Releasing of Tourniquet Before Wound Closure or not in Total Knee Arthroplasty: A Meta-Analysis of Randomized Controlled Trials

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ABSTRACT

The purpose of this study is to examine our hypothesis that releasing tourniquet intraoperatively before wound closure is better than releasing postoperatively after wound closure and bandaging. We carried out a systematic review using meta-analysis of selected randomized controlled trials comparing tourniquet releasing before and after wound closure in TKA. The results showed that tourniquet releasing before wound closure significantly increased the total blood loss ($P < 0.00001$), calculated blood loss ($P < 0.0001$) as well as postoperative blood loss ($P = 0.007$). However, it decreased the risk of both minor ($P = 0.0007$) and major complications ($P = 0.05$). The available evidence indicated that releasing tourniquet before wound closure for hemostasis increased perioperative blood loss, nevertheless, the risk of complications decreased significantly.

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Methods

We followed the methodological guidelines outlined by the Cochrane Collaboration (Oxford, United Kingdom) [3] during conducting this meta-analysis. These findings were reported according to the recommendations outlined in the Quality of Reporting of Meta-Analyses (QUOROM) statement [4].

Inclusion and Exclusion Criteria

We identified literature that met the following inclusion criteria: (1) randomized controlled trials, (2) comparison of tourniquet releasing before (release before) and after (release after) wound closure during TKA surgery. (3) Outcome measurements should include at least one of these parameters (total blood loss, minor and major complications). Exclusion criteria were: unpublished data, proceedings of meetings, non-randomized controlled trials, different tourniquet application strategy.

Literature Search

Two independent reviewers (Pengfei Zan and Yong Yang) carried out a systematic computerized search of electronic data-bases including the Cochrane Central Register of Controlled Trials, PubMed, Ovid MEDLINE and EMBASE. In addition, we also searched the Internet search engine “Google”. The key words used for the search included: “total knee replacement”, “total knee arthroplasty”, “TKR”, “TKA” and “tourniquet release”. The search was not restricted to the language of reports.
Article Selection and Validity Assessment

We included randomized controlled trials comparing tourniquet releasing before wound closure or not during TKA. Retrospective or prospective studies were excluded. The volume of blood loss and incidence of complications were regarded as primary outcomes. By scanning the title of each study we could filter those inappropriate articles. Afterwards, we independently reviewed abstracts of the remaining studies and selected those that were potentially relevant to our study. Bibliographies of each study were reviewed for any additional studies. We then critically appraised and identified the studies that were appropriate in our analysis. All disagreements were settled by discussion.

Data Extraction

Outcome data from individual study were extracted independently by Pengfei Zan and Yong Yang and checked by a third author against the original information to avoid anthropic mistakes. Whenever necessary, we contacted the authors of the studies for the missing data and additional information. One German article [5] was translated by a Germanic doctor. For any disaccord, we reached a consensus by discussion. Data extracted included publication information; participant demographics; sample size; cement or cementless; method of anesthesia; tourniquet time and operative time; usage of the drainage and the time removed; blood loss measures, including the intraoperative blood loss, postoperative blood loss, total measured blood loss, and calculated blood loss; incidence of complications (including minor complications and major complications); decrease in hemoglobin; the number of transfused patients, and amount of blood transfusion; a straight-leg raise; knee flexion; pain scores. The calculated blood loss was obtained by the method proposed by Gross[6]. With this method, the estimated blood volume was calculated based on height and weight of the patient, using a correction factor for gender. Based on the data extracted from the included studies, we defined the complication as a minor or major one according to whether a second operation was needed. Wound complications such as erythema, marginal necrosis, cellulitis, superficial infection, oozing, significant leg swelling, and DVT, which could be healed through conservative treatment and did not require another operation were defined as minor complications. Wound dehiscence, active hemorrhage, hematoma or deep infection that required drainage or debridement or revision, knee stiffness which need a second operation under anesthesia were defined as major complications.

Statistical Analysis

The results were collected using the method of variance-weighted. The presence of heterogeneity were tested using the standard chi-square test (with a level of significance of $P = 0.1$) and the $I^2$ statistic [7].

An $I^2$ statistic value of $>50\%$ indicated substantial heterogeneity. Random-effects analysis [8] was used for comparing trials with heterogeneity, otherwise fixed-effects analysis [9] was used. The mean difference or relative risk was calculated for all outcomes. If the standard deviation of a mean was not reported in a study, it was calculated by the range with use of the methods proposed by Hozo et al [10]. The meta-analysis was carried out using the RevMan 5.2 software (Cochrane Collaboration, Oxford, United Kingdom).

Results

Identified Trials

A flow chart of the studies was shown in Fig. 1. Of the 1594 studies identified by the primary search, 1574 studies were excluded based on the inclusion/exclusion criteria, leaving nineteen potentially relevant studies. This was further reduced to sixteen after critical appraisal of the full articles, eliminating three non-randomized controlled trials [11–13]. Table 1 shows the included studies with their contributions to the data pool [5,14–28].

Outcome Analysis

Blood Loss

A total of 8 studies [14,16–20,22,23] including 608 knees were included for analysis of the total measured blood loss and showed significantly more blood loss in the knees with tourniquet releasing before wound closure (Fig. 2) (mean difference = 184.19 ml; 95% confidence interval = 134.43 to 233.95; $P < 0.00001$). In four studies [5,19,21,24], the calculated blood loss proposed by Gross [6], also showed significantly more blood loss (Fig. 3) (mean difference = 268.86 ml; 95% confidence interval = 143.77 to 393.96; $P < 0.0001$). In addition, we found six studies [5,20,21,25–27] in which the decrease in hemoglobin (HB) reported showed significant difference between the two groups (Fig. 4) (mean difference = 89.56 ml; 95% confidence interval = 24.88 to 154.23; $P = 0.007$). However, four studies [5,16,20,27] in which the decrease in hemoglobin (HB) reported showed no significant difference (Fig. 5) (mean difference = 0.43; 95% confidence interval = −2.63 to 3.50; $P = 0.78$).

Complications

Based on the available data, ten studies [5,14–18,20,24,25,27] involved complications including minor complications and major complications. From Figs. 6 and 7, we could draw the conclusion that tourniquet releasing after wound closure increased the risk of both minor complications (odds ratio = 0.39; 95% confidence interval = 0.23 to 0.67; $P = 0.0007$) and major complications (odds ratio = 0.32; 95% confidence interval = 0.10 to 1.00; $P = 0.05$). With four available studies [5,16,17,20], we also conducted a subgroup analysis regarding DVT, which was which was confirmed by phlebography in clinical suspected patients. Fig. 8 showed no significant difference between


<table>
<thead>
<tr>
<th>Study (year)</th>
<th>Patients</th>
<th>Knees</th>
<th>Operative Time (min)</th>
<th>Tourniquet Time (min)</th>
<th>Total Measured Blood Loss (ml)</th>
<th>Calculated Blood loss (ml)</th>
<th>Postoperative Blood loss (ml)</th>
<th>Decrease in (HB) (g/l)</th>
<th>Minor Complications</th>
<th>Major Complications</th>
<th>DVT</th>
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<td>82/12/77</td>
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<td>nc</td>
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<tr>
<td>Schuh A 2003 [5]</td>
<td>70/35/35</td>
<td>100.2/102.4/77.12</td>
<td>18.4/26.4</td>
<td>nc</td>
<td>1201.6 (506.2/794.5)</td>
<td>nc</td>
<td>656 (363.5/393)</td>
<td>34 (14)</td>
<td>22 (11)</td>
<td>39.3 (10.4/40)</td>
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<tr>
<td>Steffin B 2009 [27]</td>
<td>37/18/19</td>
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<td>nc</td>
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<td>582 (392/532)</td>
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<td>589 (122.2/108.3)</td>
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<td>nc</td>
<td>0/2</td>
</tr>
<tr>
<td>Cemil Yildiz 2014 [28]</td>
<td>53/30/23</td>
<td>74.2/69.3/69.3</td>
<td>5.4/62.7/47.4</td>
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<td>nc</td>
<td>nc</td>
<td>nc</td>
<td>nc</td>
<td>nc</td>
<td>nc</td>
<td>0/2</td>
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</tbody>
</table>

Nc = not clear, HB = hemoglobin, DVT = deep vein thrombosis. Operative time, tourniquet time, total measured blood loss, calculated blood loss, postoperative blood loss and decrease in (HB) were described as mean (standard deviation) or mean (range). Minor complications: erythema, marginal necrosis, cellulitis, superficial infection, oozing, significant leg swelling, and DVT; major complications: wound dehiscence, active hemorrhage, hematoma or deep infection that required drainage or debridement or revision, knee stiffness which need a second operation under anesthesia. The value of total blood loss was acquired by adding intraoperative and postoperative blood loss. The value of calculated blood loss was acquired according to GROSS’ Formula. The value of postoperative blood loss was acquired by the drainage after surgery. In the study by Lotke et al [21], continuous passive motion was started 3 days postoperatively in one group (Lotke1 PA) whereas it was started immediately in the recovery room in another group (Lotke2 PA).

the two groups (odds ratio = 0.42; 95% confidence interval = 0.13 to 1.38; P = 0.15).

**Operative Time**

Nine studies [5,15,17–19,24,26,28] providing the operative time showed that the group tourniquet releasing before wound closure was associated with significantly longer surgical time compared to the other group (Fig. 9) (mean difference = 7.59; 95% confidence interval = 3.53 to 11.64; P = 0.0002). Five studies giving the tourniquet time showed that it was significantly shorter in the group tourniquet releasing before wound closure (Fig. 10) (mean difference = −13.24; 95% confidence interval = −20.56 to −5.93; P = 0.0004).

**Discussion**

A tourniquet is usually used during TKA for improving visualization of structures, reducing intraoperative bleeding for better cementation. However, a decision must be made whether to release the tourniquet before or after wound closure. This meta-analysis demonstrated that tourniquet releasing prior to wound closure for

Fig. 2. Forest plot of total measured blood loss.
hemostasis increased perioperative blood loss in TKA. Nevertheless, the risk of both minor and major complications was significantly decreased when the tourniquet was released before wound closure. Deflating the tourniquet before wound closure theoretically allows a better control of wound bleeding and patients would have better hemostasis, thus leading to less blood loss. However, there is an increase in the fibrinolytic activity in the first period after tourniquet releasing. The higher perioperative blood loss caused by fibrinolytic activity can probably be controlled after wound pressure dressing.

Releasing tourniquet before wound closure provides a window of time to the activation of fibrinolytic leading to increasing bleeding [29]. The model of prosthesis fixation (cement or cementless) was another factor that influenced perioperative blood loss in TKA. A major source of blood loss was continuous bleeding from the cut cancellous bone and cement prosthesis could reduce this bleeding [30]. In our meta-analysis, most of the included studies used the cement prosthesis with the exception of only a few studies. However, the patients with cementless prosthesis were equally allocated to the

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Mean Difference</th>
<th>IV, Random, 95% CI</th>
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<tr>
<td>n = 3736.12; Ch² = 27.13; df = 6 (P = 0.001); I² = 78%</td>
<td></td>
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</tr>
<tr>
<td>Total (95% CI)</td>
<td>205</td>
<td>295 100.0%</td>
</tr>
<tr>
<td>Test for overall effect: Z = 2.71 (P = 0.007)</td>
<td>89.56 [24.88, 154.23]</td>
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</table>

Releasing tourniquet before wound closure provides a window of time to the activation of fibrinolytic leading to increasing bleeding [29]. The model of prosthesis fixation (cement or cementless) was another factor that influenced perioperative blood loss in TKA. A major source of blood loss was continuous bleeding from the cut cancellous bone and cement prosthesis could reduce this bleeding [30]. In our meta-analysis, most of the included studies used the cement prosthesis with the exception of only a few studies. However, the patients with cementless prosthesis were equally allocated to the
group release before and release after. This increased the heterogeneity of the study but may not influence the results of the comparison. The duration of the operation might play a role in blood loss. Surgical time was significantly longer in the group release before, and this was because although the tourniquet was released, final procedure was aroused longer to additional time for controlling bleeding points. Furthermore, Harvey and Leclerc reported that longer surgical time had a greater blood loss [13].

It is important to point out that total blood loss included both visible blood loss and hidden blood loss [31,32]. Considering the measurement of blood loss, it was the calculated blood loss rather than the total measured blood loss that could represent the actual blood loss in TKA. Pattison et al [33] suggested “hemolysis” as a possible explanation for perioperative blood loss. On the other hand, Erksin using chromium-labeled red cells demonstrated that the blood loss was associated with perioperative bleeding from the wound [34]. According to the results of our meta-analysis, we speculated that it was the activation of fibrinolytic and the longer surgical time that contributed to the results of more perioperative blood loss in the group tourniquet releasing before wound closure.

No significant difference was detected in the decrease of hemoglobin between these two groups ($P = 0.78$) in the four studies [5,16,20,27]. However, differences were obviously discovered between the groups in perioperative blood loss. Theoretically, the hemoglobin is supposed to decrease proportionally with the loss of blood, which should reveal the same difference between the two groups. The small sample size, the variability in the blood transfusion rates and the criteria for transfusion among these studies may bring about this consequence.

A meta-analysis conducted by Alcelik et al [1] compared outcomes with and without a tourniquet in TKA had demonstrated that minor complications were more common in the tourniquet group. Many clinical and experimental studies [35–38] found a correlation between neuromuscular injury and the level of tourniquet pressure or the duration of tourniquet application and concluded that longer application of tourniquet could result in ischemia and mechanical muscular damage induced by tourniquet. In our included studies, the most common minor complications were wound complications, including erythema, marginal necrosis, cellulitis, superficial infection, oozing, significant leg swelling. Hematoma associated without tourniquet releasing for hemostasis and longer application of tourniquet might be
the reasons for relative higher incidence of wound complications. Secondly, it was DVT as presented by forest plot in Fig. 8. As we all know, major limb surgery is an absolute risk factor for DVT. For the group tourniquet releasing after wound closure, it was not only major limb surgery but also longer tourniquet use increases the risk for DVT on account of longer duration of venous blood stasis and probable damage to calcified vessels.

Considering major complications of our included studies, we detected six knees stiffness, three deep infections, two wounds dehiscence, two hematomas drainage, mostly in group tourniquet releasing after wound closure which were presented by forest plot in Fig. 7. These major complications could also be explained by the reasons of hematoma associated without tourniquet releasing for hemostasis and longer application of tourniquet mentioned above. These factors might lead to a delayed rehabilitation which was always accompanied with a higher incidence of the knee stiffness. Although major vascular damage in TKA was very rare, Rand [39] revealed an incidence of acute arterial damage following TKA of 0.03%. One of the included studies by Hernández-Castaños et al [14], in group tourniquet releasing after wound closure one patient needed reintervention 2 h after surgery because of a blood loss of 1200 mL treated by coagulating two medium caliber vessels that were still bleeding. It was a severe complication that needed a second operation under anesthesia and this could have been avoided if the tourniquet was released for hemostasis.

Therefore, in view of the possible complications as above, surgeons should select tourniquet releasing before wound closure for hemostasis and shorten the duration of tourniquet time to minimize the potential complications. If surgeons leave the tourniquet up until wound closure, they should pay attention to some wound complications, DVT, knee stiffness and infection induced by hematoma.

Only one of the studies referred to the pain scores, the straight-leg raising and the range of flexion [15]. Barwell et al reported that the pain scores for patients in group tourniquet releasing before wound closure were significantly higher (median scores 4 and 1 respectively; P < 0.001), and patients in group tourniquet releasing before wound closure were able to perform straight-leg raising significantly earlier (mean 2.8 and 5 days, respectively; P < 0.00001). The mean range of flexion in patients was not statistically significant. This report may provide more benefits to the earlier releasing group, and future research could focus on these aspects.

We also identified an excluded study [40] in which 64 patients were equally divided into two groups. The experimental group was a half-course strategy, tourniquet was inflated from osteotomy until the leg was wrapped with elastic bandages. And the control group used a whole-course strategy, tourniquet was inflated from incision until the leg was wrapped with elastic bandages. Chen et al concluded that the half-course tourniquet strategy could decrease the total perioperative blood loss in primary TKA. It was beneficial in helping patients to achieve earlier functional recovery by improving the pain experience and limb swelling early in the post-operative period. This report may give a new strategy of tourniquet use for TKA.

Based on the results of our meta-analysis, we suggested that patients must be evaluated preoperative carefully. If the clinical manifestation of the patients showed severe anemia, we hope the tourniquet be released after wound closure to decrease blood loss and if the patients’ general condition were just perfect, we hope the tourniquet be released before wound closure to decrease the risk of complications. However, this was not absolute, the manipulation of tourniquet depended more on a surgeon's overall judgment.

**Limitations**

Some limitations must be recognized in our meta-analysis. (1) The major limitation of this analysis is the small sample size. We could not perform statistical tests to eliminate the publication bias. However, such bias was minimized by our comprehensive search, duplicate selection process, and strict inclusion and exclusion criteria. (2) The skills of different surgeons may influence the clinical outcomes, and we need a standard to assess the surgery skills in order to avoid surgeon bias. (3) The cement and cementless TKA may affect the results. (4) The information was not consistently reported in all of the studies included in this meta-analysis.

**Conclusion**

Our meta-analysis of available studies indicates that releasing tourniquet before wound closure for hemostasis increases perioperative blood loss, including total measured blood loss, calculated blood loss and postoperative blood loss in primary TKA. Nevertheless, the risk of complications decreases significantly when the tourniquet is released before wound closure. We hope our meta-analysis presented here will enable surgeons to make an informed decision as to whether to release tourniquet before wound closure or not. Although this current meta-analysis is the one with the most studies and the largest population, more carefully and scientifically designed randomized controlled trials are required to further demonstrate the claim.

**References**


