± 6.5	56.1 ± 7.3	55.2 ± 6.9	$P = 0.66$
Incision drain (ml)	288.5 ± 97.6	276.4 ± 103.2	273.6 ± 101.5	$P = 0.32$
Opioid consumption (mg)	32.5 ± 21.7	38.3 ± 22.6	37.9 ± 20.6	* $p < 0.05$
Complication				
Nausea and vomit	2 (7.7 %)	3 (11.1 %)	2 (9.1 %)	& $P = 0.89$
Urinary retention	2 (7.7 %)	2 (7.4 %)	3 (12.5 %)	& $P = 0.78$
Postoperative hospital stays	3.6 ± 0.8	5.2 ± 1.0	4.9 ± 0.8	# $P < 0.05$
Patient satisfaction	8.3 ± 0.8	7.6 ± 1.1	7.4 ± 1.3	$P = 0.23$

* $p < 0.05$ means the total operative time in MIA group was shorter than the other two groups. # $p < 0.05$ means the postoperative hospital stays in MIA group was shorter than the other two groups. & presented as number and percent, and the P-values were calculated by chi-square and Fisher exact test

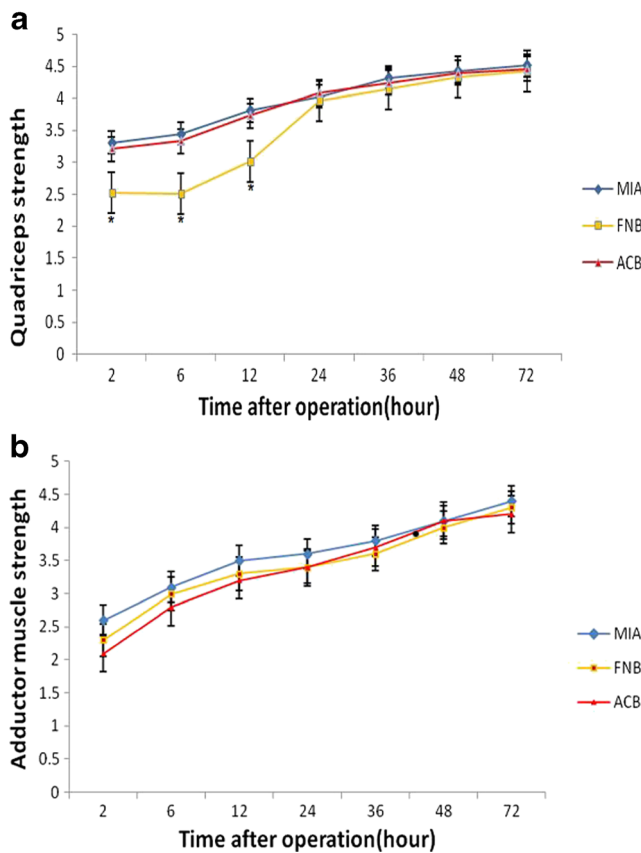


Fig. 4 Quadriceps strength (a) and hip adductor muscle strength (b) comparison among the three groups, presented as mean and standard error. * means $p < 0.05$ when FNB group compared with MIA group and ACB group in terms of quadriceps strength at 2 h, 6 h, 12 h after operation

Other outcomes

MIA groups showed less time of operation ($p < 0.05$) when compared with the FNB and ACB group. When the tourniquet time, incision drain, and patient satisfaction score were

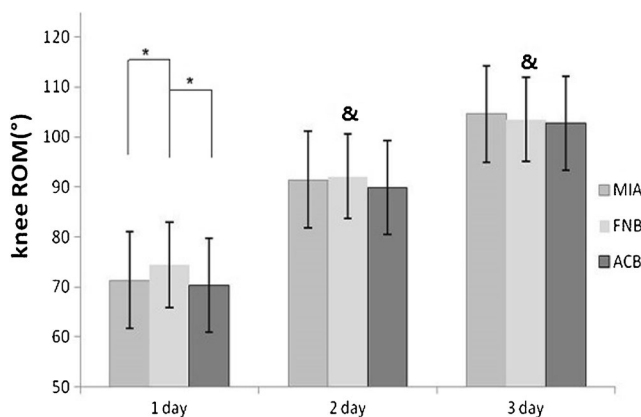


Fig. 5 Assessment of daily knee range of motion (ROM). * $p < 0.5$ when the two groups compared. & there is no significant difference among the three groups

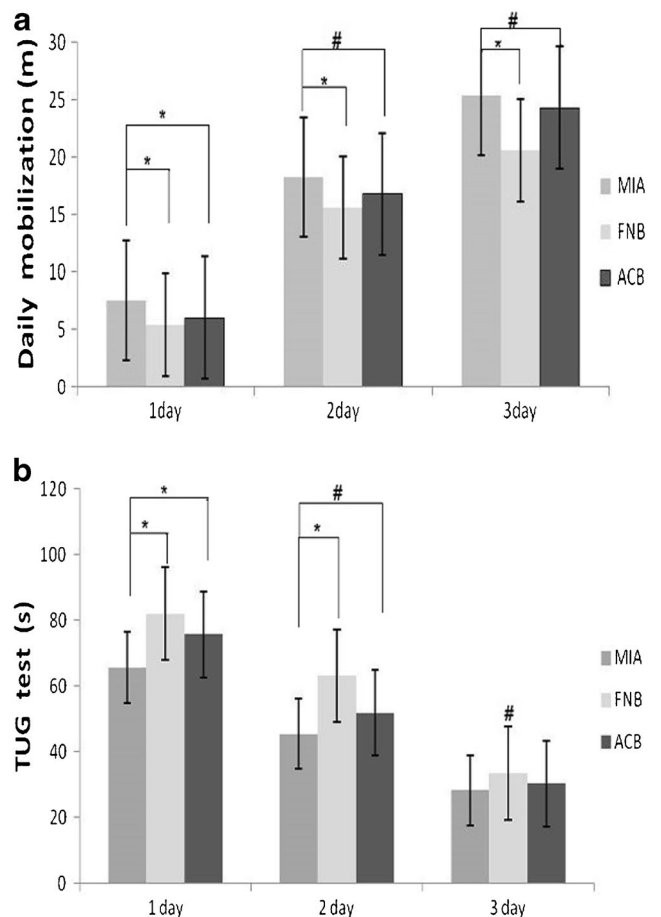


Fig. 6 (a) Daily patient mobilization recorded by the physiotherapist. (b) TUG test recorded with seconds. * $p < 0.5$ when the two groups compared. # $p > 0.05$ when the two groups are compared

evaluated there was no significant difference among the three groups ($p > 0.05$, respectively) (Table 2).

Discussion

Multimodal analgesia was a popular model for pain management for TKA. In our trial, we took analgesia measures from pre-operation to hospital discharge for patients and our results showed that all patients achieved good effects of pain control and functional recovery, but there were also some differences among the different analgesia protocol. In this study, MIA showed better pain control at rest during the first 12 hours and less opioid consumption after operation than the other two groups, and FNB was similar to ACB on these outcomes. While there are no significant differences in pain score with activity, vital signs and occurrence of complication among the three groups. When evaluated the early rehabilitation of MIA and ACB had similar outcomes on post-operative muscle strength, but they showed better quadriceps strength when compared to FNB. Although the knee ROM of the patients

with FNB showed a better result, their ambulation ability was inferior to those in the MIA group and FNB group early after the operation. Furthermore, MIA spent less time on operation and post-operative hospital stays when compared with FNB and ACB.

The comparison between LIA and nerve block on pain control for TKA had been conducted by a lot of researchers, but our study was the first time to combine intra-articular and peri-articular with wound infiltration analgesia and compare the pain management and early rehabilitation with the commonly used FNB and ACB at the same time. According to previous studies, some studies suggest LIA is superior to FNB on pain management [5, 32], some studies report an equal outcome between the two methods [9, 30, 31, 43], while other studies demonstrate LIA is inferior to FNB on pain control [44, 45]. Besides, Ashraf et al [46] conducted a RCT to compare intra-articular analgesia with single shot FNB after TKA and they demonstrated better pain control and less opiate consumption in patients that received LIA. While, Ali et al [33] suggest that continuous intra-articular analgesia after TKA has no relevant clinical effect on VAS pain and does not affect analgesic consumption, ROM, or leg-raising ability. In this trial, the MIA group showed better outcomes of pain control at the first 12 hours post-operatively with less opioid consumption, which indicated that MIA was effective in blocking the sensory nerve around the wound and can provide good performance in pain management. ACB has been reported to not be inferior to FNB on pain control by previous studies [19, 25, 47]. Although, Andersen et al [48] demonstrate that continuous saphenous nerve block that is equal to ACB [16] can act as a supplement to single-dose local infiltration analgesia for postoperative pain management after TKA, our study showed the MIA was superior to ACB when comparing the pain score between them directly. Severe pain after operation may lead to the changes of patients' hemodynamic [49], but our study revealed that vital signs were not concerning and the pain was well controlled. Furthermore, the complication occurrence and patients satisfactory score were all similar, which indicated the rehabilitation course of the three groups were all excellent.

Muscular strength is significant to post-operative exercise. Multiple studies have shown that ACB provides good performance on preserving the quadriceps strength to FNB, with no difference in opioid consumption, pain score, opioid adverse events, or mobilization ability [19, 23, 25, 48]. Some studies indicated ACB was a disadvantage in decreasing the adductor muscle [24, 25], while Saranteas et al [26] suggest that ACB does not influence the obturator nerve and the outcomes of many other studies also support this view [19, 23, 48]. In our RCT, ACB showed a better outcome of quadriceps strength compared with FNB and the adductor muscle strength is similar, which conformed to the literature and is very encouraging. Besides, the MIA was as good as ACB on muscle

strength. When evaluating the range of the knee, the FNB group was better than MIA and ACB. This was an unexpected result and may be caused by limited cases or the lost tone of the quadriceps muscle to help in gaining early range of motion. Quicker recovery requires patients achieving a fast post-operative mobilization [1–3]. According to our study, the outcomes of the daily mobilization and TUG test (s) revealed that MIA was superior to the ACB and FNB after operation but the ACB was better than FNB, which indicated that nerve block may be effective on pain control but it might reduce the strength of the related muscle and delay the post-operative mobilization and hospital stays.

This RCT was first conducted to compare the multi-site infiltration analgesia with femoral nerve block and adductor canal block after TKA directly and evaluated both the pain management and early rehabilitation. It has some strengths, but there were also limitations in this trial. First, the included objects were relatively small and studies with larger sample size are needed in the future. And then, we only studied the single-shot analgesia and whether continuous methods would have the same outcome is hard to say. Last but not least, we just used the general parameter to assess the pain management and early rehabilitation. More effective evaluation methodology should be put into research in further studies.

Conclusions

ACB was not inferior to FNB on pain control, but it was better on early mobilization. However, MIA that combine intra-articular and periarticular with wound infiltration analgesia after TKA were more effective on pain control at rest, with better efficacy on early rehabilitation and easier to perform when compared with these commonly used nerve blocks. We recommended our MIA for pain relief and fast rehabilitation after TKA.

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Compliance with ethical standards

Conflict of interest None.

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