Association of Use of Tourniquets During Total Knee Arthroplasty in the Elderly Patients With Post-operative Pain and Return to Function

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Objective: During total knee arthroplasty (TKA), tourniquet may negatively impact post-operative functional recovery. This study aimed at investigating the effects of tourniquet on pain and return to function.

Methods: PubMed, Embase, and Cochrane Library were comprehensively searched for randomized controlled trials (RCTs) published up to February 15th, 2020. Search terms included; total knee arthroplasty, tourniquet, and randomized controlled trial. RCTs evaluating the efficacies of tourniquet during and after operation were selected. Two reviewers independently extracted the data. Effect estimates with 95% CIs were pooled using the random-effects model. Dichotomous data were calculated as relative risks (RR) with 95% confidence intervals (CI). Mean differences (MD) with 95% CI were used to measure the impact of consecutive results. Primary outcomes were the range of motion (ROM) and visual analog scale (VAS) pain scores.

Results: Thirty-three RCTs involving a total of 2,393 patients were included in this study. The mean age is 65.58 years old. Compared to no tourniquet group, the use of a tourniquet resulted in suppressed ROM on the 3rd post-operative day [MD, −4.67; (95% CI, −8.00 to −1.35)] and the 1st post-operative month [MD, −3.18; (95% CI, −5.92 to −0.44)]. Pain increased significantly when using tourniquets on the third day after surgery [MD, 0.39; (95% CI, −0.19 to 0.59)]. Moreover, tourniquets can reduce intra-operative blood loss [MD, −127.67; (95% CI, −186.83 to −68.50)], shorter operation time [MD, −3.73; (95% CI, −5.98 to −1.48)], lower transfusion rate [RR, 0.85; (95% CI, 0.73–1.00)], higher superficial wound infection rates RR, 2.43; [(5% CI, 1.04–5.67)] and higher all complication rates [RR, 1.98; (95% CI, 1.22–3.22)].
INTRODUCTION

Total knee arthroplasty (TKA) is highly effective at relieving joint disease-induced pain and improving joint functions (1–3). However, blood loss during TKA is high, and is estimated to exceed 1,000 ml with 10–38% of patients requiring blood transfusion (4–6). Therefore, to reduce blood loss, tourniquets are routinely used.

Tourniquets, the tourniquet can reduce the overall blood loss and ensure that the surface operation time is clean and bloodless, can reduce total blood loss and create a clean blood-poor surface operation time, thereby achieving a long-term survival rate for cemented TKA components (7, 8). However, clinical applications of tourniquets are associated with some limitations, including delayed quadriceps strength recovery, increased risks of infections, nerve paralysis, and deep vein thrombosis, especially in obese patients (9, 10). Studies (5, 11) have reported that tourniquets can lead to weakened muscles, reduced range of motion (ROM), and increased pain, which may lead to delayed recovery. Li et al. reported that tourniquets can increase the amount of hidden blood loss after surgery (12).

Applications of tourniquets during TKA have been shown to significantly decrease blood loss without exerting adverse effects on early post-operative outcomes (8). Randomized clinical trials (RCT) have shown that the absence of tourniquets does not affect blood loss and bone cement permeability in patients with TKA. Furthermore, less inflammation and better knee functions can be realized without a tourniquet (10). However, there is no consensus regarding the advantages and disadvantages of using tourniquets in TKA. This study aimed at evaluating the effects of tourniquets on functional outcomes, pain and to determine their possible risks during TKA.

METHODS

Study Protocol

This systematic review of RCTs was performed according to the Cochrane Handbook for Systematic Reviews of Interventions (13) and the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines (14–17).

Data Sources and Searches

The Cochrane, PROSPERO, Joanna Briggs Institute (JBI), and INPLASY databases were independently searched by two reviewers (J. Z. and T. L.), to avoid duplicates in meta-analysis. Then, we searched electronic databases, including PubMed, Embase and the Cochrane Library (Supplementary Table 1). Searches were performed for publications from database inception to February 15th, 2020. References to relevant comments, editorials, and letters also need to be searched manually.

Study Selection and Data Extraction

Included Studies were based on the PICOS criteria (Supplementary Table 2).

Data Extraction

Relevant data was independently collected by two authors (J. Z. and T. L.) based on a well-designed data extraction format that contains the authors’ names, publication year, country, participant data, tourniquet pressure, anesthesia method, tourniquet duration, drainage, thrombosis prevention and follow-up.

Outcomes

Primary outcomes included ROM, pain measured at 3 days, 1, 3, 6, and 12 months post-operatively, and the need for blood transfusion. Secondary outcomes included intra-operative blood loss, post-operative blood loss, measured total blood loss, calculated total blood loss (18), operation time, transfusion, superficial wound infection, deep vein thrombosis (DVT), and all complications (including DVT, infection, revision, wound erythema/ecchymosis among others).

Quality and Risk-of-Bias Assessment

The Cochrane Collaboration’s risk-of-bias assessment tool (19) was used by two reviewers (J. Z., T. L.) to independently evaluate the included studies for potential bias (Supplementary Table 3). Disagreements between the two investigators were resolved by involving a third investigator (F-L. W.). We used the Cochrane risk of bias method to assess bias assessment (20, 21). If there are 4 or more studies per comparison, the funnel asymmetric distribution was used to estimate publication bias (22). Two reviewers (J. Z., T. L.) independently used the GRADE component (23) to categorize the quality and strength of the evidence as high, moderate, low, and very low for the ROM, pain, superficial wound infection rates and all complication rates.

Data Synthesis and Statistical Analysis

We used STATA 16.0 (Stata Corp, College Station, TX, USA) to analyze data. Data pooling was done using a random-effects model (24). Dichotomous data were evaluated by relative risks (RR) with 95% confidence intervals (CI). Mean differences (MD) with 95% CI were used to weigh effect sizes for continuous outcomes. A forest plot was used to assess effect sizes. The weight of the included study depends on the value of the event in the treatment group, the event in the control group, and the size

Conclusion: Moderate certainty evidence shows that the use of a tourniquet was associated with an increased risk of higher superficial wound infection rates and all complication rates. Therefore, the findings did not support the routine use of a tourniquet during TKA.

Keywords: total knee arthroplasty, tourniquet, function, pain, elder
of the entire sample. $P \leq 0.05$ indicates that the difference is statistically significant. Statistical heterogeneity among summary data were evaluated using the chi-square test and $I^2$ statistic. If the chi-square test showed $p < 0.10$ and $I^2 > 50\%$, data showed high heterogeneity. A subgroup analysis was conducted based on anesthesia, Tourniquet duration, drainage, thromboprophylaxis. Because these variables are categorical variables, we did not do meta regression.

**RESULTS**

**Studies Retrieved**

During our literature search, collation and analysis, no duplicate meta-analysis topics were found in the databases. The PRISMA flow chart of the selection process retrieved a total of 440 results, of which 245 (56.68%) remained after removal of duplicates (Supplementary Figure 1). Six relevant studies were added. After title/abstract curation, a total of 193 records were excluded, with 58 articles remaining. Then, the full text was read and 33 eligible RCTs (34 articles) were enrolled for final synthesis.

**Study Characteristics**

Thirty-three RCTs involving a total of 2,393 patients participated in this meta-analysis (Supplementary Table 4) (5, 6, 8, 10, 12, 25–52). The mean age is 65.58 years old. These studies come from North America, Europe, Asia, and Latin America and had been published between 1995 and 2021. Based on our defined outcomes, 12 reported ROM outcomes (5, 6, 8, 10, 12, 35, 44, 46–49, 52); 10 reported pain outcomes (6, 8, 10, 39, 44, 46, 47, 49–51); 14 reported intra-operative blood loss outcomes (5, 6, 10, 12, 28, 30, 32, 37–39, 41, 43, 48); 11 reported post-operative blood loss outcomes (6, 26, 28, 30, 32, 33, 37–40, 48); 9 reported measured total blood loss outcomes (5, 6, 10, 28, 30, 31, 34, 37, 39); 9 reported calculated total blood loss outcomes (8, 30, 32, 39, 41–43, 48, 52); 20 reported operation time outcomes (5, 6, 8, 10, 12, 28, 30, 32, 33, 35, 38, 42–44, 46–48, 51, 52); 16 reported transfusion outcomes (5, 6, 8, 10, 26, 29, 30, 32, 35, 36, 39, 42, 43, 48, 50, 52); 16 reported DVT outcomes (5, 6, 8, 25–27, 32, 33, 35, 37, 48, 51, 52); 8 reported superficial wound infection outcomes (5, 6, 8, 25, 30, 48, 49, 51); while 15 reported the outcomes for all complications (5, 6, 8, 25, 30–33, 35, 39, 42, 44, 48, 49, 51).

**Risk of Bias Assessments**

Supplementary Figures 2, 3 summarizes the assessment of the risk of bias of selected articles. Four studies were found to have a high risk for randomization sequence generation (10, 37, 38, 50), with 8 not providing this information (25, 26, 28, 30, 31, 33, 36, 43); 5 studies showed a high risk in concealing allocation (25, 26, 31, 33, 38), with 8 not providing this information (12, 27, 28, 36, 37, 39, 50, 51). Due to the nature of intervention, it is not possible to blind participants and therapists in any study. Thirteen of these studies included the objective results of blindly evaluating assessors (5, 6, 8, 32, 41, 42, 45, 46, 48, 49, 52). No study showed a high risk in selective outcome reporting.

**Primary Outcomes**

**ROM**

Pooled analysis of 12 studies showed significantly suppressed ROM when a tourniquet is put on the 3rd day after the operation [MD, $-4.67$; (95% CI, $-8.00$ to $-1.35$)] and the 1st post-operative month [MD, $-3.18$; (95% CI, $-5.92$ to $-0.44$)] (Figure 1). However, applications of a tourniquet did not have a significant impact on ROM on the 3rd, 6th and 12th post-operative months (Figure 1). More than 50% heterogeneity was found in studies reporting ROM on the 3rd post-operative day, the 1st and 3rd post-operative month (Figure 1). Supplementary Figure 4, a contour-enhanced funnel plot, showed significant deviations in the publication. Subgroup analysis revealed that inpatient, tourniquet duration, and drainage did not affect ROM, whereas thromboprophylaxis had effect on ROM on the 3rd post-operative day ($p = 0.00$) (Supplementary Figure 5). Subgroup analysis showed that drainage affected ROM on the 1st post-operative month ($p = 0.03$; Supplementary Figure 6) while thromboprophylaxis affected ROM on the 3rd post-operative month ($p = 0.00$; Supplementary Figure 7). Based on GRADE assessment, moderate-quality evidence suggests that the use of a tourniquet resulted in suppressed ROM on the 3rd post-operative day and the 1st post-operative month.

**Pain**

Pooled analysis of 10 studies showed that pain was significantly increased when a tourniquet was used on the 3rd post-operative day [MD, 0.46; (95% CI, 0.27–0.65); Figure 2]. Pain was significantly reduced when a tourniquet was applied on the 3rd post-operative day [MD, $-1.80$; (95% CI, 2.78 to $-0.82$); Figure 2]. However, tourniquets had no meaningful impact on pain in the 1st, 3rd, 6th, and 12th post-operative months (Figure 2). Supplementary Figure 8, a contour-enhanced funnel plot, did reveal significant publication bias. More than 50% heterogeneity was found in studies reporting pain on the 3rd postoperative day and the 1st post-operative month (Figure 2). Subgroup analysis showed that anesthesia, tourniquet duration, drainage, and thromboprophylaxis did not affect pain outcomes (Supplementary Figures 9, 10). Based on GRADE assessment, moderate-quality evidence suggests that pain was significantly increased when a tourniquet was used on the 3rd post-operative day.

**Secondary Outcomes**

**Blood Loss**

Pooled analysis of 14 studies showed that the use of a tourniquet resulted in low intra-operative blood loss [MD, $-127.67$; (95% CI, $-186.83$ to $-68.50$); Supplementary Figure 11]. Heterogeneity (99.12%) was found in studies reporting on intra-operative blood loss (Supplementary Figure 11). Supplementary Figure 12, contour-enhanced funnel plot, showed significant deviations in the publication. Pooled analysis revealed that tourniquets had no meaningful impact on post-operative blood loss, measured total blood loss and calculated total blood loss (Figure 3 and Supplementary Figure 11). Contour-enhanced funnel plots (Supplementary Figures 14, 16, 18) showed significant
| Study           | Tourniquet | Mean | SD  | No Tourniquet | Mean | SD  | Mean Diff with 95% CI | Weight (%) |
|-----------------|------------|------|-----|---------------|------|-----|---------------------|------------|
| 3 Days          |            |      |     |               |      |     |                     |            |
| Matziolis 2005  | 10         | 58   | 12.5| 10            | 91   | 13.75| -33.00 [-44.52, -21.48] | 1.51       |
| Li 2009         | 40         | 47   | 11  | 40            | 57   | 18  | -10.00 [-16.54, -3.46] | 2.76       |
| Ejaz 2014       | 33         | 36   | 7.9 | 31            | 48   | 9.5 | -12.00 [-16.27, -7.73] | 3.57       |
| Dennis 2016     | 28         | 73.46| 19.1| 28            | 77.72| 18.25| -4.24 [-14.02, 5.54] | 1.85       |
| Liu 2017        | 52         | 80.2 | 5.5 | 52            | 81.3 | 5.7 | -1.10 [-3.25, 1.05] | 4.27       |
| Huang 2017      | 50         | 105.1| 7   | 50            | 107.9| 7   | -2.80 [-5.54, -0.06] | 4.10       |
| Zhou 2017       | 72         | 99.8 | 13.7| 68            | 93.95| 11.15| 5.85 [1.70, 10.00] | 3.62       |
| Alexandersson 2018 | 38     | 69.9 | 1   | 43            | 73.1 | 1.575| -3.20 [-3.78, -2.62] | 4.55       |
| Wu 2018         | 50         | 97.92| 2.1 | 50            | 100.6| 1.56| -2.70 [-3.43, -1.97] | 4.54       |
| Goel 2019       | 100        | 75.9 | 15.9| 99            | 77.3 | 17  | -1.40 [-5.97, 3.17] | 3.46       |
| Zhao 2020a      | 60         | 99.91| 5.48| 60            | 106.5| 8.98| -6.59 [-9.25, -3.93] | 4.13       |
| Zhao 2020b      | 60         | 103.23| 9.23| 60            | 106.5| 8.98| -3.27 [-6.53, -0.01] | 3.93       |
| Zeng 2021a      | 50         | 100  | 5   | 50            | 104  | 6   | -4.00 [-6.16, -1.84] | 4.27       |
| Zeng 2021b      | 50         | 103  | 6   | 50            | 104  | 6   | -1.00 [-3.35, 1.35] | 4.22       |
|                 |            |      |     |               |      |     | Heterogeneity: $\tau^2 = 35.02$, $I^2 = 97.61\%$, $H^2 = 41.93$ |            |
| Test of $\Theta = \phi$: Q(13) = 80.20, p = 0.00 |            |      |     |               |      |     |                     |            |
| 1 Month         |            |      |     |               |      |     |                     |            |
| Dennis 2016     | 28         | 104.79| 14.97| 28            | 107.64| 14.68| -2.85 [-10.62, 4.92] | 2.38       |
| Wu 2018         | 50         | 104.34| 2.4 | 50            | 105.72| 2.47| -1.38 [-2.33, -0.43] | 4.51       |
| Zhao 2020a      | 60         | 108.58| 12.14| 60            | 115.58| 11.39| -7.00 [-11.21, -2.79] | 3.60       |
| Zhao 2020b      | 60         | 112.5 | 10.51| 60            | 115.58| 11.39| -3.08 [-7.00, 0.84] | 3.70       |
|                 |            |      |     |               |      |     | Heterogeneity: $\tau^2 = 4.20$, $I^2 = 57.77\%$, $H^2 = 2.37$ |            |
| Test of $\Theta = \phi$: Q(3) = 7.06, p = 0.07 |            |      |     |               |      |     |                     |            |
| 3 Months        |            |      |     |               |      |     |                     |            |
| Ejaz 2014       | 33         | 100  | 7.3 | 31            | 93   | 8.2 | 7.00 [3.23, 10.77] | 3.75       |
| Dennis 2016     | 28         | 120.88| 8.19| 28            | 122.69| 7.25| -1.81 [-5.86, 2.24] | 3.65       |
| Alexandersson 2018 | 38     | 107.1 | 2.45| 43            | 109.4| 2.05| -2.30 [-3.28, -1.32] | 4.51       |
| Goel 2019       | 93         | 102.5 | 14.8 | 96            | 101.8| 11.5| 0.70 [-3.07, 4.47] | 3.76       |
| Zhao 2020a      | 60         | 122  | 10.09| 60            | 124.75| 9.93| -2.75 [-6.33, 0.83] | 3.82       |
| Zhao 2020b      | 60         | 126.91| 9.2 | 60            | 124.75| 9.93| 2.16 [-1.10, 5.42] | 3.93       |
|                 |            |      |     |               |      |     | Heterogeneity: $\tau^2 = 10.41$, $I^2 = 93.40\%$, $H^2 = 6.02$ |            |
| Test of $\Theta = \phi$: Q(5) = 28.62, p = 0.00 |            |      |     |               |      |     |                     |            |
| 6 Months        |            |      |     |               |      |     |                     |            |
| Ejaz 2014       | 33         | 108  | 8.5 | 31            | 107 | 11 | 1.00 [-3.80, 5.80] | 3.38       |
| Wu 2018         | 50         | 107.64| 2.13| 50            | 107.64| 2.13| 0.00 [-0.83, 0.83] | 4.52       |
|                 |            |      |     |               |      |     | Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, $H^2 = 1.00$ |            |
| Test of $\Theta = \phi$: Q(1) = 0.16, p = 0.69 |            |      |     |               |      |     |                     |            |
| 12 Months       |            |      |     |               |      |     |                     |            |
| Ejaz 2014       | 33         | 113  | 8   | 31            | 113 | 8 | 0.00 [-3.92, 3.92] | 3.70       |
|                 |            |      |     |               |      |     | Heterogeneity: $\tau^2 = 0.00$, $I^2 = .0\%$, $H^2 = .0$ |            |
| Test of $\Theta = \phi$: Q(0) = 0.00, p = 0.69 |            |      |     |               |      |     |                     |            |
| Overall         |            |      |     |               |      |     |                     |            |
|                 |            |      |     |               |      |     | Heterogeneity: $\tau^2 = 17.00$, $I^2 = 95.56\%$, $H^2 = 22.52$ |            |
| Test of $\Theta = \phi$: Q(26) = 166.48, p = 0.00 |            |      |     |               |      |     |                     |            |
| Test of group differences: Qg (4) = 11.66, p = 0.02 |            |      |     |               |      |     |                     |            |

FIGURE 1 | Forest plot comparing ROM outcomes in no tourniquet and tourniquet groups.
| Study                | Tourniquet N | Tourniquet Mean | Tourniquet SD | No Tourniquet N | No Tourniquet Mean | No Tourniquet SD | Mean Diff. with 95% CI | Weight (%) |
|----------------------|--------------|-----------------|---------------|-----------------|--------------------|------------------|----------------------|------------|
| **3 Days**           |              |                 |               |                 |                    |                  |                      |            |
| Li 2008              | 30           | 6.5             | 1.6           | 30              | 6.1                | 1.3              | 0.40 [-0.34, 1.14]   | 4.45       |
| Eジャ 2014           | 33           | 5.5             | 1.6           | 31              | 4.6                | 1.4              | 0.90 [0.16, 1.64]    | 4.45       |
| Dennis 2016          | 28           | 5.2             | 1.98          | 28              | 4.76               | 2.07             | 0.44 [-0.62, 1.50]   | 3.52       |
| Liu 2017             | 52           | 5.73            | 0.6           | 52              | 4.92               | 0.57             | 0.81 [0.59, 1.03]    | 5.73       |
| Alexandersson 2018   | 38           | 2.85            | 2.06          | 43              | 2.44               | 1.63             | 0.41 [-0.39, 1.21]   | 4.25       |
| Wu 2018              | 50           | 3.98            | 0.87          | 50              | 3.62               | 0.57             | 0.36 [0.07, 0.65]    | 5.62       |
| Jawhar 2019          | 50           | 4.2             | 0.3           | 49              | 4                  | 0.4              | 0.20 [0.06, 0.34]    | 5.84       |
| Zeng 2021a           | 50           | 2.28            | 0.61          | 50              | 1.8                | 0.53             | 0.48 [0.26, 0.70]    | 5.73       |
| Zeng 2021b           | 50           | 3.44            | 1.11          | 50              | 3.08               | 1.05             | 0.36 [-0.06, 0.78]   | 5.33       |

Heterogeneity: $\tau^2 = 0.04$, $I^2 = 60.50\%$, $H^2 = 2.53$

Test of $\theta_1 = \theta_2$: Q(8) = 23.07, p = 0.00

| 1 Month              |              |                 |               |                 |                    |                  |                      |            |
|----------------------|--------------|-----------------|---------------|-----------------|--------------------|------------------|----------------------|------------|
| Dennis 2016          | 28           | 3.73            | 2.12          | 28              | 3.25               | 1.94             | 0.48 [-0.58, 1.54]   | 3.52       |
| Liu 2017             | 52           | 0.45            | 0.53          | 52              | 0.39               | 0.51             | 0.06 [-0.14, 0.26]   | 5.76       |
| Wu 2018              | 50           | 1.64            | 0.6           | 50              | 1.48               | 0.65             | 0.16 [-0.09, 0.41]   | 5.70       |
| Ozkunt 2018a         | 24           | 3.58            | 0.37          | 25              | 1.52               | 0.38             | 2.06 [1.85, 2.27]    | 5.75       |
| Ozkunt 2018b         | 20           | 1.55            | 0.47          | 25              | 1.52               | 0.38             | 0.03 [-0.22, 0.28]   | 5.69       |
| Jawhar 2019          | 47           | 1.6             | 0.3           | 45              | 2.2                | 0.4              | -0.60 [-0.74, -0.46] | 5.83       |
| Goel 2019            | 100          | 3.25            | 2.19          | 99              | 3.89               | 3.72             | -0.64 [-1.49, 0.21]  | 4.13       |

Heterogeneity: $\tau^2 = 0.82$, $I^2 = 98.14\%$, $H^2 = 53.70$

Test of $\theta_1 = \theta_2$: Q(6) = 426.76, p = 0.00

| 3 Months             |              |                 |               |                 |                    |                  |                      |            |
|----------------------|--------------|-----------------|---------------|-----------------|--------------------|------------------|----------------------|------------|
| Alexandersson 2018   | 38           | 2.9             | 2.45          | 43              | 4.7                | 2.05             | -1.80 [-2.78, -0.82] | 3.75       |

Heterogeneity: $\tau^2 = 0.00$, $I^2 = .$, $H^2 = .$

Test of $\theta_1 = \theta_2$: Q(0) = 0.00, p = .

| 6 Months             |              |                 |               |                 |                    |                  |                      |            |
|----------------------|--------------|-----------------|---------------|-----------------|--------------------|------------------|----------------------|------------|
| Dennis 2016          | 28           | 2.56            | 2.14          | 28              | 2.32               | 2.07             | 0.24 [-0.86, 1.34]   | 3.41       |
| Wu 2018              | 50           | 0.82            | 0.66          | 50              | 0.74               | 0.66             | 0.08 [-0.18, 0.34]   | 5.68       |
| Jawhar 2019          | 42           | 0.9             | 0.2           | 43              | 1.2                | 0.3              | -0.30 [-0.41, -0.19] | 5.86       |

Heterogeneity: $\tau^2 = 0.05$, $I^2 = 73.64\%$, $H^2 = 3.79$

Test of $\theta_1 = \theta_2$: Q(2) = 7.78, p = 0.02

| Overall              |              |                 |               |                 |                    |                  |                      |            |
|----------------------|--------------|-----------------|---------------|-----------------|--------------------|------------------|----------------------|------------|

Heterogeneity: $\tau^2 = 0.43$, $I^2 = 96.39\%$, $H^2 = 27.72$

Test of $\theta_1 = \theta_2$: Q(19) = 557.09, p = 0.00

Test of group differences: Q(3) = 25.87, p = 0.00

Random-effects REML model

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**FIGURE 2** Forest plot comparing pain outcomes in no tourniquet and tourniquet groups.
deviations in the publication. More than 50% heterogeneity was found in studies reporting post-operative blood loss, measured total blood loss and calculated total blood loss (Supplementary Figure 11 and Figure 3). Subgroup analyses showed that thromboprophylaxis affected intra-operative blood loss \((p = 0.00;\) Supplementary Figure 13). However, anesthesia, tourniquet duration, drainage, and thromboprophylaxis did not affect post-operative blood loss or measured total blood loss (Supplementary Figures 15, 17). In addition, anesthesia, tourniquet duration, drainage, and thromboprophylaxis affected the calculated total blood loss \((p = 0.02, 0.01,\) and 0.03, respectively; Supplementary Figure 19).

**Operation Time**

Pooled analysis of 20 studies showed that tourniquets were associated with a shorter operation time \([MD, -3.73; (95% CI])\)
CI, −5.98 to −1.48); Supplementary Figure 20. Supplementary Figure 21, a contour-enhanced funnel plot, showed significant deviations in the publication. An 84.83% heterogeneity was found across studies reporting on operation time (Supplementary Figure 20). Subgroup analysis revealed that drainage affected operation time (p = 0.00; Supplementary Figure 22).

Complications
Pooled analysis of 16 studies showed that tourniquets are associated with low transfusion rates [RR, 0.85; (95% CI, 0.73–1.00); Figure 4A]. Less than 25% heterogeneity was found in studies reporting on transfusion (Figure 4A). Pooled analysis of 16 studies showed that tourniquets had no meaningful impact on DVT (Figure 4B). A 10.43% heterogeneity was found across studies reporting on transfusion (Figure 4B). A pooled analysis of 8 studies showed that tourniquets are associated with higher superficial wound infection rates [RR, 2.43; (95% CI, 1.04–5.67); Figure 5A]. A 0% heterogeneity was found across studies reporting on superficial wound infection (Figure 5A). In addition, pooled analysis of 15 studies showed that tourniquets are associated with higher all complication rates [RR, 1.98; (95% CI, 1.22–3.22); Figure 5B]. Less than 50% heterogeneity was found across studies reporting on transfusion (Figure 5B). Contour-enhanced funnel plots (Supplementary Figures 23–26) did not show significant publication bias. Pooled analysis of 7 studies showed that tourniquets have no association with pulmonary embolism rate [RR, 1.71; (95% CI, 0.49–6.00); Supplementary Figure 27]. Contour-enhanced funnel plots (Supplementary Figure 28) showed no significant publication bias. Pooled analysis of 7 studies showed that tourniquets have no association with pulmonary embolism rate [RR, 1.71; (95% CI, 0.49–6.00); Supplementary Figure 27]. Contour-enhanced funnel plots (Supplementary Figure 28) showed no significant publication bias. Based on GRADE assessment, moderate-quality evidence suggests that the use of a tourniquet was associated with an increased risk of higher superficial wound infection rates and all complication rates.

DISCUSSION
Applications of tourniquets in TKA are not supported by sufficient data. Evidence regarding the effects of tourniquets on perioperative blood loss, post-operative function, and pain is not conclusive. We found that tourniquets are associated with increased post-operative pain and/or diminished short-term functional outcomes. However, these effects disappeared after 1 month. Our findings do not support the use of tourniquets during TKA. However, differences in outcomes were small and do not have much clinical significance (53), so interpretation of the conclusion should be cautious.

Guler et al. reported that clinical applications of tourniquets during TKA led to a 20% reduction in quadriceps volume after surgery, when measured against contralateral limb at 1-month of follow-up. There were no differences between limbs on which tourniquets were not applied (54). Dennis et al. reported simultaneous bilateral TKA, in which a tourniquet was used on one knee, and muscle weakness in the tourniquet group lasted until 3 months after surgery (46). However, Goel et al. showed that there were no clinical differences between patients who had inflated tourniquets and those who did not, by assessing functions of treated limbs (8). We found that tourniquets slow down patients’ functional recoveries and increases ischemia-associated pain. Thigh pain is common when tourniquets are used in early post-operative periods (55). Pain is unfavorable and hinders joint function recovery. The ROM is significantly decreased when tourniquets are used in TKA. Our findings are consistent with those of previous trials (5, 6, 10, 52, 56). However, differences in ROM reported in this study were within the error of goniometer, which ranges from 4 to 8 degrees, therefore, these differences might not be clinically relevant.

Total knee arthroplasty is associated with large amounts of perioperative blood loss; reduced bleeding reduces transfusion incidences. Clinical applications of tranexamic acid, hypotension-controlled anesthesia, and tourniquets are widely used in surgery (52, 57). An RCT showed that tourniquets can reduce calculated blood loss during the perioperative period (8). Moreover, it has been reported that applications of tourniquets in TKA increase total blood loss (12, 58). We found that tourniquets do not affect calculated blood loss. However, >50% heterogeneity was found across studies that reported calculated total blood loss. Subgroup analysis showed that anesthesia and thromboprophylaxis affect calculated total blood loss. A previous meta-analysis revealed that early tourniquet release is associated with greater perioperative blood loss, compared to tourniquet release after wound closure (59). The reason for this difference might be because we included more updated RCTs. The results showed that tourniquets are associated with decreased intra-operative blood loss, which can improve the surgical field of vision. Therefore, operation times are shorter when tourniquets are used.

Although there was no difference in calculated total blood loss between the two groups, tourniquets were associated with lower transfusion rates. Mori et al. reported that tourniquets are associated with a greater risk of DVT, following TKA (60). Our study found that there are no differences in DVT between the two groups, consistent with a previous meta-analysis (61). Long-term effects of tourniquets with regard to post-operative complications have not been clearly established. A matched cohort study showed that increased tourniquet times are associated with increased 30-day readmission rates (62). The longer a tourniquet is used, the higher the risk of wound complications (63). In this study, superficial wound infection rates and all complications were found to be higher in the tourniquet group. Goel et al. found that the total number of complications was high in the no-tourniquet group, however, differences in complication rates were not significant (8). Our results are consistent with those of a previous study (61).

STRENGTH AND LIMITATIONS
This study has some strengths, first, this meta-analysis was performed by a professional team including a Cochrane member. Second, the methods were inclusive and transparent, including...
**FIGURE 4** | Forest plot for transfusion rate and DVT. (A) Forest plot comparing transfusion rates between no tourniquet and tourniquet groups; (B) Forest plot comparing DVT outcomes between no tourniquet and tourniquet groups.
all software and website sources. Third, analyses were refined on Patient, Intervention, Control, Outcomes, and Study design (PICOS principle). In addition, the study included 12 outcomes to comprehensively evaluate the effects of tourniquets.

However, it is associated with some limitations. First, PubMed, Embase, and Cochrane Library were searched whereas other databases such as Web of Science, was not. PubMed, Embase, and Cochrane Library include almost all databases and a
retrieval strategy was formulated (64). Second, many studies did not clarify the duration of tourniquet use. In addition, high heterogeneity of blood loss is a disadvantage that affects result reliability. Different surgical techniques and different measurement methods may lead to this heterogeneity.

CONCLUSIONS

This meta-analysis provides insights into evidence-based medicine currently approved by the Cochrane Collaboration (65). Our findings do not support routine use of tourniquets during TKA, as inflating the tourniquet was associated with more pain, slower functional recovery and more complications. However, this conclusion should be interpreted cautiously, considering the small differences in outcomes.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author/s.

AUTHOR CONTRIBUTIONS

F-LW and JC: had full access to all the data in this study and they take responsibility for data integrity and accuracy of analysis. JC, F-LW, JZ, TL, XD, ZZ, and QG: concept and design. JC, F-LW, JZ, TL, XD, ZZ, QG, YZ, JS, and SN: acquisition, analysis, and interpretation of data. JZ, F-LW, and JC: drafting of the manuscript. TL, JZ, and F-LW: statistical analysis. JC, F-LW, JZ, TL, XD, ZZ, and QG: administrative, technical, or material support. JC, F-LW, JZ, and TL: supervision. All authors: critical revision of the manuscript for important intellectual content. All authors contributed to the article and approved the submitted version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2022.825408/full#supplementary-material

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