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ORIGINAL ARTICLE

Effects of the nontourniquet combined with controlled hypotension technique on pain and long-term prognosis in elderly patients after total knee arthroplasty: a randomized controlled study

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Abstract

Purpose The aim of this study was to confirm the alleviating effects of the nontourniquet technique on the postoperative acute and chronic pain of patients after total knee arthroplasty (TKA).

Methods 122 elderly patients undergoing TKA were randomly divided into two groups: group T ($n=58$) and group H ($n=64$). An electronic inflatable tourniquet was used during TKA in group T. The patients in group H received controlled hypotension but without tourniquet use during the operation. The numeric rating scale (NRS) score was used to evaluate pain level on day 1, day 2, day 3 and day 7 after the operation, and the incidence of chronic pain was judged at 3-month and 1-year follow-ups, and functional recovery of the knee joint was estimated by the active range of knee joint motion (AROM) at the same time points. Cognitive function was assessed by the montreal cognitive assessment scale (MoCA) for 7 days after operation.

Results There were no significant differences in the NRS scores and AROM for 7 days after surgery. The incidence rate of chronic pain in group H (25.0%) was lower than that in group T (41.4%) and the AROM in group H was greater at one year follow-up. The MoCA score in group H was lower than that in group T on day 1 and day 2.

Conclusion The nontourniquet combined with controlled hypotension technique can alleviate chronic pain and promote the long-term rehabilitation of patients after TKA.

Keywords Nontourniquet · Controlled hypotension · Knee arthroplasty · Pain · Cognitive impairment

Introduction

Total knee arthroplasty (TKA) is one of the main surgical methods for severe knee joint lesions in elderly patients, and extensive soft tissue release and osteotomy during TKA can cause massive bleeding and severe pain [1–3]. To reduce bleeding and obtain a good surgical field, TKA is often performed under tourniquet [4]. However, the use of tourniquet can cause muscle ischemia and ischemia reperfusion injury, which may further aggravate pain [5]. Acute pain is one of the main factors restricting early functional exercise and the recovery of knee joint function. TKA without tourniquet technology has been considered and adopted to avoid tourniquet-related injuries [6]. The effects of nontourniquet techniques on acute and chronic pain in elderly patients remain unclear.

In addition, the main concern for nontourniquet technology is bleeding during operation [7]. Controlled hypotension is an important technology that has been widely used in orthopedic surgery to reduce bleeding. Intraoperative hypotension and tourniquet-related ischemia reperfusion injury are possible risk factors for cognitive impairment in elderly patients after TKA [8]. It is necessary to assess impacts of controlled hypotension and nontourniquet techniques on the cognitive function and long-term prognosis of elderly patients after TKA.

The purpose of this study was to reveal the advantages of the nontourniquet technique in relieving acute pain and long-term chronic pain after TKA and to compare the effect of the controlled hypotension and the tourniquet technique on the cognitive function and prognosis of patients after TKA.

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Methods

Patients and grouping

This study was a prospective randomized controlled study lasting 2 years. The protocol was approved by the ethics committee of the First Affiliated Hospital of Chongqing Medical University (2012-2-21) and registered at ClinicalTrials.com (NCT02576015).

Patients who were 60–85 years old, undergoing unilateral TKA, NYHA classification I–III, and ASA physical status I–III, were eligible for this study. The exclusion criteria were severe cardiovascular or cerebrovascular diseases, illiteracy, mental illness, cognitive impairment, and refusal to participate in the study. Informed consent was obtained from all patients. The elimination standards were a change of operative mode and missing contact information. The patients were randomly divided into two groups according to whether tourniquet was used during knee arthroplasty: tourniquet group (group T) and nontourniquet hypotension group (group H).

Anesthetic strategies and monitoring

The patients in both groups were anesthetized by general anesthesia. General anesthesia induction drugs included midazolam 0.5 mg/kg, propofol 1.5 mg/kg, sulfentanyl 0.5 μg/kg and rocuronium 0.8 mg/kg by intravenous bolus injection. Intermittent injection of rocuronium 10 mg per 40–60 min, continuous intravenous infusion of remifentanil 0.1–0.3 μg/kg/min and propofol 2–4 mg/kg/h, and continuous inhalation of sevoflurane were used for anesthesia maintenance.

The Narcotrend Index (NTI) and spectral edge frequency (SEF maintained at 2–12 Hz) were monitored by the Anesthesia/EEG Awareness Deep Monitoring Instrument (Narcotrend-Compact, MT Monitor Technik GmbH Co. KG, D-24576 Bad Bramstedt, Germany) to assess the depth of anesthesia. The NTI of anesthesia depth was maintained at grade D (value: 46–57). The mean arterial pressure (MAP) was monitored directly through radial artery cannulation and maintained at no less than approximately 80% of the baseline in group T. Sodium nitroprusside was used for controlled hypotension from skin incision to joint prosthesis implantation in group H, and the MAP was maintained at 70–80% of the baseline, and the MAP was maintained above 80 mmHg to ensure the perfusion of vital organs.

Surgical procedures

All patients underwent TKA using a standardized technique and process. The tourniquet was tied on the operative side thigh of patients during TKA in group T; the pressure was systolic blood pressure (SBP) plus 100 mmHg. The patients underwent TKA without tourniquet binding in group H. The orthopedic surgeon injected 20 ml of a 'cocktail mixture' into the posterior capsular ligament, peripheral capsular ligament and ligamentum patellae before the artificial prosthesis was embedded to relieve pain and inflammation. The formula for the 'cocktail' is as follows: ropivacaine 100 mg, tranexamic acid 3 g, adrenaline 3 drops, methylprednisolone 40 mg, and in a total volume of 20 ml with the addition of normal saline.

Postoperative analgesia

A femoral nerve block was implemented for patients in both groups. The femoral nerve block was performed under the guidance of ultrasound before general anesthesia induction. The first dose was 0.20% ropivacaine (20 ml), and then a catheter was inserted for postoperative continuous patient-controlled femoral nerve block analgesia (PCA). We checked the effect of femoral nerve block before general anesthesia induction, pain disappeared during needling in front of the knee joint, and normal quadriceps femoris muscle myodynamia was considered satisfactory. We started PCA through a preimplanted femoral nerve catheter for patients after surgery when the anesthetic analgesics were stopped. The total volume of local anesthetic for PCA was 0.17% ropivacaine 300 ml; the PCA parameters were a background dosage of 5 ml per hour, a pressing supplementary dose of 5 ml, and a lockout time of 45 min.

Data collection and definitions

The 11-point, from 0 (no pain) to 10 (worst pain imaginable), numeric rating scale (NRS) was used to assess the degree of pain (representation by NRS score), which was evaluated before the operation and on day 1, day 2, day 3, and day 7 after the operation. The active range of motion (AROM) of the operative side knee joints was evaluated before the operation and on day 1, day 2, day 3, and day 7 after the operation. All patients were followed up for 1 year after the operation to evaluate the AROM and NRS scores. Chronic pain was diagnosed if the patient still felt pain (NRS score was 1–3 points at a resting state or more than 3 points in a moving state) after 3 months and one year. The intraoperative blood loss was measured, and total volume of blood loss within 24 h was calculated: Total volume of blood loss

within 24 h (ml) = (Hct pre-operation − Hct 24 h postoperation) × blood volume (BV), and BV (ml) = weight (kg) × 70 (ml/kg). The circumferences of the lower and middle thighs of patients were measured before the operation and on day 1, day 2, day 3 after the operation to judge the swelling of the operative side thigh.

A Montreal Cognitive Assessment Scale (MoCA) with a total score of 30 points was used to analyze the cognitive function of patients on day 1, day 2, day 3 and day 7 after the operation. MoCA value with less than 26 points was considered to be cognitive impairment [9]. The urine volume was measured during the operation. The serum creatinine and glomerular filtration rate (GFR), which was estimated according to the serum creatinine level, age, weight and sex of the patients, were used to evaluate renal function before the operation and on day 1, day 2, and day 3 after the operation. The C-reactive protein (CRP) concentration was measured before operation and on day 1, day 2, day 3, day 5, and day 7 after surgery.

Outcomes and statistical analyses

The primary outcome of this study was the difference in the incidence of chronic pain at 3 months follow-up between two groups, and secondary outcomes were the difference in acute pain level, cognitive function, knee function and biochemical parameters. Based on the previously published study and our pre-experiment, a sample size of 42 patients in each group was sufficient to detect a 15% decrease in the incidence of chronic pain with 5% significance level and 90% power. SPSS Statistics 19.0 software was used for data processing. The normal distribution measurements were expressed as the mean ± standard deviation. Analysis of variance (ANOVA) was used for comparison among groups. SNK-q was used for intergroup comparison. Repeated-measures ANOVA was used for the analysis of repeatedly measured data, and the LSD-t test was used for intragroup comparison. The Chi-squared test was used for comparison of occurrence. P values < 0.05 were considered statistically significant.

Results

General materials

A total of 129 patients were enrolled in the study, and 122 cases were actually completed and followed up (Fig. 1). A total of 58 cases were completed in group T and 64 cases were completed in group H. There was no significant difference in age, weight and years of education in the two groups (Table 1).

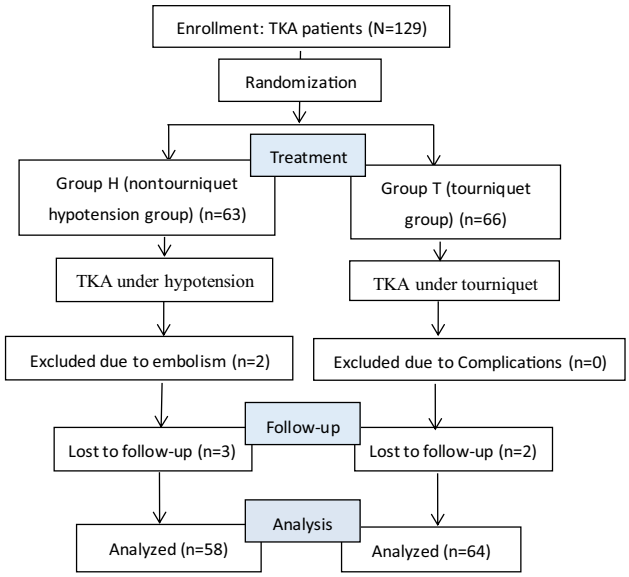

Fig. 1 Diagram of the progress through the phases of the trial

Table 1 Demographics and characteristics of patients

Variables	Tourniquet group Group T (n = 58) n (%) or mean ± SD	Nontourniquet group Group H (n = 64) n (%) or mean ± SD
Gender		
Female	38(65.5%)	41(64.1%)
Male	20(34.5%)	23(35.9%)
Age (years)	68.2 ± 17.1	69.5 ± 13.7
Weight (kg)	67.7 ± 17.6	65.9 ± 15.9
years of education (years)	8.7 ± 3.6	9.1 ± 4.7

Postoperative analgesia effect and knee function

There was no significant difference in both resting and motion state NRS score between the two groups on day 1, day 2, day 3 and day 7 after the operation, but the times of patient-controlled pressing and the total consumption dosage of ropivacaine in group T were higher. There were more chronic pain cases in group T after 3 months and 1 year, and the incidence rate of chronic pain was higher in group T. There was no significant difference in the AROM between two groups on day 1, day 2, day 3, day 7 and at 3 months after the operation, but the AROM of patients in group H was greater after 1 year (Table 2).

Tourniquet parameters and related effects

The tourniquet pressure was 234.5 ± 21.5 mmHg, and the tourniquet compression time was 47.4 ± 7.4 min in group T. There was no significant difference in the duration of

Table 2 The analgesic effect and AROM of patients after surgery

Variables	Tourniquet group Group T ($n=58$)	Nontourniquet group Group H ($n=64$)	P value
NRS score-resting state			
Preoperation	2.14 ± 0.83	2.22 ± 0.81	0.586
Post day 1	2.58 ± 0.56	2.43 ± 0.53	0.136
Post day 2	2.69 ± 0.47	2.55 ± 0.50	0.107
Post day 3	2.14 ± 0.40	2.17 ± 0.52	0.688
Post day 7	1.58 ± 0.53#	1.47 ± 0.50#	0.212
NRS score-motion state			
Preoperation	2.62 ± 0.59	2.72 ± 0.65	0.387
Post day 1	3.02 ± 0.61	2.92 ± 0.65	0.405
Post day 2	2.91 ± 0.63	2.76 ± 0.56	0.170
Post day 3	2.48 ± 0.50	2.47 ± 0.50	0.986
Post day 7	1.83 ± 0.53#	1.59 ± 0.49#,▲	0.013
PCA			
Press times	15.91 ± 1.99	9.06 ± 1.94▲	< 0.001
Local anesthetic dosage (mg)	451.93 ± 20.76	413.19 ± 11.56▲	< 0.001
AROM (degree)			
Preoperation	98.4 ± 4.91	98.7 ± 4.27	0.727
Post day 1	70.1 ± 7.24#	72.5 ± 6.35#	0.061
Post day 2	73.3 ± 6.56#	75.6 ± 6.08#	0.053
Post day 3	82.5 ± 6.26#	83.9 ± 5.51#	0.180
Post day 7	95.8 ± 6.67	96.7 ± 6.40	0.428
Post 3 months	102.6 ± 5.85#	104.5 ± 5.51#	0.063
Post 1 year	108.9 ± 4.95#	112.0 ± 4.85#,▲	0.001
Chronic pain/percentage			
Post 3 months	26/44.8%	18/28.1%▲	0.042
Post 1 year	24/41.4%	16/25.0%▲	0.042

Data are shown as means ± SD, the incidence rate is shown as percentage

Compared with group T, ▲$P<0.05$; compared with preoperation, #$P<0.05$

surgical procedure between the two groups ($P=0.106$). The intraoperative blood loss in group T was lower, but the total blood loss within 24 h in group T was higher than group H. The added value of the thigh circumference in group T was higher on day 1, day 2 and day 3 after the operation (Table 3).

Anesthesia and controlled hypotension effects

Controlled hypotension was used in group H, and the MAP during surgery in group H (85 ± 2.3 mmHg) was lower than that in group T (97 ± 3.5 mmHg) ($P<0.01$). There was no significant difference in the NTI and 95% SEF between the two groups during anesthesia ($P=0.108$). The urine volume between the two groups was not significantly different ($P=0.431$). The serum creatinine levels between the two groups were not significantly different on day 1 ($P=0.515$), day 2 ($P=0.274$) and day 3 ($P=0.276$), and there was no significant difference in glomerular filtration rate on day 1 ($P=0.576$), day 2 ($P=0.754$) and day 3 ($P=0.225$) between the two groups.

Systemic inflammatory response and postoperative cognitive function

The CRP levels were higher than the preoperative levels in group T and group H within 7 days after operation, and the CRP levels in group H were higher than those in group T on day 1, day 2, day 3, and day 5 after the operation. The MoCA total score in group H was lower than that in group T on day 1 and day 2 after the operation. The incidence of cognitive impairment in group H (24 cases) was higher than that in group T (12 cases) within 7 days. The total incidence rate of cognitive impairment in group H (37.5%) was higher than that in group T (20.7%) within 7 days ($P=0.033$) (Fig. 2).

Discussion

Severe pain after TKA can be caused by many factors, such as trauma, tourniquet pressure injury, inflammatory reaction and tissue edema [10]. The multimodal stratified

Table 3 Blood loss and the added value of thigh swelling

Variables	Tourniquet group Group T ($n=58$)	Nontourniquet group Group H ($n=64$)	P value
Duration of the surgeries (min)	**71.60 ± 9.48**	**72.91 ± 8.35**	0.106
Intraoperative blood loss (ml)	56.02 ± 12.53	82.34 ± 17.62▲	< 0.001
Blood loss within 24 h (ml)	455.45 ± 69.47	258.34 ± 40.85▲	< 0.001
Thigh swelling value (cm)			
Post day 1	5.21 ± 1.44	2.34 ± 1.06▲	< 0.001
Post day 2	6.02 ± 1.24	2.35 ± 0.95▲	< 0.001
Post day 3	5.25 ± 1.04	1.42 ± 0.59▲	< 0.001

Bold—duration of the surgeries was the time from the beginning of skin incision to the end of suture

Data are shown as means ± SD; compared with group T, ▲$P<0.05$

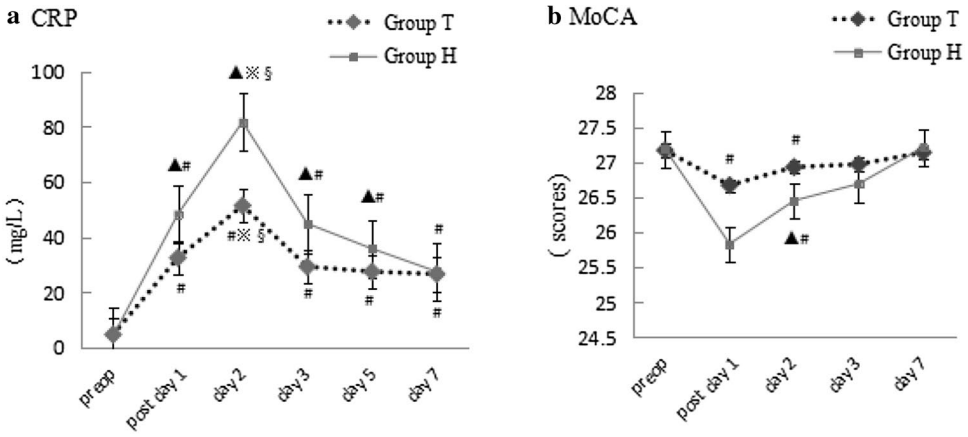

Fig. 2 Systemic inflammatory response and postoperative cognitive function. Changes in C-reactive protein concentration (**a**) and the MoCA score (**b**). Data are shown as means ± SD, compared with group T, $^{▲}P < 0.05$; compared with preoperative day 1, $^{\#}P < 0.05$; compared with postoperative day 1, $^{※}P < 0.05$; compared with postoperative day 3, $^{§}P < 0.05$

analgesia scheme based on continuous femoral nerve block was adopted in the study. Our study shows that the continuous femoral nerve block is a suitable way to control acute pain within 3 days after operation and that is one of the best recommended analgesic methods at present [11]. Although there was no difference in NRS score between the two groups, the number of PCA pressing and the total dosage of ropivacaine in patients receiving tourniquet technology were significantly higher than those in nontourniquet patients. So, our study revealed that the use of a nontourniquet technique in total knee arthroplasty may reduce postoperative acute pain. Postoperative hemarthrosis and swelling of the knee joint caused by tourniquet application are considered to be important causes of postoperative pain aggravation [12]. Less bleeding during the operation may benefit from the application of a tourniquet, but high total blood loss occurred within 24 h after the operation in this study, which indicated that hidden hemorrhage increased after the operation and that hidden bleeding in the knee joint can aggravate pain. Excessive high pressure and the prolonged use of tourniquet, especially over 280 mmHg and for more than 90 min, can cause severe swelling of the thigh [13]. The average tourniquet pressure was less than 250 mmHg and the time was controlled within 60 min in this study, but the thigh of patients swelled significantly and lasted for three days in tourniquet patients after the operation. Hemarthrosis, joint swelling and pain are important factors limiting the functional exercise and recovery of patients after TKA [14]. There was no significant difference in the AROM of all patients within 3 days after TKA, which was attributed to the good analgesia and effective functional exercise.

Long-term rehabilitation after total knee arthroplasty is closely related to pain. Some studies have shown that the incidence of chronic pain after TKA is as high as 30–50%. [15]. To evaluate the long-term prognosis of patients, the number and incidence of chronic pain in patients after surgery were analyzed. There was a lower incidence of chronic pain in the nontourniquet group at 3 months and 1 year, which indicated that the lack of tourniquet use could reduce the occurrence of long-term chronic pain. Additionally, the quadriceps activity of patients with tourniquet may be significantly lower after the operation. This kind of tourniquet-related skeletal muscle activity damage may last for 6 months and recover basically after 12 months [11, 16]. We found that the improvement of the AROM in the nontourniquet group was better at one year after operation, which indicates that the application of tourniquet may affect the function of quadriceps for a long time.

Controlled hypotension was performed to control bleeding in the nontourniquet group during the operation. Previous studies have confirmed that tourniquet can reduce intraoperative bleeding and provide a good environment for the sclerosis of bone cement. Although tranexamic acid infusion and controlled hypotension were performed, the blood loss during TKA operation without tourniquet was still higher in the present study, but the total amount was controlled within 100 ml, which did not increase the risk of allogenic blood transfusion in elderly patients. To ensure the safety of controlled hypotension technology for elderly patients, we controlled an appropriate depth of anesthesia according to EEG waveform (NTI) and 95% SEF. The MAP in both groups was maintained above 80 mmHg to maintain sufficient perfusion of the kidney, brain and other important organs. The intraoperative urine volume and postoperative renal function showed no difference between the two groups in our study. These results suggest that controlled hypotension based on maintaining an adequate depth of anesthesia and tissue perfusion is safe for elderly patients after TKA.

TKA surgical stress and fat particles entering the blood during the treatment of the knee joint marrow cavity can also produce a strong systemic inflammatory response [17]. Previous studies have suggested that the ischemia–reperfusion injury after the release of tourniquet may activate the inflammatory response after operation, but whether nontourniquet technology can alleviate the inflammatory response is still uncertain. We found that the increase in C-reactive protein

(CRP) appeared on the first day but lasted for more than 7 days in all patients. The level of CRP is closely related to bone marrow injury in TKA [18]. The tourniquet blocking the blood flow in the lower limbs may occlude the veins and prevent tiny emboli from entering the systemic circulation during operation; however, this kind of protective effect may disappear in the nontourniquet group. The continuous entry of tiny emboli into the systemic circulation may activate the systemic inflammatory response and cause a temporary and significant increase in CRP. The persistent inflammatory response is one of the important causes of cognitive impairment after surgery operation [19, 20]. The cognitive function of patients evaluated by MoCA decreased early in both groups after operation, and the MoCA score of patients in the nontourniquet group was lower within two days. Postoperative cognitive decline is associated with both anesthesia and surgery [21, 22]. We compared the trend and time curve of CRP elevation in the two groups and speculated that the more serious early cognitive decline in the nontourniquet group in our study may be related to a more serious inflammatory reaction. Some cerebral protective measures were taken in this trial for group H. Firstly, appropriate MAP was maintained to ensure cerebral perfusion. Secondly, the depth of anesthesia was monitored to avoid excessive inhibition of brain function. Thirdly, preoperative nerve block was performed to reduce surgical stress. However, the cognitive function of group H still decreased, which indicated that powerful anti-inflammatory treatments lacked in our trail during perioperative period may be the important protection measures for cognitive function.

The study had two limitations. First, the study did not reveal the causes of higher cognitive impairment in the non-tourniquet group. Second, in addition to CRP, more inflammatory response indicators are needed to evaluate inflammatory response, and the relationship between CRP and marrow cavity destruction still needs to be confirmed by TEE.

Conclusion

Our study indicates that reasonably controlled hypotension is one of the safe and effective methods to reduce intraoperative bleeding, and the nontourniquet technique can alleviate chronic pain after operation and promote the long-term rehabilitation of TKA patients. Notably, the nontourniquet technique may cause more severe systemic inflammation and transient cognitive impairment, so anti-inflammatory and cerebral protection methods should be strengthened during the perioperative period.

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