# Effect of Femoral Nerve Block with Different Concentrations of Chloroprocaine on the Recovery of Joint Function in Rehabilitation Training after Knee Replacement: A Prospective, Double-Blind, Randomized, Controlled Clinical Study

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**Research Article**

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# Abstract

**Background:** Patients who undergo total knee arthroplasty (TKA) experience severe pain after surgery. Especially active pain in early postoperative rehabilitation training of the knee joint is particularly severe, and it should receive people’s attention.

**Methods:** A total of 90 patients who only received unilateral TKA in our hospital were randomly and equally divided into three groups (group C1: 1% chloroprocaine, group C2: 2% chloroprocaine, and group NS: 0.9% sodium chloride solution 0.2 ml/kg; the dosage was fixed at 0.2 ml/kg for all three groups). All patients received femoral nerve catheterization before TKA and started rehabilitation training 48 h after TKA. The visual analogue scale (VAS) scores of active exercises before and after administration were observed and recorded. VAS scores, maximum knee flexion and extension angles, the incidence of knee flexion angle ≥100° in each group, the American knee society(AKS) scores, together with postoperative rehabilitation training satisfaction and adverse effects were recorded at 7 days and 3 months after surgery.

**Results:** Compared with the NS group, VAS scores after administration of patients in the group C1 and C2 were decreased significantly at each time point ($P < 0.05$), and the maximum knee flexion angles were increased significantly ($P < 0.05$), as well as the proportion of maximum knee angle ≥100° ($P < 0.05$). The postoperative rehabilitation training satisfaction of patients in group C1 and C2 were more than that of patients in the NS group ($P < 0.05$).

**Conclusion:** The administration of 1% chloroprocaine for femoral nerve block before rehabilitation training after TKA could improve the knee flexion angle at the early postoperative stage, increase the proportion of patients who could squat, and cause fewer side effects.


# Introduction

End-stage knee joint disease seriously affects the quality of life of the patients and causes great pain. At present, knee replacement is one of the effective methods to restore knee function. Besides the influence of surgery, the early postoperative rehabilitation exercises play an important role in the recovery of knee joint function after surgery. It is difficult to complete essential rehabilitation training because of postoperative trauma and pain. The quality of completed rehabilitation training is unsatisfactory. Thus, a small number of patients might have joint stiffness that affects the normal movement of joints and increases the risk of paralytic ileus, urinary retention, and deep vein thrombosis [1]. Therefore, administration of good analgesia intervention has become the focus and difficulty in early functional exercises after total knee arthroplasty (TKA).

Postoperative analgesia can be used to reduce the pain during rehabilitation training after TKA, and a better functional exercise of the knee joint could be carried out, which has already been reported [2–4]. It is believed that the administration of an appropriate dose of local anesthetics to block the femoral nerve can significantly reduce the pain during rehabilitation training and help the patients to overcome their fear of training. However, there is no literature introducing the whole process of postoperative functional exercise, especially the influence of the control of active pain 72 h after surgery on knee joint function, as well as the evaluation of functions that are important in daily life, such as squatting. As a short-acting local anesthetic, chloroprocaine has the characteristics, such as fast onset, strong analgesic efficacy, rapid metabolism, synchronous recovery of motor sensation after drug withdrawal, and low toxicity. In real clinical practice, the recommended concentration for nerve block is 1–2%, but the appropriate concentration and dose for femoral nerve block for post-TKA rehabilitation training have not been studied. The purpose of this study was to investigate the effect of femoral nerve block with different concentrations of chloroprocaine on rehabilitation training after TKA.

## Material And Methods

# Study Design and Participants

Patients scheduled for primary unilateral TKA in our hospital from September 2017 to December 2019 were selected for the study. The exclusion criteria were as follows: A history of TKA, American Society of Anesthesiologists (ASA) classification III-V, age less than 65 y or more than 80 y, allergy to morphine or local anesthetic, continuous use of analgesics for two weeks or more, history of gastrointestinal ulcers or bleeding, peripheral neuropathy, morbid obesity [Body Mass Index (BMI) $> 30$ kg/m$^2$], platelet count $<$ $8\times10^9$/L, coagulation dysfunction, puncture site infection, history of mental illness, and inability to understand visual analog scale (VAS). A total of 90 cases were enrolled and divided into three groups via computer-generated randomization. Large angle rehabilitation training of the knee joint began 48 h after the operation. Before training, 1% chloroprocaine 0.2 ml/kg (group C1), 2% chloroprocaine 0.2 ml/kg (group C2), or 0.9% sodium chloride solution 0.2 ml/kg (group NS) was given through femoral nerve catheterization.

# Femoral Nerve Catheterization

After entering the operation room, the patient was monitored by pulse oximetry, non-invasive blood pressure, and ECG, and then the vein was opened. Guided by a 12-mHz high-frequency linear probe (HFL 50/13 – 6 MHz, M-Turbo, SonoSite, Bothell, WA, USA) and a nerve stimulator (Stimuplex HNS 11, B Braun Medical, Melsongen, Germany), a femoral nerve catheter was introduced into the patient using a nerve stimulator kit (lot no. 1290, Pajunk, Geisingen, Germany).

After local infiltration anesthesia of the skin, a stimulating needle was inserted at a 30°–45° angle to the skin about 0.5 cm outside of the ultrasonic probe using an in-plane technique. When the needle tip reached near the femoral nerve, the nerve stimulation current was turned on to 0.5 mA to induce quadriceps contraction or patellar lift. After the current was reduced to 0.3 mA that still led to the above reactions, 0.9% sodium chloride solution 10 ml was injected, and a nerve catheter was inserted for about 11 cm. Then the puncture needle was removed and the catheter secured properly. When administration of 1% lidocaine hydrochloride injection 15 ml could decrease the pain or temperature sensation of skin on the surface of the knee joint within 15 min, the catheterization was confirmed to be successful; otherwise, the catheter was excluded.

# Rehabilitation Training Methods

This was a double-blind, randomized, controlled study in which neither the subjects nor the trainers were aware of the drug used. The patients were randomly allocated to 1 of the 3 groups (group C1: 1% chloroprocaine 0.2 ml /kg, group C2: 2% chloroprocaine 0.2 ml/kg, and group NS: 0.9% sodium chloride solution 0.2 ml /kg) via computer-generated randomization conducted by a team member who was not involved in operations or rehabilitation training after surgery. This member prepared opaque envelopes in which the intervention type was concealed. These envelopes were opened a few minutes before attempting ultrasound-guided femoral nerve catheterization. Patients were anesthetized prior to surgery by 1 of the 2 physicians. Combined lumbar epidural anesthesia in the lumbar 3–4 intervertebral space was selected. The knee drainage tube and epidural analgesia pump (long-acting low-concentration local anesthetic + morphine/hydromorone) were removed 48 h after the operation, and large angle rehabilitation training of the operative limb was started. Training and patient assessment were carried out by other members of the team who did not participate in randomization and anesthesia procedures. Flurbiprofen axetil injection 100 mg was administered routinely for intravenous analgesia twice a day in the morning and afternoon. Before rehabilitation training, each participant underwent pulse oximetry, non-invasive arterial blood pressure, and electrocardiogram monitoring, followed by injection of corresponding drugs into the femoral nerve catheter. After 10 min, the patients were instructed to complete rehabilitation training (flexion and extension of the knee joint). The training began with passive movement in which the researcher could help the patients to overcome fear and direct them to move the affected limbs followed by active movement. They received femoral nerve block and training three times every day, and the interval between each administration was at least 4 h. One group of exercises was performed after each block on days 1 and 2 of rehabilitation training, and each group of exercises included 10 active and 10 passive exercises. Two groups of exercises were performed from day 3 of rehabilitation training. After completing the whole training, the femoral nerve catheter was removed.

# Outcome Measures

VAS scores (scores 0–10: 0 = no pain, 1-2-3 = mild pain, 4-5-6 = moderate pain, 7-8-9 = severe pain, and 10 = worst possible pain) of the three groups of patients were recorded during active exercises at the third time of training before (after) and after (before) administration on postoperative day 3 (3 d), day 4 (4 d), day 5 (5 d), and day 6 (6 d). VAS scores for active exercises as well as maximum knee flexion and knee extension angles, the incidence of knee flexion angle ≥ 100° in each group, and AKS scores on the 7th day (7d) and 3 months (3m) after surgery were recorded, as well as postoperative rehabilitation training satisfaction (scores 0–10: 0-1-2 = very dissatisfied, 3-4-5 = dissatisfied, 6–7 = generally satisfied, 8–9 = satisfactory, and 10 = very satisfied) and adverse effects (nausea, vomiting, irritability, drowsiness, confusion, decreased muscle strength, and other complications related to the nervous system) after anesthesia during rehabilitation training. The landmarks used to measure the angles were the greater trochanter of the femur, the proximal head of the fibula, and the lateral malleolus[5].

# Statistical Analysis

Data were statistically analyzed using SPSS 25.0 software. Patients' age, BMI, maximum knee flexion and knee extension angles, VAS score, AKS score, and rehabilitation training satisfaction belonged to quantitative variables, which were expressed as the mean and standard deviation; and all of them were in accordance with normal distribution. One-way analysis of variance was used for comparison between groups, and the Least-Significant Difference method was used for pairwise comparison. Gender composition, ASA classification, limb composition, and incidence of maximum knee flexion angle ≥ 100° in each group were count data, and they were compared between groups using the $\chi^2$ test. Significance was set at $P < 0.05$.

# Sample Size Estimation

According to the pre-experiment results, the mean of maximum knee flexion angles in the group C1, C2 and NS on the 7th day after surgery were 102.5 ± 7.1°, 103.8 ± 6.2° and 97.7 ± 5.8°, respectively. The sample size of each group calculated by PASS 15 software was 25 cases to provide 80% power with a two-sided alpha value of 0.05. A sample size of 30 participants per group was needed, assuming a 20% dropout rate.

## Results

Finally, 80 patients were left for analysis (as shown in Fig. 1). In group C1, three patients were lost to follow-up, one patient had femoral nerve catheter blockage, and one patient withdrew due to postoperative delirium. In group C2, one patient was lost to follow-up, and one patient pulled out the femoral nerve catheter accidentally. In group NS, two patients refused training due to severe pain, and one patient unexpectedly pulled out the femoral nerve catheter .

# Comparison of the Information on Characteristics Among the Three Groups

There were no significant differences in gender, ASA physical status, age, body mass index (BMI), and limb composition among the three groups ($P > 0.05$), as shown in Table 1.

Table 1 Patient Characteristics Information

| Group | C1<br>(n = 25) | C2<br>(n = 28) | NS<br>(n = 27) | F/ $\chi^2$ | *P* Value |
|---|---|---|---|---|---|
| Gender<br>Male<br>Female | 8<br>17 | 10<br>18 | 7<br>20 | 0.623 | 0.733 |
| ASA physical status<br>[illegible]<br>[illegible] | 9<br>16 | 6<br>22 | 7<br>20 | 1.457 | 0.483 |
| Age(year)<br>Mean ± SD | 70.6 ± 3.7 | 71.5 ± 3.8 | 71.7 ± 4.7 | 0.547 | 0.581 |
| Body mass index(kg/m²)<br>Mean ± SD | 24.5 ± 3.0 | 25.7 ± 2.7 | 25.8 ± 2.3 | 1.852 | 0.164 |
| Limb composition<br>Left knee<br>Right knee | 9<br>16 | 7<br>21 | 13<br>14 | 3.188 | 0.203 |

Abbreviation: C1, 1% Chloroprocaine; C2, 2% Chloroprocaine; NS, 0.9% sodium chloride solution; ASA, American Association of Anesthesiologists.

## Comparison of Postoperative VAS Scores

There were no significant differences in VAS scores before administration at each time point in three groups ($P > 0.05$),as shown in Fig. 2A. VAS scores after administration of patients in group C1 and C2 were decreased significantly compared with those in group NS at each time point ($P < 0.05$), as shown in Fig. 2B.

### Comparison of the Maximum Knee Flexion Angles and Knee Extension Angles Among the Three Groups

The maximum flexion angles of patients in groups C1 and C2 on the 7th day and 3 months after surgery were significantly higher than those of patients in the NS group ($P$<0.05). There was no significant difference in the maximum knee extension angle among the three groups at these two-time points ($P$>0.05), as shown in Fig. 3.

### Comparison of the Incidence of the Maximum Knee Flexion Angle ≥100° Among the Three Groups of Patients on the 7th Day and 3 Months after Surgery

Compared with group NS, patients in groups C1 and C2 had a higher incidence of maximum knee flexion angle ≥100° on the 7th day (as shown in Fig. 4A) and 3 months after surgery (as shown in Fig. 4B) ($P$<0.05).

### Comparison of the AKS Scores among the Three Groups on the 7th Day and 3 Months After Surgery

AKS knee and functional scores showed no significant difference among the three groups on the 7th day and 3 months after surgery ($P$>0.05), as shown in Table 2.

### Comparison of VAS Scores and Rehabilitation Training Satisfaction in the Three Groups on the 7th Day after Surgery

The VAS scores of patients in the three groups on the 7th day after the operation showed no significant difference ($P$>0.05), while patients in groups C1 and C2 showed higher rehabilitation training satisfaction than those in group NS ($P$<0.05), as shown in Table 2.

Table 2
Comparison of the AKS scores and rehabilitation training satisfaction among the patients of three groups

| Group | | C1 (n = 25) | C2 (n = 28) | NS (n = 27) | *F* | *P* Value |
|---|---|---|---|---|---|---|
| VAS scores on the 7th day after surgery | | 3.2 ± 1.0 | 3.1 ± 1.1 | 3.8 ± 1.6 | 2.598 | 0.081 |
| AKS scores on the 7th day after surgery | Knee score | 66.8 ± 7.5 | 64.7 ± 5.7 | 65.1 ± 7.7 | 0.633 | 0.534 |
| | Functional score | 39.2 ± 10.0 | 40.7 ± 7.0 | 36.3 ± 8.4 | 1.912 | 0.155 |
| AKS scores 3 months after surgery | Knee score | 86.4 ± 5.1 | 88.3 ± 5.3 | 87.1 ± 6.7 | 0.782 | 0.461 |
| | Functional score | 82.8 ± 12.4 | 79.6 ± 14.0 | 74.3 ± 14.1 | 2.660 | 0.076 |
| Rehabilitation training satisfaction | | 8.7 ± 1.2** | 8.6 ± 1.1** | 7.3 ± 1.6 | 8.957 | 0.002 |

Values reported as mean ± SD. Compared with Group NS, *$P$ < 0.05, **$P$ < 0.01.

Abbreviation: C1, 1% Chloroprocaine; C2, 2% Chloroprocaine; NS, 0.9% sodium chloride solution; VAS, Visual Analogue Scale; AKS, American Knee Society.

### Comparison of Adverse Reactions

One patient had difficulty in active knee movement during training in group C1, while in group C2, six patients had the same problem. However, all patients returned to the normal level 1 h after administration.

There were no postoperative adverse reactions, such as nausea, vomiting, restlessness, drowsiness, unconsciousness, and other complications of the nervous system after anesthesia.

# Discussion

According to the results, the knee flexion angles of patients in groups C1 and C2 on the 7th day and 3 months after surgery were better than those of patients in the control group, and the pairwise comparison also showed a significant difference. At this time, the knee flexion angle was obtained on the basis that no local anesthetic was used after removing the femoral nerve catheter, and the VAS scores of the three groups showed no significant difference, which could be considered as an evaluation in a completely natural state and of high value for the analysis of recent knee joint function. In group NS, the standard deviation of the flexion angle on the 7th day after surgery was relatively large, and some patients could achieve an angle of 120°, while some patients could only achieve an angle of about 90°. One of the reasons was the individual's pain tolerance during training. The standard deviation of the flexion angle at 3 months after surgery did not decrease, which may be strongly associated with the influence of periarticular adhesion and psychological factors during training. Therefore, during postoperative rehabilitation training, femoral nerve block before training can improve the effect of rehabilitation training, especially in patients with poor pain tolerance. Escramilla et al.[6] believed that knee flexion angle above 100° is considered to be able to squat, which enables people to complete the movements of kneeling and cross-legged sitting, which can greatly improve the standard of daily life. Thus, in our study, we further compared the number of patients with a knee flexion angle above 100° in the three groups, and we found that there were more patients in groups C1 and C2 than in the control group on the 7th day and at 3 months after surgery. AKS scoring is a commonly used method to evaluate knee joint function [7,8]. In our study, AKS scores on 7$^{th}$ day and at 3 months after surgery showed no significant difference among the three groups, which was consistent with the results reported by Sakai et al. [9]. We took into account that active pain occupies a greater weight in the AKS knee score, and the functional score mainly focuses on daily basic functions (walking and stairs) without squatting and other actions. If there is little difference in active pain among the patients of different groups or the knee flexion angles reach above 90°, then the function of the knee joint cannot be further distinguished. Therefore, the evaluation of the effect of knee rehabilitation training after surgery should have a specific scale to make the evaluation more scientific and reasonable. Previous studies [9,10] have focused on continuous femoral nerve block (CFNB) continuous infusion within 3 days after surgery. It is believed that the enhancement effect of CFNB on postoperative training is mainly through reducing postoperative pain, postoperative knee swelling, and muscle spasms.

Local anesthetics play an important role in the recovery of knee joint function by reducing peripheral inflammation[11,12] and inhibiting the release of pro-inflammatory mediators[13,14]. Combined with the results, the VAS score at 3–6 days after the operation still showed active pain; thus, it was more significant to continue the use of nerve block to reduce the inflammatory response at this stage to achieve a better training effect.

A possible decline in the quadriceps femoris muscle strength is considered as a defect of CFNB [15,16]. Ilfeld et al. [17] believed that continuous infusion will cause a decrease in the quadriceps muscle strength, while other researchers [18,19] believed that it can improve the postoperative walking training ability and achieve the rehabilitation standards earlier. However, if local anesthetics affect the quadriceps muscle strength for a long time, it will not only increase the risk of falling, but it is also not conducive to early joint function exercise. Therefore, in this study, chloroprocaine with an onset time of 6–10 min and a duration of action of about 45–60 min was used as a local anesthetic. The results showed that one patient in group C1 and six patients in group C2 had difficulty in active knee joint movement during training due to the quadriceps femoris muscle weakness. It interfered with the training by waiting for the quadriceps muscle strength to recover before the training was performed during active joint movement. All of them returned to normal levels about 1 h after administration. However, it remains to be explored whether it is possible to further reduce the concentration of chloroprocaine combined with a certain amount of non-steroidal drugs to avoid the impact on quadriceps muscle strength while maintaining optimal analgesia. Adductor canal block (ACB) is considered to be a blocking method that can retain femoral nerve analgesia and has little influence on quadriceps femoris muscle strength [20]. However, some authors believed that femoral nerve block (FNB) was associated with the perception of less severe pain after TKAs [21]. Kim et al. [22] reported that FNB may be superior to ACB in analgesic intensity. From the results, the active pain is still very severe during rehabilitation training, and some patients achieve the degree of severe pain. The effect of ACB may not be as good as that of FNB, and further study is needed.

Long-term CFNB is considered to have a risk of infection [9,10] ; thus, there are very few literary works on CFNB for more than 3 days. In this study, it took 6 days to remove the femoral nerve catheter from the insertion of the catheter, and none of the patients had local or systemic infections. This is closely related to strict aseptic operation during catheterization, and two sessions of disinfection during rehabilitation training and replacement of the film.

A total of 90 patients were enrolled in this study, among which 4 cases were lost to follow-up, 1 case developed femoral nerve catheter blockage, 2 cases pulled out the catheter unexpectedly, 1 case withdrew due to postoperative delirium, and 2 cases refused training. Other shortcomings were that only relatively old (65–80 years old) and ASA I-II grade patients were taken as subjects, and there was no further study of postoperative rehabilitation in the elderly and patients with poor physical condition. In addition, obese patients were not included in the study, and the effect of this method on postoperative recovery in this population could not be analyzed. In the next step, we can continue to study these two populations.

# Conclusion

In conclusion, in the early rehabilitation training after TKA, injection of 1% chloroprocaine 0.2 ml/kg through a femoral nerve catheter can improve the early postoperative knee flexion angle with fewer side effects.

# Abbreviations

TKA: Total Knee Arthroplasty; C1: 1% Chloroprocaine; C2: 2% Chloroprocaine; NS: 0.9% sodium chloride solution; VAS: Visual Analogue Scale; AKS: American Knee Society; ASA: American Association of Anesthesiologists；BMI: Body Mass Index; CFNB: Continuous Femoral Nerve Block; FNB: Femoral Nerve Block; ACB: Adductor canal block.

# Declarations

### Ethics approval and Consent to participate

This study was approved by the Ethics Committee of the authors' affiliated institution (Medical Technology Review No. 2017-09-72).The trial was registered prior to patient enrollment at Chinese Clinical Trial Registry (ChiCTR-INR-17012787, 25/09/2017). All participants were informed about the study and written consents were obtained.

### Consent for publication

All authors made an agreement for publication.

### Availability of data and materials

All data are available from the corresponding author on reasonable request.

### Competing interests

The authors have no conflicts of interest to declare.


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### Authors' contributions

JJL conceived and designed the study, analysed and interpreted of data and drafted the article. RQX, CCZ, HW, HRL and ZHW helped to acquire the data. HXW helped to revise the draft. JL provided administrative and technical support. JFM conceived and designed the study, submitted protocol to Ethics and Governance, provided administrative and technical support. All authors read and approved the final manuscript.


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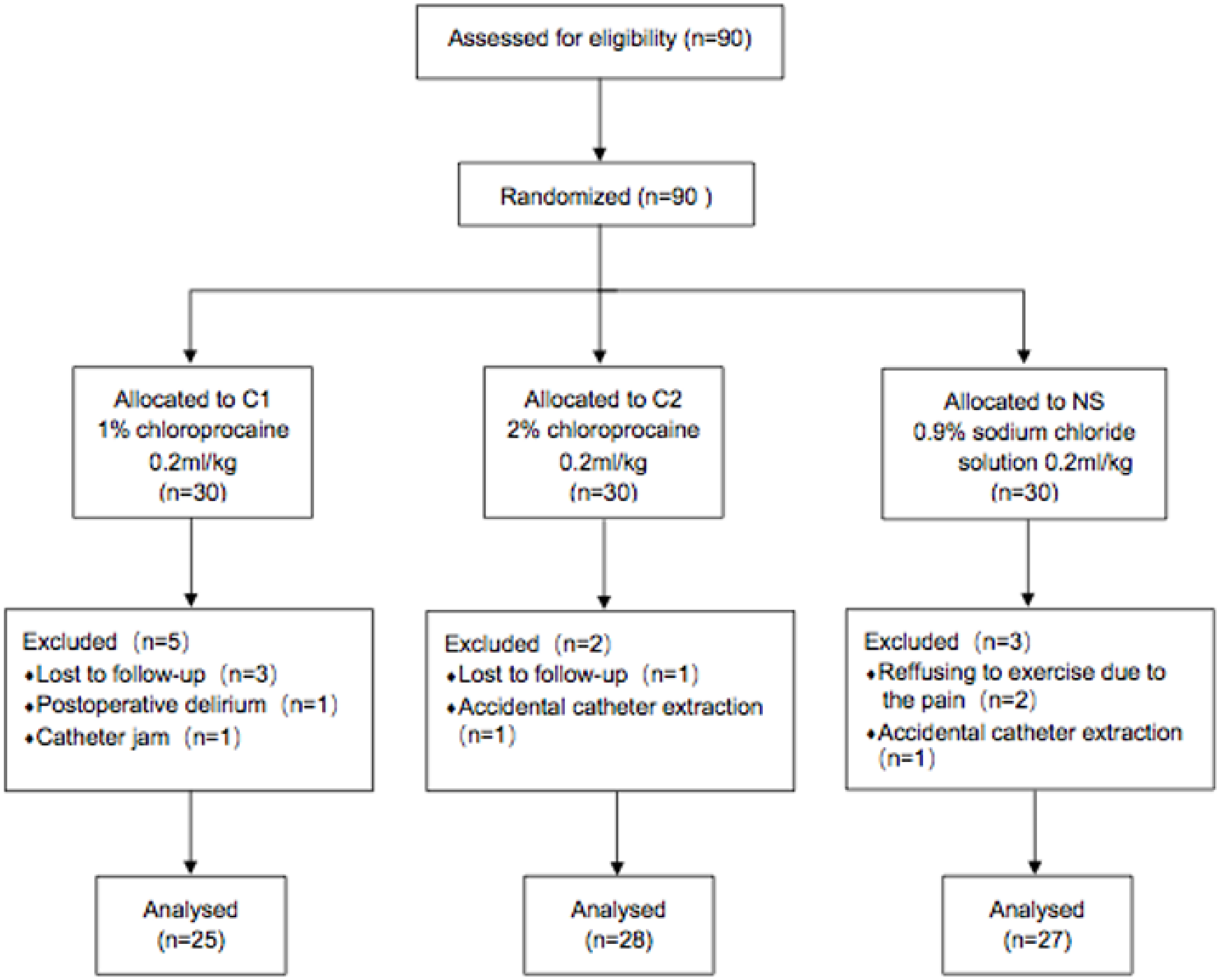
# Figures




## Figure 1

Consort flow diagram for study participation. C1 indicates 1% Chloroprocaine; C2, 2% Chloroprocaine; NS, 0.9% sodium chloride solution.

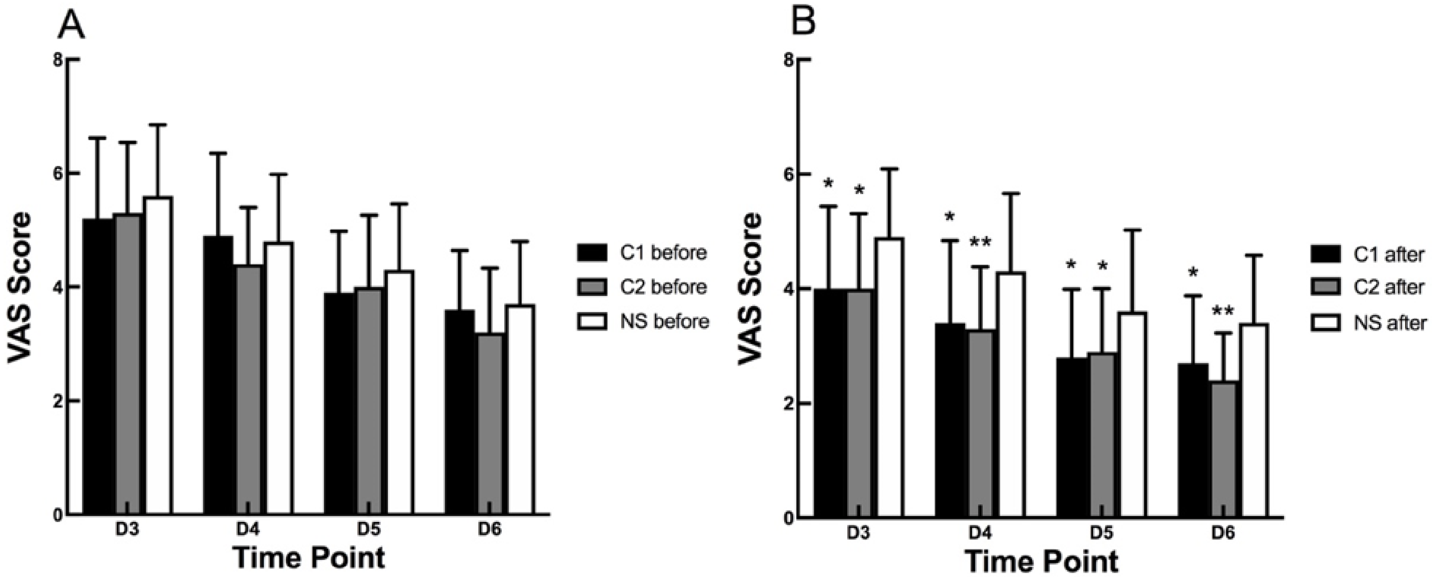



**Figure 2**

VAS scores of three groups before and after administration. A, VAS scores of group C1. B, VAS scores of group C2. C, VAS scores of group NS.Compared with Group NS, *P<0.05, **P<0.01. C1 indicates 1% Chloroprocaine; C2, 2% Chloroprocaine; NS, 0.9% sodium chloride solution; VAS, Visual Analogue Scale; 3d, postoperative day 3; 4d, postoperative day 4; 5d, postoperative day 5; 6d, postoperative day 6.

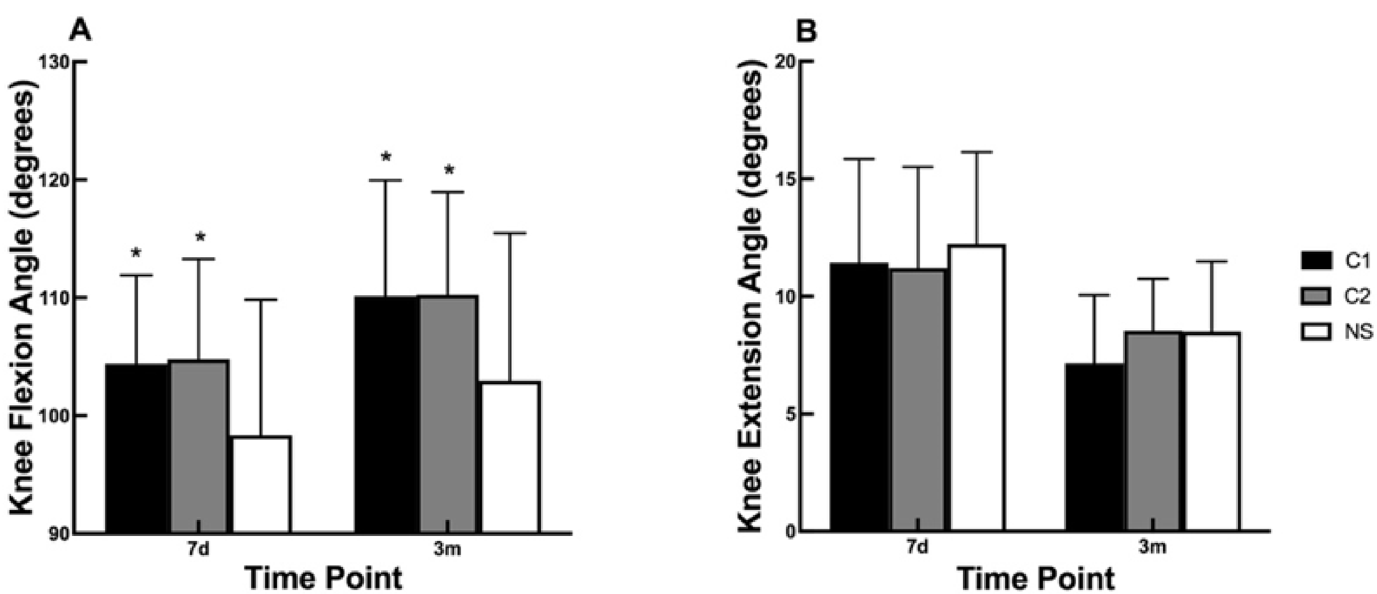
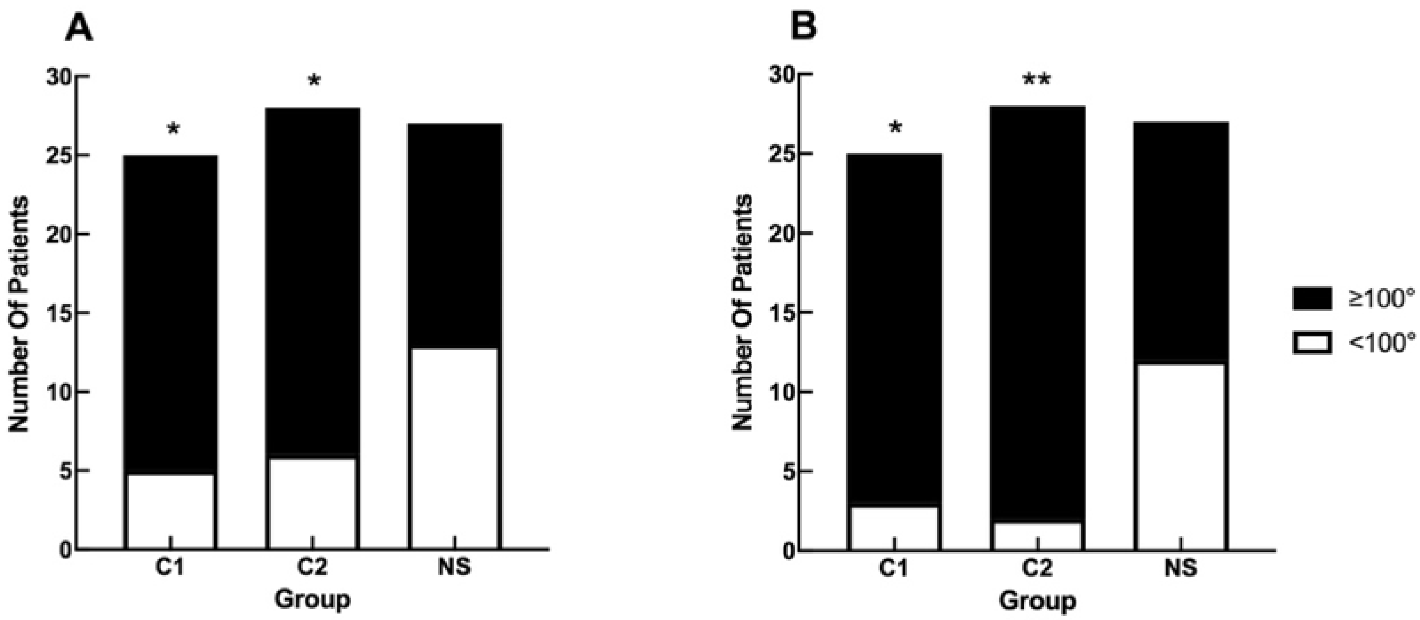



**Figure 3**

Knee activity of three groups 7th day after surgery and 3 months after TKA. A, knee flexion angles of three groups 7th day after surgery and 3 months after TKA. B, knee extension angles of three groups 7th day after surgery and 3 months after TKA. Compared with Group NS, *P<0.05, **P<0.01. TKA indicates Total

Knee Arthroplasty; C1, 1% Chloroprocaine; C2, 2% Chloroprocaine; NS, 0.9% sodium chloride solution; 7d, 7th day after surgery; 3m, 3 months after surgery.




## Figure 4

Comparison of the incidence of maximum flexion Angle ≥100 degrees in patients of three groups on the 7th day after surgery and 3 months after TKA. A, the incidence of maximum flexion Angle ≥100 degrees in patients of three groups on the 7th day after surgery. B, the incidence of maximum flexion Angle ≥100 degrees in patients of three groups 3 months after surgery. Compared with Group NS, *P<0.05, **P<0.01. TKA indicates Total Knee Arthroplasty; C1, 1% Chloroprocaine; C2, 2% Chloroprocaine; NS, 0.9% sodium chloride solution.