Total knee arthroplasty (TKA) is a major treatment for end-stage osteoarthritis (OA). As the aging population continues to grow, more individuals suffer from obesity or knee-joint injury, and the number of TKAs performed has increased yearly,¹ which has resulted in the emergence of many problems relevant to TKA surgery.

Perioperative blood loss is a major concern with TKA. Most orthopedic surgeons believe the application of a tourniquet can effectively reduce intraoperative blood loss, provide better visualization, facilitate surgical procedures, reduce operative time especially during the cementing of the prosthesis, and provide optimal conditions for the combined bone cement and bone cutting interface. A meta-analysis by Alcelik et al² concluded that the application of a tourniquet reduces intraoperative and perioperative blood loss. Although it has been reported that using tourniquets in TKA results in more relevant complications,³-⁶ tourniquet application during TKA is common because long-term use has proven the reliability of this practice, and most surgeons rely on this technique. A survey of the membership of the American Association of Hip

Effects of Tourniquet Release on Total Knee Arthroplasty

Kai Tie, MD; Dongcai Hu, MD; Yongjian Qi, MD; Hua Wang, MD; Liaobin Chen, MD, PhD

This study investigated the clinical outcomes of early and late tourniquet release (tourniquet release after cementing the prosthesis vs tourniquet release after wound closure and pressure dressing) in total knee arthroplasty (TKA). The study was conducted by searching PubMed, Embase, Web of Science, and Cochrane Central databases for articles on randomized controlled trials comparing early and late tourniquet release in primary TKA that were published from 1966 to March 2015. Relevant data were extracted, and the Physiotherapy Evidence Database (PEDro) Scale was used to assess the methodologic quality. Stata software (StatCorp, College Station, Texas) was used to perform a meta-analysis. Sixteen articles were included with a total of 1073 patients and 1097 knees. For blood loss, there were no significant differences between the 2 groups in calculated blood loss, decrease in hemoglobin level, drop in hematocrit level, and measured postoperative blood loss, although total measured blood loss and postoperative blood transfusion rate were significantly higher in the early tourniquet release group than in the late tourniquet release group. No statistical differences were found for operative time and incidence of deep venous thrombosis (DVT) between the 2 groups. Wound complication rate in the early tourniquet release group was significantly lower than in the late tourniquet release group. Primary TKA with early tourniquet release is similar to TKA with late tourniquet release regarding perioperative blood loss, operative time, and incidence of DVT. Early tourniquet release reduced the incidence of wound complications compared with late tourniquet release. [Orthopedics. 2016; 39(4):e642-e650.]
and Knee Surgeons reported that 95% use tourniquets in TKA.\textsuperscript{7}

In this context, various methods of using a tourniquet were proposed by different researchers; of these, 2 methods are widely adopted. The first widely used method is to release the tourniquet after cementing the prosthesis (early release) to reduce tourniquet time and the incidence of relevant complications.\textsuperscript{8} The second widely used method is to release the tourniquet after wound closure and pressure dressing (late release), which is believed to decrease blood loss effectively, decrease operative time, reduce the pressure of the articular cavity hematoma on the synovium, and relieve postoperative pain, thus increasing function and postoperative recovery.\textsuperscript{9} Many independent comparative studies have been conducted on these 2 methods of tourniquet application in primary TKA, but their conclusions for perioperative blood loss are controversial, which might be due to the limited sample size of each study. Therefore, the conclusions are less clinically instructive.

The current study pooled the effective sizes by using meta-analysis to compare the 2 methods on perioperative blood loss and the incidence of relevant complications by searching the latest databases for randomized controlled trials (RCTs) on timing of tourniquet release.

\textbf{MATERIALS AND METHODS}

\textbf{Searching Strategy}

Two researchers independently searched international databases from 1966 to March 2015. Databases included PubMed, Embase, Web of Science, and Cochrane Central, with no restriction to specific languages or years of publication, and manually searched all reference lists contained in the literature. The following search terms were used: total knee arthroplasty, TKA, total knee replacement (TKR), TKR, tourniquet, and random.

\textbf{Eligibility Criteria}

Inclusion criteria were: (1) patients underwent primary TKA, (2) clinical results of early tourniquet release versus late tourniquet release in TKA were compared, (3) studies reported clinical outcomes of TKA (at least 1 desirable outcome), and (4) studies were RCTs.

Exclusion criteria were: (1) nonprospective RCTs, (2) animal or cadaver studies, (3) comparative studies on the different timings of tourniquet release in other operations but not TKA, and (4) revision TKA.

\textbf{Article Selection and Validity Assessment}

Two researchers independently selected articles according to the criteria above and assessed the quality of each literature. All disagreements were resolved by the corresponding researcher. The Physiotherapy Evidence Database (PEDro) Scale, which contains 11 items based on the Delphi list, was used to assess the methodologic quality of each article.\textsuperscript{10} Each item was scored as having either satisfied the criterion or not satisfied the criterion, with a maximum score of 10 because criterion 1 was not scored. A trial with a score of 6 or higher was considered to be a high-quality trial.

\textbf{Data Extraction}

Two researchers independently extracted the data from the articles using the same format, after which the data were compared and disagreements were resolved by extracting and reviewing the data again, including information about the study, such as authors and years of publication, participant demographics, sample size, operative time, types of prosthesis, and outcome indicators. Data from any non-English articles were extracted only after professional translation.\textsuperscript{11} The authors of some of the articles were contacted by e-mail to acquire missing data, including data such as sample size\textsuperscript{12} and measured perioperative blood loss.\textsuperscript{13} Total
measured blood loss was defined as the sum of intraoperative and measured postoperative blood loss, intraoperative blood loss was measured by weighing the swabs and measuring the blood in the suction drain, the calculated blood loss was estimated with formulas, and deep venous thrombosis (DVT) was considered to be present if confirmed by phlebography or ultrasound examination.

### Statistical Analysis

The meta-analysis was conducted using Stata/SE version 12.0 (StatCorp, College Station, Texas). All extracted data were checked and input by reviewers. When the outcome indicator was dichotomous outcomes, relative risk (RR) was calculated for effect size. For continuous outcomes, a weighted mean difference (WMD) was calculated when using the same measurement criterion, otherwise a standardized mean difference (SMD) was calculated; both used 95% confidence intervals (CI). The intervening effect of an indicator was considered as zero difference if 95% CI for WMD or SMD contained “0” and 95% CI for RR contained “1.”

The heterogeneity (chi-square test) was tested on the involved studies with a level of significance of \( \alpha = 0.10 \) to calculate heterogeneity index \( I^2 \). The value of \( I^2 > 50\% \) or \( I^2 = 0 \) was considered as low statistical heterogeneity, using a fixed-effects model to pool effect size; \( I^2 > 50\% \), existing heterogeneity, used random-effects model. Begg’s test was used to check the publication bias of involved articles.

### Results

#### Study Selection

Of the 606 articles retrieved by the search, 354 were excluded after checking for duplicates; 236 were excluded after reviewing the titles and the abstracts; and a meeting summary was excluded by reading the full text. Therefore, a total of 16 articles were included in the meta-analysis. The review process is summarized in Figure 1.

#### Study Characteristics

Sixteen articles were included in this meta-analysis. One study was published in German, and the other studies were all published in English. The types of prostheses were posterior cruciate ligament retaining and posterior stabilized. This meta-analysis involved a total of 1073 patients and 1097 knees, with 534 patients and 545 knees in the early tourniquet release group, and 539 patients and 552 knees in the late tourniquet release group. All basic information regarding the articles is summarized in Table 1.

#### Quality of Included Articles

The methodologic quality of the 16 RCT articles was assessed in accordance with the PEDro Scale. The results showed 2 articles scored 5 and were rated as low quality; the remaining 14 articles scored 6 or higher and were rated as high quality. The methodologic score for each of the RCTs is shown in Table 2.

#### Outcomes of Meta-analysis

**Calculated Blood Loss**

Four articles reported calculated blood loss, and the study by Lotke et al\(^7\) was included as 2 independent studies because the authors divided the TKA cases into 2 groups according to the beginning time of postoperative continuous passive motion, and then compared the difference between early and late tourniquet release in each group. There was heterogeneity \( (P = 0.000, I^2 = 96.9\% ) \) between each study. A total of

### Table 1

**Description of Included Trials**

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Mean Age, y</th>
<th>Male/Female</th>
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<th>Late Release</th>
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<td>Enoxaparin</td>
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<tr>
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<td>Enoxaparin/ warfarin</td>
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</table>

Abbreviation: NA, not available.
106 knees in the early release group and 113 knees in the late release group were analyzed by random-effects model; the result showed no significant difference between the 2 groups (WMD=204.22; 95% CI, -4.25 to 412.69; *P*=.055) (Figure 2).

### Decrease in Hemoglobin Level

The decrease in hemoglobin levels on the second or third postoperative day was reported in 6 studies. Heterogeneity among the studies was low (*P*=.091, *I*²=47.4%). A total of 261 knees in the early release group and 257 knees in the late group were analyzed by fixed-effects model, which indicated no significant difference between the 2 groups regarding the drop in hemoglobin level (WMD=0.18; 95% CI, -0.08 to 0.43; *P*=.170) (Figure 3).

### Drop in Hematocrit Level

Four articles reported a decrease in the hematocrit level 2 days or more after the operation. No heterogeneity existed among the studies (*P*=.528, *I*²=0%). Using the fixed-effects model, with 175 knees in the early release group and 178 knees in the late release group, the result showed no significant difference between the 2 groups (WMD=0.97; 95% CI, -0.02 to 1.97; *P*=.055) (Figure 4).

### Measured Postoperative Blood Loss

Seven articles demonstrated measured postoperative blood loss, and the study by Lotke et al17 was included as 2 independent studies as mentioned previously. Heterogeneity existed among the studies (*P*=.000, *I*²=95%). Using the random-effects model, 220 knees in the early release group and 214 knees in the late release group were analyzed; measured postoper-

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### Table 2

PEDro Critical Appraisal Tool Results

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Abbreviation: PEDro, Physiotherapy Evidence Database Scale.

*Criteria: 1. Eligibility criteria were specified; 2. Subjects were randomly allocated to groups (in a crossover study, subjects were randomly allocated an order in which treatments were received); 3. Allocation was concealed; 4. The groups were similar at baseline regarding the most important prognostic indicators; 5. There was blinding of all subjects; 6. There was blinding of all therapists who administered the therapy; 7. There was blinding of all assessors who measured at least one key outcome; 8. Measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups; 9. All subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analyzed by “intention to treat”; 10. The results of between-group statistical comparisons are reported for at least one key outcome; 11. The study provides both point measures and measures of variability for at least one key outcome.

*Maximum score is 10 because criterion 1 is not scored.

* x = not satisfied criterion.
* ✓ = satisfied criterion.
ative blood loss in the 2 groups showed no significant difference (WMD=7.76; 95% CI, -97.88 to 113.40; \(P=0.886\)) (Figure 5).

**Total Measured Blood Loss**

Eleven articles described total measured blood loss, and there was heterogeneity (\(P=0.000, \tau^2=90.9\%\)) among the studies. A total of 429 knees in the early release group and 432 knees in the late release group were analyzed using the random-effects model, which showed that total measured blood loss in the 2 groups was significantly different (WMD=153.41; 95% CI, 37.29 to 269.53; \(P=0.010\)). Late tourniquet release had less total measured blood loss (Figure 6).

**Operative Time**

Twelve studies reported the operative time for the 2 groups. There was heterogeneity between the studies (\(P=0.000, \tau^2=81.6\%\)). Using the random-effects model, the results of analyzing 430 knees in the early release group and 430 knees in the late release group showed no significant difference in operative time between the 2 groups (WMD=3.85; 95% CI, -0.50 to 8.20; \(P=0.083\)) (Figure 7).

**Transfusion Rate**

Eight articles compared the rate of postoperative blood transfusion, including the study by Lotke et al,\(^{17}\) which was deemed as 2 independent studies. No heterogeneity existed among the studies (\(P=0.518, \tau^2=0\%\)). Using the fixed-effects model to analyze 278 knees in the early release group and 298 knees in the late release group, the results indicated a significant difference in the rate of postoperative blood transfusion, with a higher rate in the early release group (RR=1.23; 95% CI, 1.01 to 1.49; \(P=0.035\)) (Figure 8).

**Incidence of Postoperative DVT**

Six articles compared the incidence of postoperative DVT. No heterogeneity existed among these studies (\(P=0.768, \tau^2=0\%\)). The fixed-effects model was used to analyze 229 knees in the early release group and 235 knees in the late release group.
group, showing no significant difference in the incidence of DVT between the 2 groups (RR=0.69; 95% CI, 0.34 to 1.36; \( P = .282 \)) (Figure 9).

**Wound Complications**

Eight articles compared the incidence of postoperative wound complications. Wound complications were mainly erythema, hematoma, oozing, infection, and cellulitis. No heterogeneity was found among these studies (\( P = .672, I^2 = 0\% \)). The fixed-effects model was used to analyze 321 knees in the early release group and 307 knees in the late release group, showing a significant difference in the incidence of postoperative wound complications (RR=0.59; 95% CI, 0.37 to 0.95; \( P = .030 \)). The incidence of wound complications was significantly lower in the early release group (Figure 10).

**Publication Bias**

Taking total measured blood loss, involved as an indicator in most of the studies, as an example, Begg’s test was used to test publication bias. The test showed there was no publication bias existing in the meta-analysis of total measured blood loss (\( P = .732, \) continuity corrected).

**Discussion**

The current study showed no significant difference existed in calculated blood loss, decrease in hemoglobin and hematocrit levels, and postoperative blood loss, indicating the actual total blood losses of early and late tourniquet release are almost equal. Sehat et al reported total blood loss in TKA included both visible and hidden blood loss. In addition, the mean hidden loss accounted for 50% of the total blood loss, which was attributed to hemolysis. However, by using tagged red blood cells, Erskine et al and McManus et al demonstrated that the hidden blood loss in TKA was due to peri-

![Figure 6: Forest plot of total measured blood loss. Abbreviations: CI, confidence interval; ID, identification; WMD, weighted mean difference.](image6)

![Figure 7: Forest plot of operative time. Abbreviations: CI, confidence interval; ID, identification; WMD, weighted mean difference.](image7)

![Figure 8: Forest plot of transfusion rates. Abbreviations: CI, confidence interval; ID, identification; RR, relative risk.](image8)

![Figure 9: Forest plot of incidence of postoperative deep venous thrombosis. Abbreviations: CI, confidence interval; ID, identification; RR, relative risk.](image9)
operative bleeding into the tissue and the joint. As for the finding of more total measured blood loss in TKAs with early tourniquet release, the probable reason is that only visible blood loss was taken into account for this outcome indicator and that the hidden blood loss was not included.

Reactive hyperemia and increase in fibrinolytic activity have been demonstrated to occur a few minutes after tourniquet release, leading to excessive bleeding. A closed wound and pressure dressing can produce a local compressive effect and control this bleeding. Some studies showed that the visible, intraoperative blood loss of early tourniquet release was notable whereas that of late tourniquet release was zero. Based on this, early tourniquet release theoretically would result in more intraoperative blood loss. The current study found no significant difference in postoperative blood loss between early and late tourniquet release. Taking the results of postoperative blood loss and calculated blood loss into account together, one can deduce that early tourniquet release did not increase intraoperative blood loss as well. This might be because under direct view, visible bleeding points could be stopped immediately after tourniquet release.

Although no difference was found in postoperative hemoglobin levels between early and late tourniquet release, the transfusion rate was significantly higher when the tourniquet was released early. This seems to indicate that the transfusion rate was not directly associated with the level of hemoglobin decrease. Moráis et al analyzed the factors affecting perioperative transfusion rate in TKA and found the rate had no significant relevance with application time of tourniquet, but was relevant with preoperative hemoglobin level and body mass index. The difference in transfusion rate between early and late tourniquet release TKAs may have resulted from the different preoperative hemoglobin levels and the different criteria for transfusion.

This study demonstrated that early tourniquet release remarkably reduced the incidence of postoperative wound complications. It is widely accepted that oxygen supply in the soft tissue around the incision is one of the key limitations for sound incision healing. Any factor that weakens the oxygen content in the soft tissue can delay healing of the incision. Clarke et al reported that tourniquet in TKA sharply decreased the oxygen content in the soft tissue around the incision because ischemia-reperfusion injuries due to the application of the tourniquet caused damage to capillaries and blocked capillary lumen. Tetro and Rudan held that the longer a tourniquet was used in TKA, the more serious the anoxia. Late tourniquet release further worsened the low oxygen content in the soft tissue around the incision and consequently increased the incidence of wound complications due to the extension of using a tourniquet. In addition, inadequate control of subcutaneous bleeding points, caused by tourniquet release after the incision is closed, may lead to wound hematomas. Such hematomas may produce local ischemia and anoxia that will affect wound healing.

Separated from the other complications, DVT was assessed individually in this study, and no difference was found in DVT incidence between early and late tourniquet release. Hernandez et al showed operative time longer than 120 minutes increased the incidence of DVT after TKA. According to the study by Olivecrona et al, using a tourniquet for more than 100 minutes in TKA would increase the risk of DVT. In the current study, use of a tourniquet was less than 100 minutes, and there was no difference in operative time between early and late tourniquet release. This may partially account for the similar incidence of DVT in the 2 groups.

There are several limitations of this analysis. First, there was high heterogeneity in the indicators of blood loss including calculated blood loss, measured total blood loss, and postoperative measured blood loss, which may be related to the long publication intervals and the difference in operative technique. Second, the involved complications in the studies in-
cluded in this research did not encompass systemic ones such as pulmonary and cardiovascular complications, and it has been reported that using a tourniquet is associated with an increased risk of perioperative pulmonary and cardiovascular complications. Third, in this research, no direct data proved that there was no significant difference in intraoperative blood loss between the early and late tourniquet release TKAs. The outcome was only a deduction based on the pooled results of calculated blood loss and postoperative blood loss.

**Conclusion**

Primary TKA with early tourniquet release is similar to that with late tourniquet release regarding perioperative blood loss, operative time, and DVT incidence. Early tourniquet release reduced the incidence of wound complications compared with late tourniquet release.

**References**

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