Systematic Review and Meta-Analysis

Medicine®

OPEN

Efficacy of tranexamic acid plus drain-clamping to reduce blood loss in total knee arthroplasty

A meta-analysis

Yan Zhang, MD*, Jun-Wei Zhang, MD, Bao-Hua Wang, MD

Abstract

Background: Perioperative blood loss is still an unsolved problem in total knee arthroplasty (TKA). The efficacy of the preoperative use of tranexamic acid (TXA) plus drain-clamping to reduce blood loss in TKA has been debated. This meta-analysis aimed to illustrate the efficacy of TXA plus drain-clamping to reduce blood loss in patients who underwent a TKA.

Methods: In February 2017, a systematic computer-based search was conducted in PubMed, EMBASE, Web of Science, the Cochrane Database of Systematic Reviews, and Google Scholar. Data from patients prepared for TKA in studies that compared TXA plus drain-clamping versus TXA alone, drain-clamping alone, or controls were retrieved. The primary endpoint was the need for transfusion. The secondary outcomes were total blood loss, blood loss in drainage, the decrease in hemoglobin, and the occurrence of deep venous thrombosis. After testing for publication bias and heterogeneity between studies, data were aggregated for random-effects models when necessary.

Results: Ultimately, 5 clinical studies with 618 patients (TXA plus drain-clamping group = 249, control group = 130, TXA-alone group = 60, and drain-clamping group = 179) were included. TXA plus drain-clamping could decrease the need for transfusion, total blood loss, blood loss in drainage, and the decrease in hemoglobin than could the control group, the TXA-alone group, and the drain-clamping group ($P < .05$). There was no significant difference between the occurrence of deep venous thrombosis between the included groups ($P > .05$).

Conclusions: TXA plus drain-clamping can achieve the maximum effects of hemostasis in patients prepared for primary TKA. Because the number and the quality of the included studies were limited, more high-quality randomized controlled trials are needed to identify the optimal dose of TXA and the clamping hours in patients prepared for TKA.

Abbreviations: CI = confidence interval, DVT = deep venous thrombosis, PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-analyses, RCTs = randomized controlled trials, RR = relative risk, SD = standard deviation, TKA = total knee arthroplasty, TXA = tranexamic acid, WMD = weight mean difference.

Keywords: drain-clamping, meta-analysis, total knee arthroplasty, tranexamic acid

1. Introduction

Total knee arthroplasty (TKA) is 1 of the effective alternative treatments for severe knee osteoarthritis or osteoarthritis.[1] It is reported that the number of primary TKA procedures will reach 3.48 million in the United States by the year of 2030, which would be an 8-fold increase from the year 2005.[2] However, considerable blood loss is a problematic complication after TKA. It has been reported that patients who underwent TKA may have a resultant blood loss that ranges from 1450 to 1790 mL.[3,4]

Several methods including fibrin sealant, tranexamic acid (TXA), and drain-clamping have been reported to reduce postoperative blood loss and avoid homologous blood transfusion.[5–8] Various protocols for drain-clamping with antibiotics, epinephrine, or TXA have been reported.[9–11] All the above studies proved that drain-clamping can decrease the early period of blood loss in TKA. However, some studies reported that drain-clamping has no benefit in primary TKA.[12]

Tranexamic acid is a synthetic antifibrinolytic agent that is routinely used to prevent bleeding after TKA. The optimal procedure and dose of TXA remain unclear. In the previous references, researchers recommended that TXA combined with drain-clamping can be more effective than drain-clamping alone.

Nevertheless, the evidence is low and included number is limited. Thus, we conducted a meta-analysis to compare the efficacy of TXA plus drain-clamping versus TXA alone, drain-clamping alone, or a control group regarding blood loss in TKA patients.

2. Materials and methods

This systematic review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses

Editor: Giovanni Tarantino.

The authors report no conflicts of interest.

Department of Orthopaedics, North China university of science and technology affiliated hospital, Tangshan, China.

* Correspondence: Yan Zhang, Department of Orthopaedics, North China University of Science and Technology Affiliated Hospital, 73 Jianshenan Road, Lubei District, Tangshan, Hebei Province 063000, China (e-mail: wangminsci@qq.com).

Medicine (2017) 96:26(e7363)

Received: 16 February 2017 / Received in final form: 31 May 2017 / Accepted: 1 June 2017

http://dx.doi.org/10.1097/MD.0000000000007363

(PRISMA) guidelines.[13] This review is registered in Research Registry: Review registry 263 (http://www.researchregistry.com/).

2.1. Search strategies

The following databases were searched in September 2016 without restrictions on location or publication type: PubMed (1950–February 2017), EMBASE (1974–February 2017), the Cochrane Library (February 2017 Issue 3), and the Google database (1950–February 2017). The Mesh terms and their combinations used in the search were as follows: "blood loss" OR "blood" OR "tranexamic acid" OR "drain" OR "drain tube" OR "clamping" AND "total knee arthroplasty" [Mesh terms]. The reference lists of related reviews and original articles were searched for any relevant studies, including randomized controlled trials (RCTs) involving adult humans. Moreover, gray literature and relevant books were manually searched to identify any omitted studies. No language was restricted. When multiple reports describing the same sample were published, the most recent or complete report was used. Since this is a meta-analysis, no ethic approval was need for this meta-analysis.

2.2. Inclusion criteria

2.2.1. Patients. We included adults who have undergone unilateral TKA surgery (no restriction on the sex, disease severity, or comorbidities).

2.2.2. Intervention. Perioperative intra-articularly or intravenous TXA plus drain-clamping was chosen as an intervention group, and there was no restriction on the dose of TXA and timing of clamp.

2.2.3. Comparison. Placebo, TXA only, or drain-clamping only was identified as a comparison group.

2.2.4. Outcomes. Primary outcomes were the need for transfusion, total blood loss, blood loss in drainage, and a decrease in hemoglobin. Secondary outcome was the occurrence of deep venous thrombosis (DVT).

2.2.5. Study design. Randomized controlled trials and non-RCTs were included in this meta-analysis. When multiple reports describing the same sample were published, the most recent or complete report was used.

2.3. Study selection

Two independent reviewers (Y.Z. and J.-W.Z.) screened the titles and abstracts of the identified studies after removing duplicates from the search results. Any disagreements about the inclusion or exclusion of a study were mitigated by discussion or consultation with an expert. The reliability of the study selection was determined by Cohen kappa test, and the acceptable threshold value was set at 0.61.[6,7]

2.4. Data abstraction

A specific extraction was conducted to collect data in a pregenerated standard Microsoft Excel (Microsoft Corporation, Redmond, Washington, D.C.) file. The items extracted from relevant studies were as follows: first author and publication year, country, sample size of the intervention and control groups, transfusion criteria, study type, and follow-up. Outcomes such as the need for transfusion, total blood loss, blood loss in drainage, a decrease in hemoglobin, and the occurrence of DVT were abstracted and recorded in the spreadsheet. Data in other forms (ie, median, interquartile range, and mean ± 95% confidence interval [CI]) were converted to the mean ± standard deviation (SD) according to the Cochrane Handbook.[14] If the data were not reported numerically, we extracted these data from the published figures using "GetData Graph Digitizer" software. All the data were extracted by 2 independent reviewers, and disagreements were mitigated by discussion.

2.5. Quality assessment

The quality of all included trials was independently assessed by 2 reviewers based on the Cochrane Handbook for Systematic Reviews of Interventions, version 5.1.0 (http://www.cochrane-handbook.org/).[14] A total of 7 domains were used to assess the overall quality: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias. Each domain was measured as low bias, unclear bias, or high bias. The methodologic quality of the RCTs was evaluated using the modified Jadad scale,[15] which is a numeric scale that evaluates the quality of the randomization, double blinding, and withdraws and dropouts. Studies scoring 4 or more out of a total possible of 8 were considered to be of high quality. The Newcastle–Ottawa quality assessment scale (NOS) was used to assess the quality of the included non-RCTs. The NOS scale assigns 9 points for non-RCTs. Validity scores of NOS scale were evaluated as follows: 8 to 9, high quality; 6 to 7, medium quality; 5, low quality.

2.6. Outcome measures and statistical analysis

Continuous outcomes (total blood loss, blood loss in drainage, and the decrease in hemoglobin) were expressed as the weighted mean differences (WMDs) with 95% CI. Dichotomous outcomes (the need for transfusion and the occurrence of DVT) were expressed as a risk ratio (RR) with a 95% CI. Statistical significance was set at $P < .05$ to summarize the findings across the trials. Variables in the meta-analysis were calculated using Stata software, version 12.0 (Stata Corp., College Station, TX). Statistical heterogeneity was evaluated using the chi-square test and the I^2 statistic. A random-effects model was applied to estimate the pooled outcomes without regarding heterogeneity.[16,17] Publication bias was visually assessed using funnel plots and was quantitatively assessed using Begg test. If there was a large heterogeneity, we perform sensitivity analysis to find out the source of heterogeneity.

3. Results

3.1. Search results

The process of study selection can be seen in Figure 1. In the initial search, a total of 203 studies were identified from the electronic databases (PubMed = 65, EMBASE = 74, Web of Science = 32, Cochrane Library = 30, and Google database = 2). A total of 189 papers were reviewed, and 184 papers were removed according to the inclusion criteria at the abstract and title levels. One study compared drain-clamping alone versus nonclamping after TKA and was excluded.[12] Ultimately, 5 clinical studies with 618 patients (TXA plus drain-clamping group = 249, control group = 130, TXA alone group = 60, and drain-clamping group = 179)

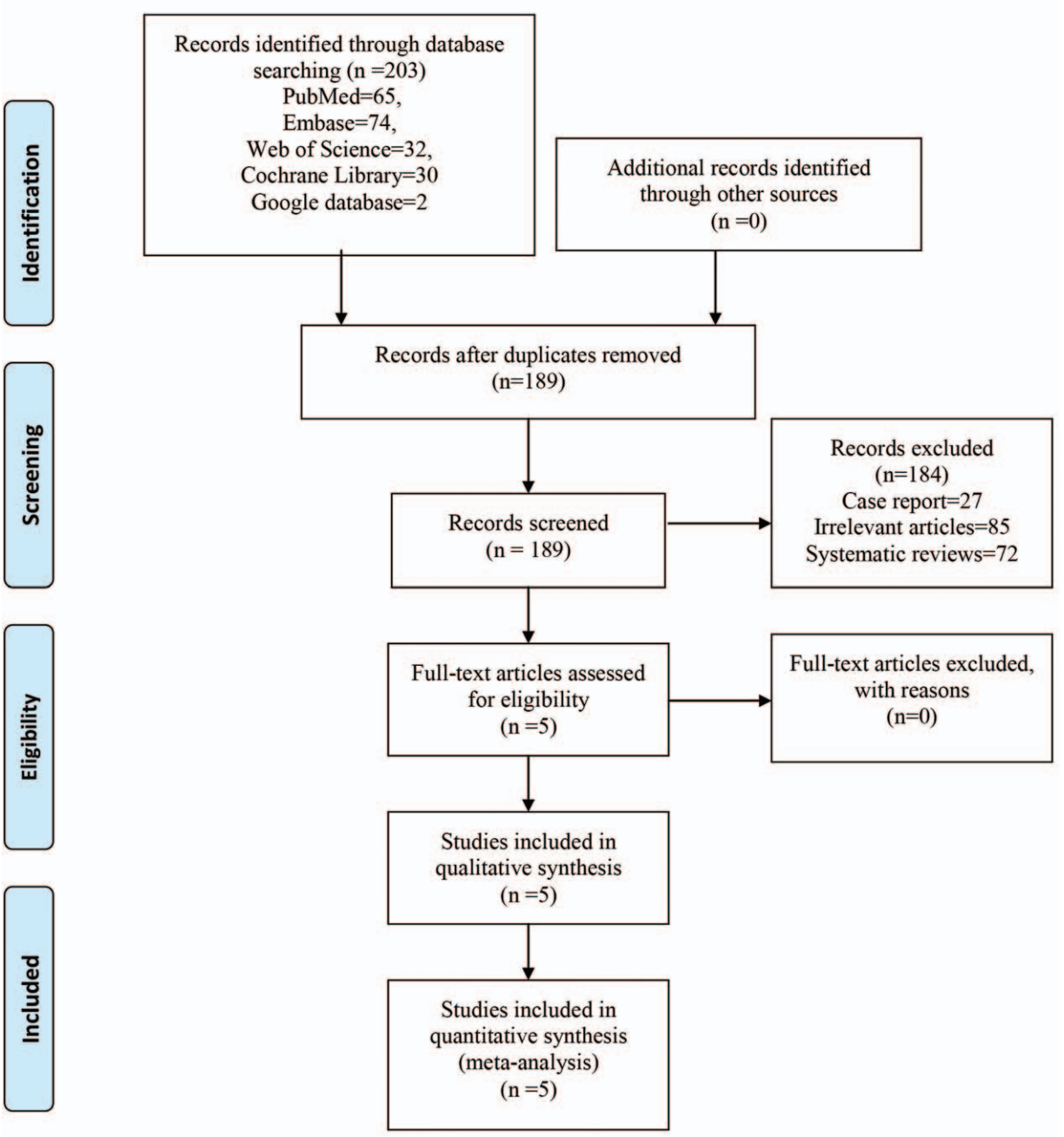

Figure 1. The PRISMA flow chart of retrieved studies. PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-analyses.

were included in the meta-analysis.[11,18–21] The clamping hours ranged from 1 to 3 hours. The dose of TXA ranged from 250 to 1000 mg. Detailed information on the general characteristics of the studies can be seen in Table 1.

3.2. Quality assessment

Details regarding the Jadad scores of the included studies can be seen in Table 2. The total Jadad score of the included studies ranged from 5 to 7. The risk of bias summary and risk of bias graph can be seen in Figures 2 and 3, respectively. Random sequence generation, allocation concealment, blinding of participants, personnel, and outcome assessors are appropriate in 4 studies.[11,19–21] Three studies did not report incomplete outcomes data.[11,20,21] The NOS was used to assess the quality of the non-RCTs, and the results can be seen in Table 3. Mutsuzaki and Ikeda[18] reported 8 scores (high quality). The Kappa value between the reviewers was 0.796, which indicated that there was good consistency between the included studies.

3.3. Results of the meta-analysis

3.3.1. Need for transfusion. Pooled results indicated that preoperative TXA plus drain-clamping can decrease the need for transfusion (RR = 0.30, 95% CI 0.22, 0.42, $P = .000$; Fig. 4) compared with the control group. Compared with the group that included drain-clamping only, TXA plus drain-clamping group was associated with a lower transfusion need (RR = 0.41, 95% CI 0.30, 0.57, $P = .000$; Fig. 4). Compared with the TXA group, the

Table 1

The general characteristics of the included studies.

Author	Country	Control group: No. of patients	Control group: Doses	Surgery	Intervention group: No. of patients	Intervention group: TXA dose	Intervention group: No. of hours for clamping the tube	Outcomes	Follow-up	Study
Chareancholvanich et al, 2012[11]	Thailand	60	Control	TKA	60	10 mg/kg	3	1, 3, 4, 5	6 mos	RCT
		60	Arm1 = TXA							
		60	Arm2 = Clamp							
Mutsuzaki and Ikeda, 2012[18]	Japan	70	Control	TKA	70	1000 mg	1	1, 2, 3	7 d	RCS
Onodera et al, 2012[19]	Japan	50	Clamp	TKA	50	1000 mg	1	1, 2, 4, 5	2 mos	RCT
Sa-Ngasoongsong et al, 2011[20]	Thailand	24	Clamp	TKA	24	250 mg	2	1, 2, 5	3 d	RCT
Sa-Ngasoongsong et al, 2013[21]	Thailand	45	Clamp	TKA	45	250 mg	2	1, 2, 5	3 mos	RCT

In all, 618 patients were included in the meta-analysis. 1, need for transfusion; 2, total blood loss; 3, blood loss in drainage; 4, hemoglobin drop; 5, the occurrence of deep venous thrombosis (DVT). RCS = retrospective controlled studies, RCTs = randomized controlled trials, TXA = tranexamic acid.

Table 2

The risk of bias of the included studies.

Study	A	B	C	D	E	F	Total
Chareancholvanich et al, 2012[11]	√	√	√	√	?	?	4
Onodera et al, 2012[19]	√	√	√	?	?	?	3
Sa-Ngasoongsong et al, 2011[20]	√	√	√	√	√	√	6
Sa-Ngasoongsong et al, 2013[21]	√	√	√	√	√	√	6

A = sequence generation, B = allocation concealment, C = blinding of participants, personnel, and outcome assessors, D = incomplete outcome data, E = no selective outcome reporting, F = other source of bias, √ = low risk of bias, ? = unclear risk of bias.

TXA plus drain-clamping group was associated with a lower transfusion need (RR = 0.68, 95% CI 0.46, 1.00, $P = .049$; Fig. 4).

3.3.2. Total blood loss. Total blood loss was presented in 6 studies. The pooled results indicated that TXA plus drain-clamping can reduce total blood loss when compared with the control group (WMD = −642.20, 95% CI −748.94, −535.46, $P = .000$; Fig. 5). Compared with drain-clamping, TXA plus drain-clamping was associated with less total blood loss (WMD = −130.96, 95% CI −230.91, −31.00, $P = .010$; Fig. 5).

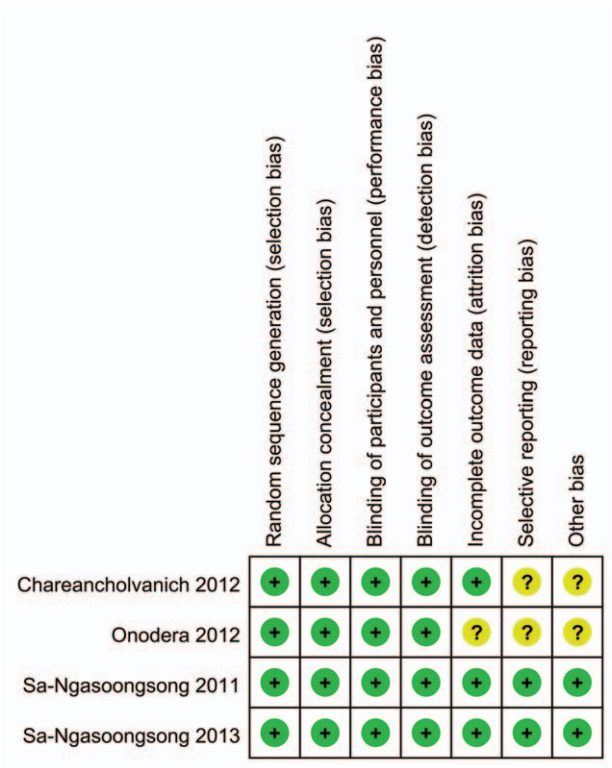

Figure 2. Risk of bias summary.

3.3.3. Blood loss in drainage. Total blood loss was presented in 2 studies. The pooled results indicated that TXA plus drain-clamping could reduce the blood loss in drainage when compared with the control group (WMD = −443.14, 95% CI −855.39, −30.89, $P = .035$; Fig. 6). Compared with drain-clamping, TXA plus drain-clamping was associated with less total blood loss (WMD = −176.12, 95% CI −286.15, −66.09, $P = .002$; Fig. 6). Compared with the TXA group, the TXA plus drain-clamping group was associated with a lower transfusion need (WMD = −198.00, 95% CI −281.66, −114.34, $P = .000$; Fig. 6).

3.3.4. Decrease of hemoglobin. The decrease of hemoglobin was presented in 1 study. The pooled results indicated that TXA plus drain-clamping could reduce the decrease in hemoglobin when compared with the control group (WMD = −1.50, 95%CI −1.79, −1.21, $P = 0.000$; Fig. 7). Compared with drain-clamping, TXA plus drain-clamping was associated with less of a decrease in hemoglobin (WMD = −0.87, 95% CI −1.04, −0.70, $P = .000$; Fig. 7). Compared with the TXA group, TXA plus drain-clamping was associated with a lower transfusion need (WMD = −0.30, 95% CI −0.53, −0.07, $P = .012$; Fig. 7).

3.3.5. The occurrence of DVT. Pooled results indicated that there was no significant difference between TXA plus drain-clamping than with drain-clamping alone (RR = 2.33, 95% CI 0.35, 15.46, $P = .380$; Fig. 8).

3.4. Publication bias

Funnel plot and Begg test of the need for transfusion can be seen in Figures 9 and 10, respectively. Results indicated that effect size

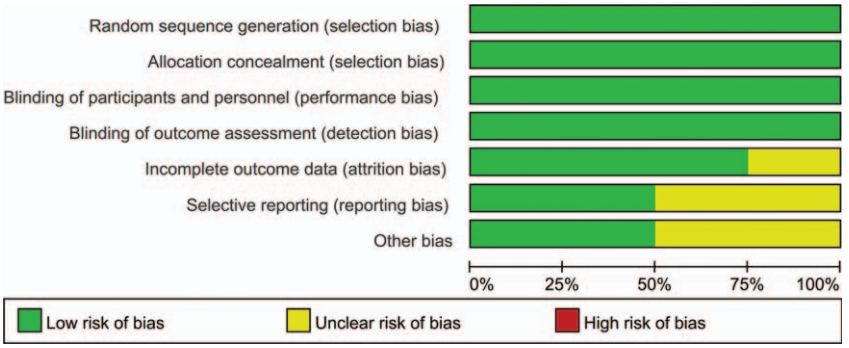

Figure 3. Risk of bias graph.

Table 3

Quality assessment of included non-RCTs according to NOS.

Quality assessment for non-RCTs	Mutsuzaki and Ikeda, 2012
Election point	3
Comparability point	2
Outcome point	3
Total score	8

NOS = Newcastle–Ottawa quality assessment scale, RCT = randomized controlled trial.

was symmetrical and thus no publication bias existed. The *P* value drawn from Begg test was 0.844 and indicated that there was no publication bias.

4. Discussion

This is the first systematic review and meta-analysis that compares the efficacy of TXA plus drain-clamping to reduce blood loss in TKA patients. A total of 5 studies were ultimately included in this meta-analysis. Pooled results indicated that TXA plus drain-clamping could reach the maximum effects of hemostasis than could TXA alone, drain-clamping alone, or control groups. Meanwhile, the occurrence of DVT was not statistically significant between the groups. The major strengths of the current meta-analysis were the comprehensive search and the rigorous statistical calculation. The databases of PubMed, EMBASE, the Cochrane Library, and the Google scholar were searched from inception to February 2017.

Pooled results indicated that compared with drain-clamping, TXA and controls alone, TXA plus drain-clamping could decrease the need for transfusion, total blood loss, and blood loss in drainage to an extreme. The differences between the groups were clinically important. When compared with controls, TXA plus drain-clamping was associated with a reduction of need for transfusion by 53.1% (RR = 0.30, 95% CI 0.22, 0.42, *P* = .000). The blood-saving effects of TXA are certain and have been identified in several previous studies and meta-analyses.[22,23] The effects of drain-clamping for blood loss has been dubiously reported in previous studies.[12] Previous studies have reported that most of the blood loss in TKA occurs during the first postoperative day[24,25]; thus, it seems reasonable to clamp the drain in the early postoperative period to control blood loss. A

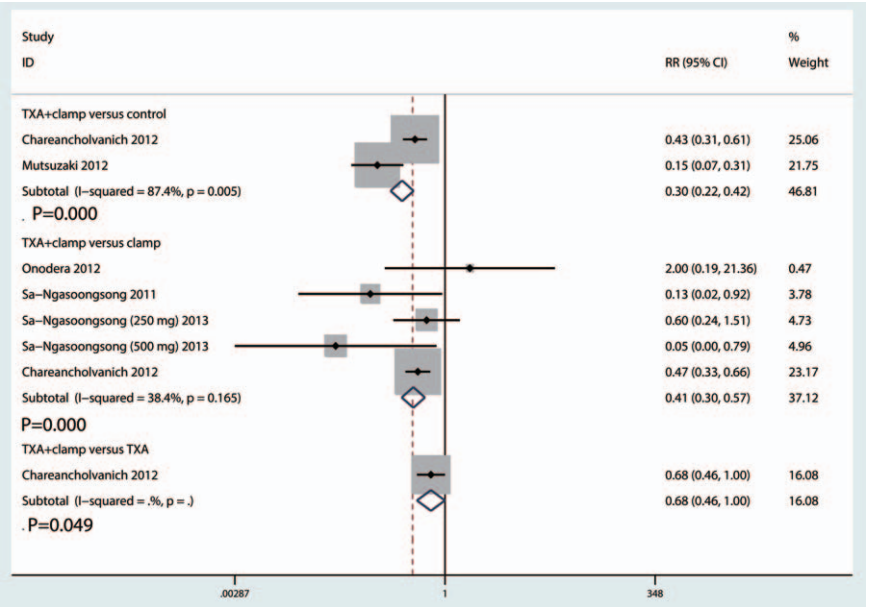

Figure 4. Forest plot comparing the need for transfusion between the 2 groups.

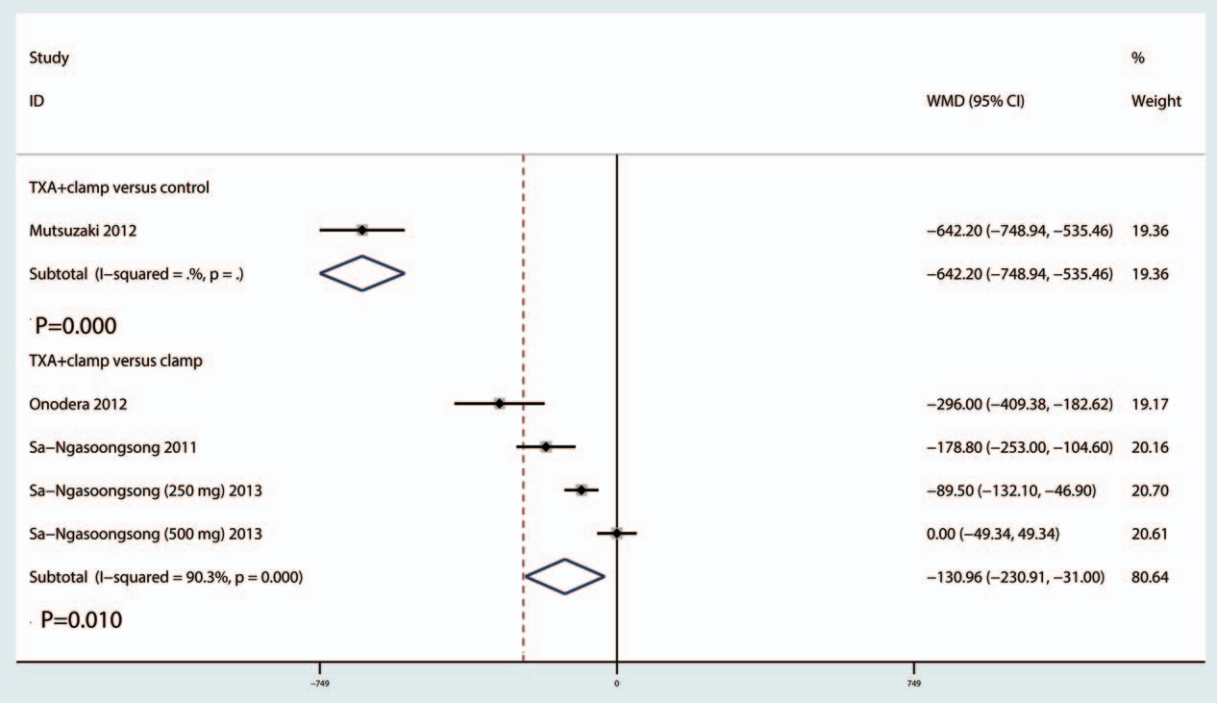

Figure 5. Forest plot comparing the total blood loss between the 2 groups.

single administration with drain-clamping is not sufficient to control the blood loss as reported by a previous study.[7,26] Another issue that should be addressed is the clamping hours for the drain. Yamada et al[27] reported that one-hour clamping is preferable to 24-hour clamping when using the drain-clamping method for minimizing complications.

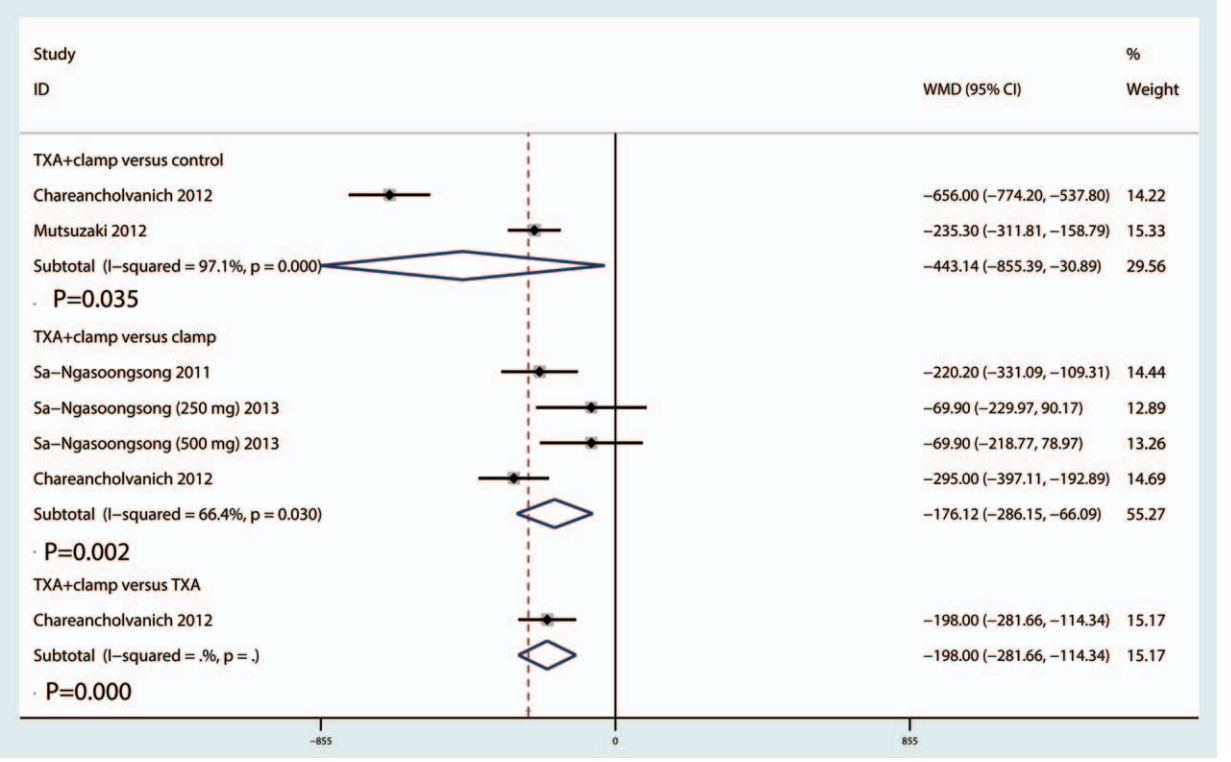

Figure 6. Forest plot comparing the blood loss in drainage between the 2 groups.

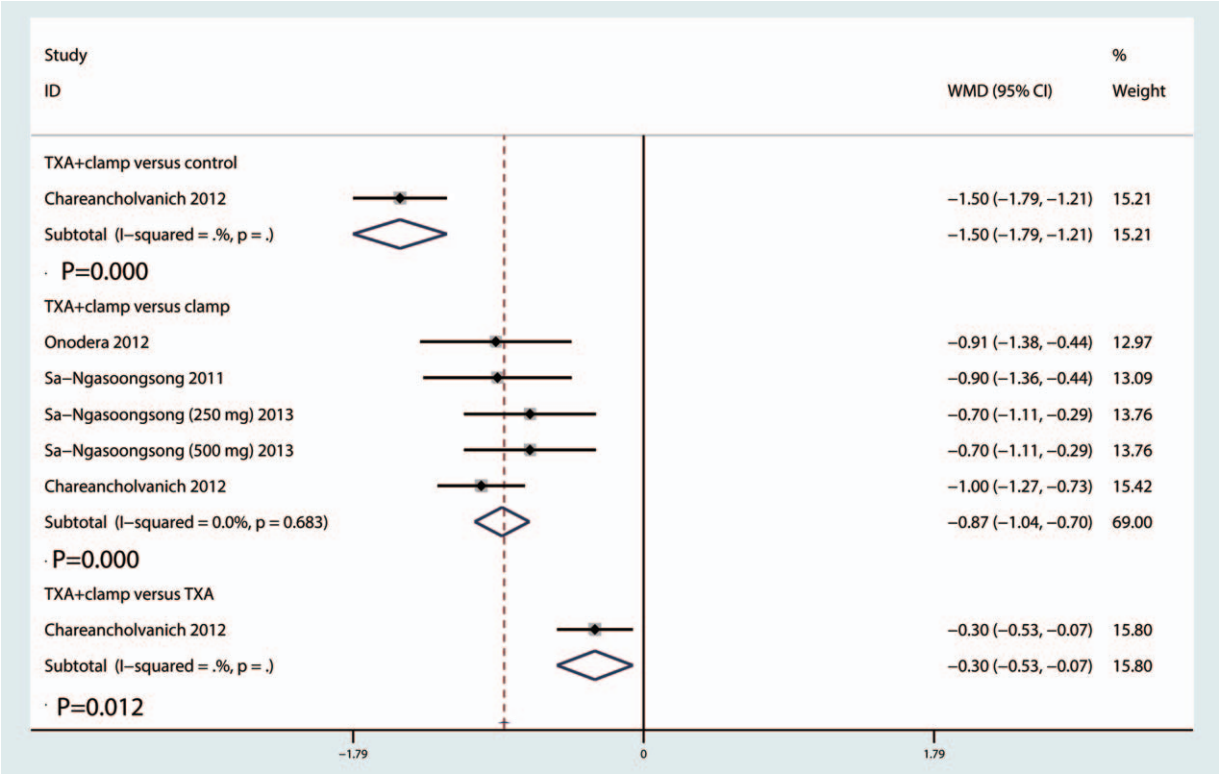

Figure 7. Forest plot comparing the decrease in hemoglobin between the 2s groups.

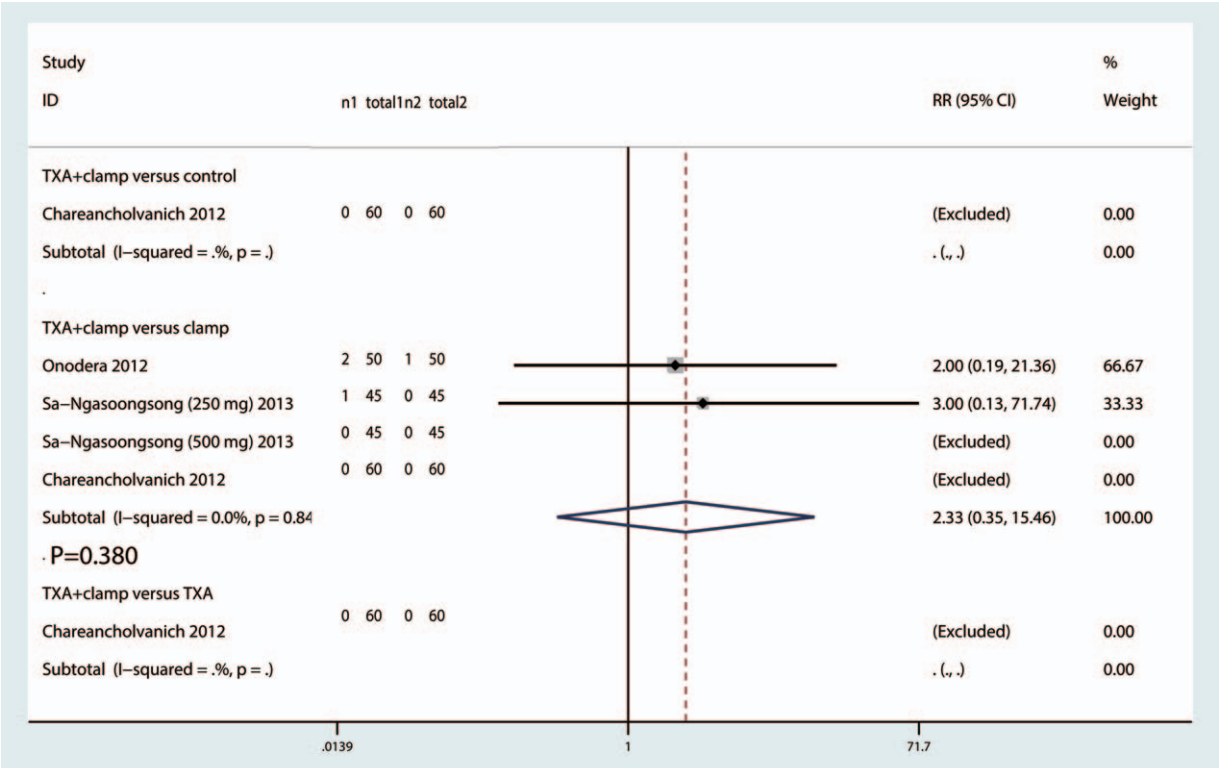

Figure 8. Forest plot comparing the occurrence of deep venous thrombosis (DVT) between the 2 groups.

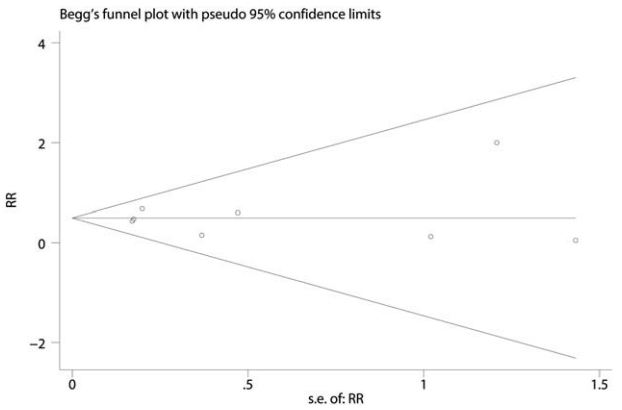

Figure 9. Begg test for need for transfusion.

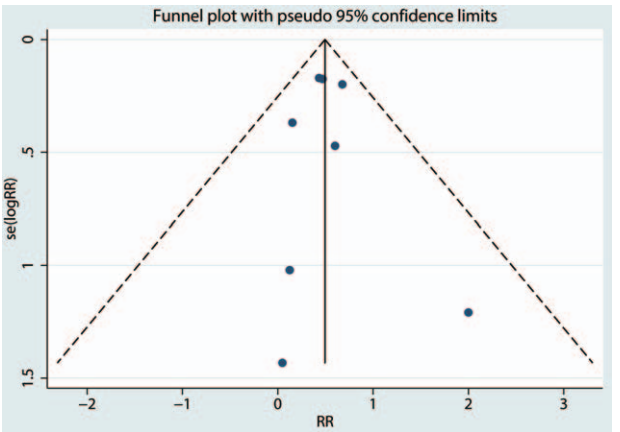

Figure 10. Funnel plot of the need for transfusion.

The most concerning complication regarding drain-clamping is ecchymosis. Chareancholvanich et al[11] reported that TXA plus drain-clamping did not increase the incidence of ecchymosis when compared with the control group or to a group of patients without drain-clamping. Another complication is the incidence of DVT when combined with TXA. This outcome is consistent with other reports in that TXA will not increase the incidence of thrombotic diseases.[28] We used I^2 to assess the heterogeneity between the studies; I^2 is largely affected by the size of the included studies. Because the number of the included studies is limited, there was potential bias between the included studies.[29]

There were several limitations to this meta-analysis: only 5 studies were included, and the sample sizes of the included studies were relatively small, which might have affected the precision of the effect size estimations; several studies had relatively short periods of follow-up that ranged from 3 to 7 days; the dosage and timing of TXA administration differed between the studies, which could affect largely the observed treatment effect; the drain-clamping hours were different and may have influenced the final results; and publication bias may have existed due to the limited number of included studies.

5. Conclusions

In conclusion, this is the first meta-analysis that compares the use of TXA plus drain-clamping for the control of blood loss after primary TKA. Some blood-saving effects were observed with the administration of TXA plus drain-clamping that did not increase complications. Due to the sample size and the limited number of included studies, a multicenter RCT is needed to identify the effects of TXA plus drain-clamping for the reduction of blood loss after primary TKA.

References

[1] Lin C, Qi Y, Jie L, et al. Is combined topical with intravenous tranexamic acid superior than topical, intravenous tranexamic acid alone and control groups for blood loss controlling after total knee arthroplasty: a meta-analysis. Medicine (Baltimore) 2016;95:e5344.
[2] Kurtz S, Ong K, Lau E, et al. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. J Bone Joint Surg Am 2007;89:780–5.
[3] Good L, Peterson E, Lisander B. Tranexamic acid decreases external blood loss but not hidden blood loss in total knee replacement. Br J Anaesth 2003;90:596–9.
[4] Hiippala ST, Strid LJ, Wennerstrand MI, et al. Tranexamic acid radically decreases blood loss and transfusions associated with total knee arthroplasty. Anesth Analg 1997;84:839–44.
[5] Li J, Li HB, Zhai XC, et al. Topical use of topical fibrin sealant can reduce the need for transfusion, total blood loss and the volume of drainage in total knee and hip arthroplasty: a systematic review and meta-analysis of 1489 patients. Int J Surg 2016;36(Pt A):127–37.
[6] Li JF, Li H, Zhao H, et al. Combined use of intravenous and topical versus intravenous tranexamic acid in primary total knee and hip arthroplasty: a meta-analysis of randomised controlled trials. J Orthop Surg Res 2017;12:22.
[7] Li B, Liu ZT, Shen P, et al. Comparison of therapeutic effects between drainage blood reinfusion and temporary clamping drainage after total knee arthroplasty in patients with rheumatoid arthritis. Clinics (Sao Paulo) 2015;70:202–6.
[8] Shen PC, Jou IM, Lin YT, et al. Comparison between 4-hour clamping drainage and nonclamping drainage after total knee arthroplasty. J Arthroplasty 2005;20:909–13.
[9] Tsumara N, Yoshiya S, Chin T, et al. A prospective comparison of clamping the drain or post-operative salvage of blood in reducing blood loss after total knee arthroplasty. J Bone Joint Surg Br 2006;88:49–53.
[10] Sakata H, Maekawa K, Okajima K, et al. The role of microfibrillar collagen hemostat to control postoperative bleeding after total knee arthroplasty. Orthoped Traumatol 1996;45:816–7.
[11] Chareancholvanich K, Siriwattanasakul P, Narkbunnam R, et al. Temporary clamping of drain combined with tranexamic acid reduce blood loss after total knee arthroplasty: a prospective randomized controlled trial. BMC Musculoskelet Disord 2012;13:124.
[12] Kiely N, Hockings M, Gambhir A. Does temporary clamping of drains following knee arthroplasty reduce blood loss? A randomised controlled trial. Knee 2001;8:325–7.
[13] Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ 2009;339: b2700.
[14] GS, H. J. Cochrane handbook for systematic reviews of interventions version 5.1.0. 2011. Available at: http://handbook.cochrane.org/. access date 2011.
[15] Huang Z, Ma J, Pei F, et al. Meta-analysis of temporary versus no clamping in TKA. Orthopedics 2013;36:543–50.
[16] DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986;7:177–88.
[17] Higgins JP. Commentary: heterogeneity in meta-analysis should be expected and appropriately quantified. Int J Epidemiol 2008;37: 1158–60.
[18] Mutsuzaki H, Ikeda K. Intra-articular injection of tranexamic acid via a drain plus drain-clamping to reduce blood loss in cementless total knee arthroplasty. J Orthop Surg Res 2012;7:32.
[19] Onodera T, Majima T, Sawaguchi N, et al. Risk of deep venous thrombosis in drain clamping with tranexamic acid and carbazochrome sodium sulfonate hydrate in total knee arthroplasty. J Arthroplasty 2012;27:105–8.
[20] Sa-Ngasoongsong P, Channoom T, Kawinwonggowit V, et al. Postoperative blood loss reduction in computer-assisted surgery total knee replacement by low dose intra-articular tranexamic acid injection together with 2-hour clamp drain: a prospective triple-blinded randomized controlled trial. Orthop Rev (Pavia) 2011;3:e12.

[21] Sa-Ngasoongsong P, Wongsak S, Chanplakorn P, et al. Efficacy of low-dose intra-articular tranexamic acid in total knee replacement; a prospective triple-blinded randomized controlled trial. BMC Musculoskelet Disord 2013;14:340.
[22] Chen TP, Chen YM, Jiao JB, et al. Comparison of the effectiveness and safety of topical versus intravenous tranexamic acid in primary total knee arthroplasty: a meta-analysis of randomized controlled trials. J Orthop Surg Res 2017;12:11.
[23] Fu Y, Shi Z, Han B, et al. Comparing efficacy and safety of 2 methods of tranexamic acid administration in reducing blood loss following total knee arthroplasty: a meta-analysis. Medicine (Baltimore) 2016;95: e5583.
[24] Fan CH, Hung HH, Chiu KH. Rate of drainage following total knee replacement. J Orthopaed Surg 2006;10:10–3.
[25] Senthil KG, Von Arx OA, Pozo JL. Rate of blood loss over 48 hours following total knee replacement. Knee 2005;12:307–9.
[26] Liu XH, Fu PL, Wang SY, et al. The effect of drainage tube on bleeding and prognosis after total knee arthroplasty: a prospective cohort study. J Orthop Surg Res 2014;9:27.
[27] Yamada K, Imaizumi T, Uemura M, et al. Comparison between 1-hour and 24-hour drain clamping using diluted epinephrine solution after total knee arthroplasty. J Arthroplasty 2001;16:458–62.
[28] Wei Z, Liu M. The effectiveness and safety of tranexamic acid in total hip or knee arthroplasty: a meta-analysis of 2720 cases. Transfus Med 2015;25:151–62.
[29] Borenstein M, Higgins JP, Hedges LV, et al. Basics of meta-analysis: I2 is not an absolute measure of heterogeneity. Res Synth Methods 2017;8:5–18.