Efficacy of acetaminophen on preemptive multimodal analgesia in total knee arthroplasty: a prospective, double-blind, randomized placebo-controlled trial

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Research Article

Keywords: total knee arthroplasty, preemptive analgesia, pain, acetaminophen

Posted Date: August 5th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1794721/v1

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Abstract

Background

Preemptive multimodal analgesia is a commonly used method to control pain following total knee arthroplasty (TKA). This study aimed to evaluate the efficacy of preemptive acetaminophen for pain management in patients who underwent TKA.

Methods

In this prospective, double-blind, randomized placebo-controlled trial, 80 patients were randomized to the acetaminophen or control group. Patients in the acetaminophen group received celecoxib 400mg, pregabalin 150mg, and acetaminophen 325mg 2 hours before TKA. Patients in the control group received celecoxib, pregabalin, and placebo. Primary outcome was postoperative consumption of morphine hydrochloride used for rescue analgesia. Secondary outcomes included the time to the first rescue analgesia, postoperative pain as assessed by visual analogue scale (VAS), functional recovery as assessed by range of knee motion and ambulation distance, the time to hospital discharge, and complication rates.

Results

There was no significant difference between the control group and the acetaminophen group in postoperative 0–24 h morphine consumption (average 11.3 mg vs. 12.3 mg, p = 0.445) and total morphine consumption (average 17.3 mg vs. 19.3 mg, p = 0.242). There was no significant difference in the time to the first rescue analgesia, postoperative VAS pain scores at any time points, postoperative functional recovery of knee, and the time to hospital discharge. The two groups had a similar occurrence of postoperative complications.

Conclusions

The addition of acetaminophen to preoperative preemptive multimodal analgesia could not reduce postoperative morphine consumption or improve pain relief. Orthopedic surgeons should reconsider routine use of preemptive acetaminophen in TKA.

Trial registration: The study was prospectively registered on Chinese Clinical Trial Registry (identification number: ChiCTR2100052732) on 04/11/2021.


Background

Total knee arthroplasty (TKA) has been regarded as one of the most painful orthopedic surgeries [1]. Inadequate pain management can delay recovery, and reduce patient satisfaction [2, 3]. Multimodal
analgesia incorporates the use of analgesic drugs with different mechanisms of action to enhance postoperative analgesia [4]. Preemptive multimodal analgesia is an important part of multimodal analgesia [5], wherein multimodal analgesia is initiated before the painful stimulus with the goals of preventing central sensitization and amplification of pain during surgery [6]. In the last two decades, preoperative preemptive multimodal analgesia was widely adopted in centers performing total joint arthroplasty [7–12].

The preemptive multimodal analgesia regimens typically consist of a selective cyclooxygenase-2 (COX-2) inhibitor and an extended-release opioid [7–9, 11–15], with some centers adding other medications such as antiepileptic drugs [16–18] and acetaminophen [19–21]. The conceptual framework of preemptive multimodal analgesia makes sense intuitively, aiding its widespread adoption across many orthopedic centers without rigorous analysis of the individual components of the regimen [22]. Therefore, there is a possibility that some components of the preemptive multimodal analgesia regimen may not be helpful. Previous studies have confirmed the efficacy of some medications for preemptive multimodal analgesia in TKA, including celecoxib (a selective COX-2 inhibitor) and pregabalin (an antiepileptic drug) [16, 17, 23, 24]. However, a recent retrospective cohort study which included 550 patients undergoing elective, primary total joint arthroplasty reported that patients who were given preemptive opioids immediately before surgery experienced more pain, consumed more postoperative opioids, and exhibited impaired early function as compared to those who were not given preemptive opioids. To our knowledge, there is no study to confirm the efficacy of acetaminophen on preemptive multimodal analgesia. Thus, we designed this prospective, double-blind, randomized placebo-controlled trial to investigate the efficacy of acetaminophen as a component of the preemptive multimodal analgesia regimen for patients undergoing TKA.

Methods

This study was designed as a prospective, double-blind, randomized placebo-controlled trial and approved by the Clinical Trials and Biomedical Ethics Committee of Sichuan University West China Hospital. All procedures performed on this study were in accordance with the ethical standards of the 1964 Helsinki declaration. Written informed consent was obtained from all participants. The study was prospectively registered on Chinese Clinical Trial Registry (identification number: ChiCTR2100052732) on 04/11/2021.

The methods section including patient recruitment, randomization, perioperative analgesia and management, outcomes and follow-up, and statistical analysis refers to our previous studies [25–28].

Patient recruitment

This study recruited osteoarthritis patients undergoing primary unilateral TKA at our institution. Patients with an American Society of Anesthesiologists (ASA) functional status of I–III were included. We excluded patients with a diagnosis of non-osteoarthritis (including rheumatoid arthritis, traumatic
arthritis, and septic arthritis), a knee flexion deformity of $\geq 30^\circ$, a varus-valgus deformity of $\geq 30^\circ$, or known allergies to the drugs being used in this study. We also excluded those with a history of open surgery of knee, knee infection, narcotic dependency, or recognized neuromuscular disorders. Patients who were unwilling to give informed consent were also excluded.

**Randomization**

All patients were classified into two groups using a computer-generated list of random numbers (Excel, Microsoft Corporation, Redmond, WA, USA). Based on this list, Investigator 1 who was blinded to group allocation and study design prepared sealed opaque envelopes for each patient. On the morning of their surgery, Investigator 2 assigned the patients to the control group or acetaminophen group based on the number in the sealed envelopes. Investigator 2 prepared corresponding analgesic medications in the central pharmacy then ensured that the patients took these drugs in the bed ward 2 hours before surgery. The outcome assessor (Investigator 3) and surgeon were both blind to the treatment group. Statistical analysis was performed by Investigator 4, who was also blind to group allocation.

**Perioperative analgesia and management**

As preemptive multimodal analgesia regimen, patients in the acetaminophen group received celecoxib 400mg, pregabalin 150mg, and acetaminophen 325mg. Patients in the control group received celecoxib 400mg, pregabalin 150mg, and placebo. All medications were given orally 2 hours prior to surgery.

Thirty minutes before general anesthesia, the adductor canal block was performed by the same senior anesthesiologist refer to previous studies [25]. A total of 20 mL local anesthetic consisting of 0.25% ropivacaine and 2.0 µg/mL of epinephrine was administered for adductor canal block.

All surgical procedures in this study were performed by the same surgeon in our institution. Surgery was performed by making a midline skin incision with a medial parapatellar approach after general anesthesia. During the surgery, cemented prostheses (DePuy Synthes, New Brunswick, NJ, USA) were used, but not pneumatic tourniquets.

During surgery, the periarticular local infiltration analgesia was performed by the surgeon. The analgesic cocktail consisted of 0.25% ropivacaine and 2.0 µg/mL of epinephrine. Prior to prosthesis implantation, 10 mL of cocktail was injected into the posterior aspect of the capsule, and 10 mL of cocktail was used as an infiltration analgesia for the medial and lateral collateral ligaments. After implantation, the quadriceps and retinacular tissues were infiltrated with 10 mL of cocktail; the adipose and subcutaneous tissues were infiltrated with 20 mL of cocktail. Drainage tubes were not used before the wound was sutured.

After awakening from general anesthesia, patients were sent to the bed ward and an ice compress was applied around the incision. Oral celecoxib (200 mg) and pregabalin (150 mg) were administered twice daily to control postoperative pain. If the patient was unable to tolerate the pain, a further 10 mg of
morphine hydrochloride as rescue analgesia was injected subcutaneously. During their postoperative hospitalization, patients were required to walk with a walking aid.

Outcomes and follow-up

The primary outcome was postoperative consumption of morphine hydrochloride used for rescue analgesia.

Secondary outcomes included the time to the first rescue analgesia, postoperative pain as assessed by visual analogue scale (VAS), functional recovery as assessed by range of knee motion and ambulation distance, the time to hospital discharge and complication rates.

Postoperative pain at rest and during motion (knee flexion as much as possible) was measured using a visual analogue scale (VAS) score [29]. The scale ranged from 0 to 10, where 0 indicates no pain and 10 indicates extreme pain. Pain was measured at 3, 6, 12, 24, 36 and 48 h after surgery. If the patient’s hospital stay was less than 48 hours, the pain score at discharge was recorded instead of 48 hours after surgery.

The functional recovery of the knee was measured by range of motion and daily ambulation distance. The range of motion was measured using a protractor, three times per day, 6 h apart, and the best value was used as the day’s value. For daily ambulation distance, the patient was asked to walk the longest distance possible in one attempt, and the distance was measured.

The time to hospital discharge was recorded. The discharge criteria of patients included: adequate pain control on oral pain medication; independent transfer; ambulation of at least 200 feet alone; and the ability to climb stairs.

The occurrence of complications was recorded. The complications included nausea, vomiting, wound complications (including wound oozing and delayed wound healing), venous thrombotic events, and falls after surgery.

Statistical Analysis

The sample size was based on the power analysis from a pilot study involving 20 patients not enrolled in the main study. In order to achieve the minimal clinically important difference of 0–24 h opioid consumption (relative 40%) [30], we calculated that 36 individuals per group would be required to detect a statistically significant difference between groups with a two-sided alpha level of 0.05 and a power of 90%. Therefore, we decided to include 40 patients in each group.

Statistical analysis was performed using SPSS 26.0 (IBM, Chicago, IL, USA). The normality of data was assessed using histograms and quantile-quantile plots. Continuous data were presented as mean and standard deviation. Categorical data were presented as numbers or percentages. Inter-group differences in normally distributed data were assessed for significance using Student’s t test; differences in skewed and ordinal data, using the Mann-Whitney U test; and differences in categorical data, using Pearson's chi-
squared test or Fisher’s exact probabilities test. The time to first rescue analgesia and the time to hospital discharge were analyzed using survival analysis (Kaplan-Meier method with log-rank test). Differences were considered significant if \( p < 0.05 \).

**Results**

**Baseline characteristics of patients**

A total of 156 patients were assessed for eligibility, of whom 32 did not meet the eligibility criteria and another 44 were unwilling to give consent. The remaining 80 patients were randomized into two groups. During postoperative outcome assessments, no patients dropped out of the study (Fig. 1). Before surgery, the two groups showed no significant differences in baseline data (Table 1).

**Primary outcome**

There was no significant difference between the control group and the acetaminophen group in postoperative 0–24 h morphine consumption (11.3 ± 6.5 mg vs. 12.3 ± 7.7 mg, \( p = 0.445 \)) and total morphine consumption (17.3 ± 10.1 mg vs. 19.3 ± 9.4 mg, \( p = 0.242 \)) (Table 2). There was also no significant difference in the proportion of patients who received rescue analgesia between the two groups (36 cases, 90.0% vs. 36 cases, 90.0%, \( p = 0.709 \)).

**Secondary outcomes**

**The time to the first rescue analgesia**

The time to the first rescue analgesia did not differ significantly between the control group and the acetaminophen group (13.5 ± 6.0 hours vs. 14.1 ± 8.0 hours, \( p = 0.837 \)) (Table 2, Fig. 2).

**VAS pain scores**

There was no significant difference in postoperative VAS pain scores at rest or during motion at any time points between the two groups (Fig. 3).

**Functional recovery**

After surgery, the two groups showed no significant difference in range of knee motion (postoperative day 1: 94.0 ± 9.9 degrees vs. 98.6 ± 11.2 degrees, \( p = 0.092 \); postoperative day 2: 107.8 ± 10.5 degrees vs. 110.5 ± 9.5 degrees, \( p = 0.190 \)), and ambulation distance (postoperative day 1: 19.2 ± 9.8 meters vs. 20.3 ± 8.3 meters, \( p = 0.399 \); postoperative day 2: 36.4 ± 14.4 meters vs. 35.6 ± 13.3 meters, \( p = 0.977 \)) during hospitalization (Table 3).

The time to hospital discharge

There was no significant difference in the time to hospital discharge between the control group and the acetaminophen group (58.1 ± 13.1 hours vs. 61.5 ± 12.5 hours, \( p = 0.335 \)) (Table 3, Fig. 4).
Complication rates

During postoperative hospitalization, the two groups showed similar incidence of nausea (11 cases, 27.5% vs. 9 cases, 22.5%, p = 0.606), vomiting (7 cases, 17.5% vs. 6 cases, 15.0%, p = 0.762) and wound complications (3 cases, 7.5% vs. 2 cases, 5.0%, p = 1.000) (Table 4). Postoperative falls or venous thrombotic events did not occur in any group.

Discussion

The most important finding of the present study was that adding acetaminophen to preoperative preemptive multimodal analgesia did not reduce postoperative morphine consumption or improve pain relief in patients undergoing TKA.

Previous studies have reported that preemptive multimodal analgesia could achieve a better pain control, faster postoperative functional recovery, and leads to less adverse events by preventing the establishment of altered central processing of afferent input, which amplifies pain after TKA [31, 32]. However, the optimal combination of medications for preemptive multimodal analgesia was still unclear. Previous studies have confirmed the efficacy of some medications such as celecoxib (a selective COX-2 inhibitor) and pregabalin (an antiepileptic drug) [16, 17, 23, 24]. Some researchers recommended the use of well-established combined celecoxib and pregabalin as routine preemptive analgesia after TKA [16]. In previous clinical practice, most researchers advocated for the use of preoperative long-acting opioids [7–15]. However, A recent retrospective cohort study which included 550 patients undergoing elective, primary total joint arthroplasty (320 patients received total hip arthroplasty, 230 patients received TKA) evaluated the efficacy of opioids as a component of preemptive multimodal analgesia [22]. They found that patients who received opioids in preoperative holding reported significantly greater VAS pain scores on postoperative day 1, when compared to those who did not. These patients also walked shorter distances on postoperative day 0 and consumed greater morphine equivalents per hospital day over the course of their hospital stay. These differences remained significant when stratified by procedure, TKA or total hip arthroplasty. Their study casted doubt on the use of preoperative preemptive opioids. To date, there is no clinical evidence to support or oppose the routine use of acetaminophen for preemptive multimodal analgesia in TKA. Therefore, we designed this study to verify the efficacy of acetaminophen based on the well-established combined celecoxib and pregabalin.

Acetaminophen is a commonly used antipyretic and analgesic drug. It is commonly used for fever caused by a cold and can also be used to relieve mild to moderate pain such as headache and joint pain [33, 34]. At present, acetaminophen is still a commonly used medication for the non-surgical management of knee osteoarthritis [35, 36]. Some medical centers also administered it as a part of the preemptive multimodal analgesia regimen after TKA [19–22]. However, our results suggested that the addition of acetaminophen to preemptive multimodal analgesia regimen did not provide any clinical benefits. Patients who received acetaminophen before surgery did not show any advantage in terms of postoperative morphine
consumption, VAS pain scores, or functional recovery. Orthopedic surgeons should reconsider routine use of preemptive acetaminophen in patients undergoing TKA.

Celecoxib can provide analgesia via inhibition of the COX-2 that are involved in the formation of prostaglandins in the periphery and central nervous system [37]. Pregabalin, a γ-aminobutyric acid receptor agonist, mainly acts on presynaptic α2-δ subunits to inhibit peripheral and central pain sensitization. α2-δ subunit is a voltage-dependent calcium channel widely distributed in the peripheral and central nervous system, and its upregulation plays an important role in hypersensitization of nociceptive nerves [38]. The analgesia mechanism of acetaminophen is controversial and currently unknown [39]. The inhibition of centrally expressed cyclooxygenase-1 (COX-1) and COX-2 enzymes is not considered the primary mechanism for analgesia [39]. Previous studies reported that loss of cannabinoid receptor CB1 activity attenuates acetaminophen-mediated analgesia in rodents, implicating the endocannabinoid system played a role in mechanisms of action of acetaminophen [40]. In addition, acetaminophen may also produce analgesia through inhibiting the pronociceptive N-Methyl-d-aspartic acid/nitric oxide signaling in the spinal cord or activation of voltage-gated potassium channels in the dorsal horn [41]. Finally, pre-clinical evidence also suggests that the analgesics efficacy of acetaminophen may involve prolonged activation and desensitization of the transient receptor potential (TRP) family of nonselective cation channels [42]. Theoretically, celecoxib, pregabalin, and acetaminophen produce analgesia through different mechanisms of action, and the combination of the three medications can enhance the analgesia. However, interestingly, no improvement was observed when acetaminophen was added to the combination of celecoxib and pregabalin. Since the analgesic mechanism of acetaminophen is not completely clear, the cause and exact mechanism of our results need to be further explored.

This is the first study to evaluate the efficacy of acetaminophen as a component of preemptive multimodal analgesia regimen for patients undergoing TKA. However, the results of the study should be interpreted with caution in light of several limitations. First, the multimodal analgesia regimen including preemptive multimodal analgesia regimen used in this study may be different from that in other medical centers or other regions. For example, the types and dosages of drugs used for preemptive analgesia vary greatly among medical centers [7–15]. Different multimodal pain regimens may affect the results. Second, our study was limited to the hospitalization period, so we were not able to assess differences in outcomes and complications after discharge. The lack of any form of outcome measure beyond hospital discharge is another limitation of our study. Third, this study included only patients undergoing TKA, so the results may not be generalizable to all patients undergoing other orthopedic surgeries. Fourth, all surgeries were finished by one single surgeon in this study. The surgeon’s surgical proficiency may affect postoperative pain. The results of this study need to be further verified by multiple surgeons.

Conclusions

Compared to those who were not given preemptive acetaminophen, patients who received preemptive acetaminophen did not show any clinical improvements or benefits. The addition of acetaminophen to
preemptive multimodal analgesia regimen could not reduce postoperative morphine consumption or improve pain relief. Orthopedic surgeons should reconsider routine use of preemptive acetaminophen in TKA.

**Abbreviations**

ASA
American Society of Anesthesiologists
COX-1
cyclooxygenase-1
COX-2
cyclooxygenase-2
TKA
Total knee arthroplasty
TRP
transient receptor potential
VAS
visual analogue scale.

**Declarations**

*Ethics approval and consent to participate*

This study was approved by the Clinical Trials and Biomedical Ethics Committee of Sichuan University West China Hospital (grant no.2021-1035). All procedures performed on this study were in accordance with the ethical standards of the 1964 Helsinki declaration. Written informed consent was obtained from all participants.

*Consent for publication*

Not applicable.

*Availability of data and materials*

The data collected and analyzed in the present study are not publicly available due to ethical restrictions but are available from the corresponding author upon request.

*Competing interests*

The authors declare that they have no competing interests.

*Funding*
This study was funded by 1.3.5 Project of Sichuan University West China Hospital. Grant ID: ZYJC18040.

**Author contributions**

Q.W and Z.W were responsible for manuscript writing. T.M was responsible for data collection. L.W and C.Z. was responsible for data analysis and manuscript writing. P.K. was responsible for the study design and correspondence. All authors read and approved the final manuscript.

**Acknowledgements**

We want to express our sincere appreciation for all the patients that joined this study.

**References**


**Tables**

**Table 1** Baseline characteristics of patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Control group (n=40)</th>
<th>Acetaminophen group (n=40)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65.7±6.3</td>
<td>65.9±8.5</td>
<td>0.870(^a)</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>14/26</td>
<td>13/27</td>
<td>0.813(^b)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>68.3±9.3</td>
<td>66.4±10.7</td>
<td>0.393(^a)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>160.8±9.0</td>
<td>161.7±8.3</td>
<td>0.653(^a)</td>
</tr>
<tr>
<td>Body mass index (kg/m(^2))</td>
<td>26.4±2.8</td>
<td>25.4±3.4</td>
<td>0.139(^a)</td>
</tr>
<tr>
<td>Surgery side (right/left)</td>
<td>22/18</td>
<td>25/15</td>
<td>0.496(^b)</td>
</tr>
<tr>
<td>Preoperative measures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VAS pain score</td>
<td>4.50±0.93</td>
<td>4.43±0.87</td>
<td>0.730(^c)</td>
</tr>
<tr>
<td>Knee ROM</td>
<td>109.4±15.5</td>
<td>107.3±15.1</td>
<td>0.591(^c)</td>
</tr>
<tr>
<td>ASA status (I/II/III)</td>
<td>1/27/12</td>
<td>0/31/9</td>
<td>0.581(^c)</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>65.4±8.9</td>
<td>63.5±8.4</td>
<td>0.238(^c)</td>
</tr>
</tbody>
</table>

Values are mean ± SD or n

ASA, American Society of Anesthesiologists; ROM, range of motion; VAS, visual analogue scale

\(^a\) Student's t test

\(^b\) Pearson's chi-squared test
Table 2 Postoperative rescue analgesia

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Control group (n=40)</th>
<th>Acetaminophen group (n=40)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine consumption within 24 hours (mg)</td>
<td>11.3±6.5</td>
<td>12.3±7.7</td>
<td>0.445</td>
</tr>
<tr>
<td>Total morphine consumption (mg)</td>
<td>17.3±10.1</td>
<td>19.3±9.4</td>
<td>0.242</td>
</tr>
<tr>
<td>Time to first rescue analgesia (hours) *</td>
<td>13.5±6.0</td>
<td>14.1±8.0</td>
<td>0.837</td>
</tr>
<tr>
<td>Proportion of patients who received remedial analgesia (n, %)</td>
<td>36 (90.0%)</td>
<td>36 (90.0%)</td>
<td>0.709</td>
</tr>
</tbody>
</table>

Values are mean ± SD or n (%)

- a Mann-Whitney U test
- b Kaplan-Meier method with log-rank test
- c Pearson's chi-squared test

* Patients who did not receive rescue analgesia were excluded
Table 3 Postoperative functional recovery

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Control group (n=40)</th>
<th>Acetaminophen group (n=40)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knee ROM (degrees)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postoperative day 1</td>
<td>94.0±9.9</td>
<td>98.6±11.2</td>
<td>0.092&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Postoperative day 2</td>
<td>107.8±10.5</td>
<td>110.5±9.5</td>
<td>0.190&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Ambulation distance (m)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postoperative day 1</td>
<td>19.2±9.8</td>
<td>20.3±8.3</td>
<td>0.399&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Postoperative day 2</td>
<td>36.4±14.4</td>
<td>35.6±13.3</td>
<td>0.977&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Time to hospital discharge (hours)</td>
<td>58.1±13.1</td>
<td>61.5±12.5</td>
<td>0.335&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Values are mean ± SD

ROM, range of motion

<sup>a</sup> Mann-Whitney U test

<sup>b</sup> Kaplan-Meier method with log-rank test

Table 4 Postoperative complications

<table>
<thead>
<tr>
<th>Complication</th>
<th>Control group (n=40)</th>
<th>Acetaminophen group (n=40)</th>
<th>p&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>11 (27.5%)</td>
<td>9 (22.5%)</td>
<td>0.606</td>
</tr>
<tr>
<td>Vomiting</td>
<td>7 (17.5%)</td>
<td>6 (15.0%)</td>
<td>0.762</td>
</tr>
<tr>
<td>Wound complications</td>
<td>3 (7.5%)</td>
<td>2 (5.0%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Venous thrombotic events</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Fall after surgery</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
</tbody>
</table>

Values are n (%)

<sup>a</sup> Pearson's chi-squared test

Figures
Figure 1

Flow diagram of patients' selection and exclusion.
Figure 2

The survival analysis function of the time to first rescue analgesia.
Figure 3

The average postoperative VAS pain scores at rest (A) and during motion (B) of patients in both groups. The error bars indicate the standard deviation of the mean.
Figure 4

The survival analysis function of the time to hospital discharge.