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The use of tranexamic acid reduces blood loss in osteotomy at knee level: a systematic review

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Abstract

Purpose Aim of this systematic review was to evaluate the literature regarding the effect of tranexamic acid (TXA) on the outcome after knee osteotomy.

Methods A systematic literature search was carried out in various databases on studies on the use of tranexamic acid in osteotomies around the knee. Primary outcome criterion was the hemoglobin (drop). Secondary outcome criteria were total blood loss, drainage volume, adverse effects such as thromboembolic events, blood transfusions, wound complications and clinical scores. A meta-analysis was performed for quantitative measures. The present study was registered prospectively (www.crd.york.ac.uk/PROSPERO; no.: CRD42021229624).

Results Seven studies with 584 patients (TXA group: 282 patients, non TXA group: 302 patients) Hemoglobin decrease (1.54 g/dl vs. 2.28 g/dl), blood loss (394.49 ml vs. 595.54 ml) and drainage volume (266.5 ml vs. 359.05 ml) were significantly less in the TXA group compared to the non TXA group. No thromboembolic event was noted in any study. In the non TXA group four blood transfusions were given. Eleven wound complications occurred in the non TXA group in comparison to two wound complications in the TXA group.

Conclusions The results of the present study show that the application of TXA reduces hemoglobin drop, blood loss and drainage volume. These effects could be responsible for the lesser rate of side effects after administration of TXA during knee osteotomy.

Keywords High tibial osteotomy · Medial open wedge osteotomy · Distal femoral osteotomy · HTO · DFO · Osteotomy and tranexamic acid

Introduction

The osteotomy to correct deformities is an established method for the treatment of unicompartmental arthrosis [4, 20, 21]. The open wedge technique allows precise correction and has the advantage of protecting the peroneal nerve on the tibia [20]. Risks of the open wedge technique are bleeding and hematoma due to the exposed osteotomy surfaces [12]. The rate of this complication vary between 2 and 5% [12, 22]. Risks of postoperative hematomas are wound complications with delayed healing and superficial or deep infections. The proximal tibial metaphysis is particularly prone to these types of complications due to the small amount of subcutaneous tissue [17].

It is known from various surgical disciplines that intraoperative and postoperative bleeding can be significantly reduced by the use of tranexamic acid (TXA) [5, 6]. In knee and hip arthroplasty, the use of TXA for intra- and postoperative bleeding reduction has proven its worth [5]. There has been no increased risk of symptomatic thromboembolic events after administration of TXA [5]. However, the transfusion rates after TKA could be reduced significantly [5, 13].

The use of TXA in combination with intra-articular infiltration anesthesia is therefore an integral part of TKA today. These concepts for reducing postoperative complications are also called "fast track" or "enhanced recovery" concepts [6].

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Various studies have shown that the use of TXA also reduces hemoglobin (Hb) decline and blood loss after osteotomies around the knee joint [7, 16, 17, 23]. Nevertheless, the use of TXA in knee osteotomies remains controversial, as no study has so far been able to show that the use of TXA can lower the transfusion rate after knee osteotomy [10]. The problem with these studies, however, is that the rate of anemia in the typical patient population for an osteotomy is significantly lower than in patients for whom a TKA is an option. Transfusion rates after osteotomy near the knee are known to be lower after osteotomy compared to TKA and they would probably only be measurable for case numbers of more than 300 patients. However, the number of cases in previous studies on the use of TXA for osteotomy fluctuated between 30 and 150 patients [17, 23, 24]. An option would be a systematic review in which the results of the various studies are evaluated in a meta-analysis. That is the aim of the present work.

The hypothesis of the present study was that the use of TXA in osteotomies around the knee joint leads to less blood loss, but also to lower transfusion rates or wound complications. Analogous to the studies from knee arthroplasty, an increase in the thrombosis rate is not expected.

Methods

Search details

Between November 15, 2020 and December 15, 2020, a systematic literature search was carried out in various databases (PubMed, MEDLINE, EMBASE, Scopus, Google scholar) according to PRISMA criteria to identify work in which the long-term results after the use of tranexamic acid in osteotomies around the knee were examined (Fig. 1). The present study was registered prospectively (www.crd.york.ac.uk/PROSPERO; no.: CRD42021229624).

The following search terms were used: High tibial osteotomy, medial open wedge osteotomy, distal femoral osteotomy, HTO, DFO, osteotomy and tranexamic acid.

The main search was carried out by two reviewers (MB and WP). Inclusion criteria were: 1. Study about osteotomy at the distal femur or proximal tibia (metaphysis and epiphysis), 2. Topical or systemic use of tranexamic acid (TXA) in this study, and 3. English language. Exclusion criteria were: 1. No control group without the use of tranexamic acid, 2. Recommendation and guideline papers, 3. Previous systematic reviews, previous meta-analysis.

If multiple articles of one clinical trial were available, the study with the shorter follow up was excluded.

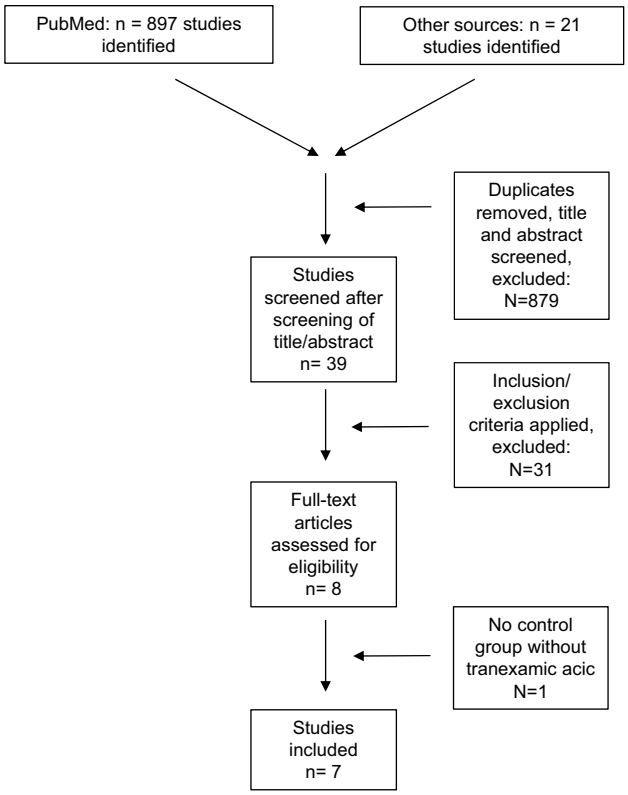

Fig. 1 Flow chart of literature search and review process

Risk of bias (quality) assessment

Quality assessment was conducted by the first authors. The PEDro scale is used for randomized controlled trials [11]. The Newcastle Ottawa scale (NOS) is used for retrospective cohort studies [3]. With full points on the NOS, a maximum of 9 stars can be achieved. A result of ≥ 8 stars applies as high quality, < 6 stars applies as low quality.

Data extraction (selection and coding)

Two reviewers have extracted the following data from the selected studies:

1. Study details such as author and publication date, study design, level of evidence, number of patients and number of patients in the different treatment groups.
2. Results such as blood loss, Hb decrease, and drainage volume
3. Adverse events such as blood transfusions, thromboembolic events and wound complications
4. Other outcome measures (pain, PROM)

Primary and secondary outcome measures

Primary outcome measure is the Hb decrease. Blood loss, drainage volume, adverse events (thrombembolic complications, blood transfusions and wound complications) and other outcome measures are secondary outcome measures. In most studies blood volume were estimated according to the method of Nadler et al. 1962 taking sex, body mass index (BMI) and height into account [15]. For males BV = (0.366 9 × height3) + (0.03219 × weight) + 0.6041 and for females BV = (0.3561 × height3) + (0.03308 × weight) + 0.1833. Total blood loss is calculated from total hemoglobin loss, which in turn is calculated from the difference between preoperative Hb and the minimum Hb during the hospital stay.

Calculation:

Blood loss (in mL) = 100 mL/dL × Hbloss/Hbi

Hbloss = BV x (Hbi – Hbe) × 0 dL/L + Hbt

Hbi = Hb concentration before surgery (g/dL)

Hbe = Hb concentration during hospital stay (g/dL)

Hbt = Total amount of allogeneic Hb transfused (g). Because there were no transfusions, this variable was dropped from the equation in our study.

The formula for blood volume (Nadler et al.) were used by Ni et al., Kim et al., Chen et al. and Palanisamy et al.

Strategy for data synthesis

After extraction of the data tables have been developed to aid the presentation of the data along. A formal meta-analysis was performed for the primary outcome measure (Hb decrease) and for blood loss, drainage volume and for adverse events such as thromboembolic complications, blood transfusions and wound complications. For the cumulative transfusion rate and wound complication rate, the number of patients and number of events for two different treatment groups (TXA and non-TXA) were summarized and the overall percentages were calculated.

Statistics

Mean Hb, blood loss and drainage volume were calculated by adding the mean reported values for each measure and dividing these values by the summarized number of patients in each treatment group. The rate of adverse events was calculated using the total number of subjects in the included studies and the number of reported events.

The STATA 15 program was used. A standardized mean difference according to Cohen with a confidence interval (standardized mean difference) was used for the metric variables (blood loss, Hb decrease and drainage volume). The odds ratio with the confidence interval was calculated for side effects on. For values of 0 in the 4-field table, the principle of small numbers was used. A random effects model was calculated to summarize the results and presented as a forest plot. The level of significance was set at p value: 0.05.

Results

Search results and study design

The search results of this systematic review and detailed information about the study designs is provided in Table 1. Out of 8 articles about the use of TXA in osteotomies around the knee, one had to be excluded due to a missing control group without the administration of TXA [8].

A total of 7 articles with a total of 636 patients were identified (Table 1). All included articles reported about the use of TXA during a tibial or femoral osteotomy close to the knee joint [2, 7, 16, 17, 19, 23, 24]. A total of 314 patients could be identified in the TXA group and 328 patients could be identified in the non TXA group (Table 1).

The majority of studies identified were retrospective case series with a control group. One study focused on the use of TXA at femoral osteotomies whereas the other five reported about the use of TXA in high tibial osteotomies.

One study was level of evidence (LOE) Ib, the other 6 articles were LOE IIb.

The dosing protocols varied among the included studies (Table 1). Four studies used intravenous (i.v.) administration of TXA (Table 1). One study used a topical application of TXA at the osteotomy site [24] and one study combined i.v. and topical administration of TXA [2].

Quality assessment

Tables 2 and 3 show the results of the study quality analysis incorporating the NOS for evaluating the methodological quality of the included studies. In NOS, most studies achieved 7 of 9 possible points which is an acceptable result for a non-randomized study (Table 2). The only RCT which was included received 8 of 10 possible points on the PEDro scale.

Blood parameters

Table 4 shows the results of different blood parameters (blood loss, Hb decrease, and drainage volume) as found in the different studies. Hb decrease was significantly less in the TXA group compared to the non TXA group (1.56 g/dl vs. 2.32 g/dl, Fig. 2). The same applies to blood volume (394.49 ml vs. 560.52 ml, Fig. 3) and drainage volume (239.09 ml vs. 331.91 ml, Fig. 4). These differences were statistically significant (p values: Hb decreased $p = 0.000$, blood loss $p = 0.008$; drainage volume $p = 0.099$ (not significant)).

Table 1 Studies about the use of tranexamic acid (TXA) in knee osteotomy

Author and year	Study design (RCT, prospective cohort study, retrospective)	Level of evidence (LOE)	Number of patients	Dosage	Follow up	Treatment groups with number of patients
Ni, Liu, Zhang et al. [16] (2020)	prospective single blinded, placebo controlled RCT	Ib	100	One dose TXA i.v., 50 mg/kg 10 min before the tourniquet deflated	Blood examination 1,2 and 5 days after surgery, Drainage volume 1 and 3 days after surgery, DVT and PE assessed 3 months	TXA group: 50 Non-TXA group: 50
Kim, Kim, Kim et al. [7]	Retrospective	IIb	150	Three doses of 10 mg/kg of TXA, 1st before tourniquet deflation; 2nd 6 h after surgery, 3rd 24 h after surgery	Blood examination 1,2 and 5 days after surgery, Drainage volume 1 and 2 days after surgery, DVT and PE assessed 3 months	TXA group: 75 Non-TXA group: 75
Chen, Zu, Wang et al. [2]	retrospective cohort study	IIb	100	1 g TXA i.v. before tourniquet and 1 g topical TXA at osteo-tomy site	Blood examination 3 days after surgery, hospital stay 10 days (mean)	TXA group: 52 Non-TXA group: 48
Suh, Kyung, Han et al. [24]	Retrospective	IIb	30	Topical administration of 2 g TXA in 20 mL saline	Blood examination on day 1, 6, and 13 after surgery, Drainage volume 1, 2, and 3 after surgery	TXA group: 15 Non-TXA group: 15
Palanisamy, Das, Moon et al. [17]	Retrospective	IIb	152	2-g TXA i.v. prior to incision, 2-g TXA i.v. 3 h later	Blood examination 2 days after surgery. drainage volume at 72 h	TXA group: 66 Non-TXA group: 86
Steinhaus, Buksbaum, Eisenman [23]	Retrospective	IIb	52	1-g TXA prior to incision, 1-g TXA 4 h later	Blood examination 1 day after surgery, drainage volume at 24 h	TXA group: 24 Non-TXA group: 28
Petersen, Bentzin, Häner et al. [19]	Prospective, non-randomized comparative study	IIa	52	1 g TXA i.v. preoperatively	Blood examination 2 days after surgery, drainage volume at 48 h	TXA group: 26 Non-TXA group: 26
Overall	One RCT, one prospective, five retrospective studies	One LOE Ib, one IIa, five LOE IIb	636	–		TXA group: 314 Non TXA group: 328

RCT randomized controlled trial, *i.v.* intravenous

Table 2 Quality assessment of non-randomized trials about the effect of tranexamic acid (TXA) in patients with osteotomy around the knee with the Newcastle Ottawa scale (NOS)

NOS items/references	Kim et al. [7]	Chen et al. [2]	Suh et al. [24]	Steinhaus et al. [23]	Palanisamy et al. [17]	Petersen, Bentzin, Häner et al. [19]
Representativeness of the exposed cohort	1	1	1	1	1	1
Selection of the non-exposed cohort	1	1	1	1	1	1
Ascertainment of exposure	1	1	1	1	1	1
Demonstration that outcome of interest was not present at start of study	1	1	1	1	1	1
Comparability of cohorts on basis of design or analysis	1	1	2	1	1	1
Assessment of outcome	0	1	0	1	1	1
Was follow-up long enough for outcomes to occur	1	1	1	1	1	1
Adequacy of follow up of cohorts	1	1	0	1	1	1
Total score	7	8	7	8	8	8

Table 3 Quality assessment of RCT about the effect of tranexamic acid (TXA) in patients with osteotomy around the knee with the PEDro Scale

Criteria	Ni, Liu, Zhang et al. [16]
1. Eligibility criteria were specified	1
2. Subjects were randomly allocated to groups (in a crossover study, subjects were randomly allocated an order in which treatments were received)	1
3. Allocation was concealed	1
4. The groups were similar at baseline regarding the most important prognostic indicators	1
5. There was blinding of all subjects	1
6. There was blinding of all therapists who administered the therapy	0
7. There was blinding of all assessors who measured at least one key outcome	0
8. Measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups	1
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 analysed by "intention to treat"	1
10. The results of between-group statistical comparisons are reported for at least one key outcome	1
11. The study provides both point measures and measures of variability for at least one key outcome	1
Total points	8 (criterion 1 will not be used to calculate the PEDro score)

Table 4 Blood loss, Hb decrease and drainage volume of studies about the use of tranexamic acid in knee osteotomy

References	Blood loss (mean in ml)		Hb decrease (mean)		Drainage volume (total in ml)	
	TXA group	Non TXA group	TXA group	Non TXA group	TXA group	Non TXA group
Ni, Liu, Zhang et al. [16]	477.9 ± 138.4	834.6 ± 213.5	1.4 ± 1.1 (g/dl)	2.5 ± 1.3 (g/dl)	282.3 ± 105.5	413.2 ± 114.8
Kim, Kim, Kim et al. [7]	502.4 ± 294.9	882.7 ± 482.0	1.4 ± 1.2 (g/dl)	2.6 ± 1.0 (g/dl)	330.4 ± 196.5	269.3 ± 126.6
Chen, Zu, Wang et al. [2]	296.0 ± 128.7	383.3 ± 181.3	19.2 ± 15.2 (g/l)	27.9 ± 13.8 (g/l)	/	/
Suh, Kyung, Han et al. [24]	/	/	1.1 (g/dl)	1.7 (g/dl)	137.7	276.7
Steinhaus, Buksbaum, Eisenman [23]	184.2 (one dose: 250; Two dose:162.2)[1]	242.1	2.12 g/dl	1.91 g/dl	/	/
Palanisamy, Das, Moon et al. [17]	372 ± 36	635 ± 53	1.3 ± 0.4 (g/dl)	2.2 ± 1.1 (g/dl)	315 ± 95	537 ± 340
Petersen, Bentzin, Häner et al. [19]	/	/	1.0 ± 0.7 (g/dl)	2.3 ± 0.8 (g/dl)	275.6 ± 202.8	476.7 ± 216.3
Average value	359.94 ml	560.52 ml	1.56 g/dl	2.32 g/dl	239.09 ml	331.91 ml

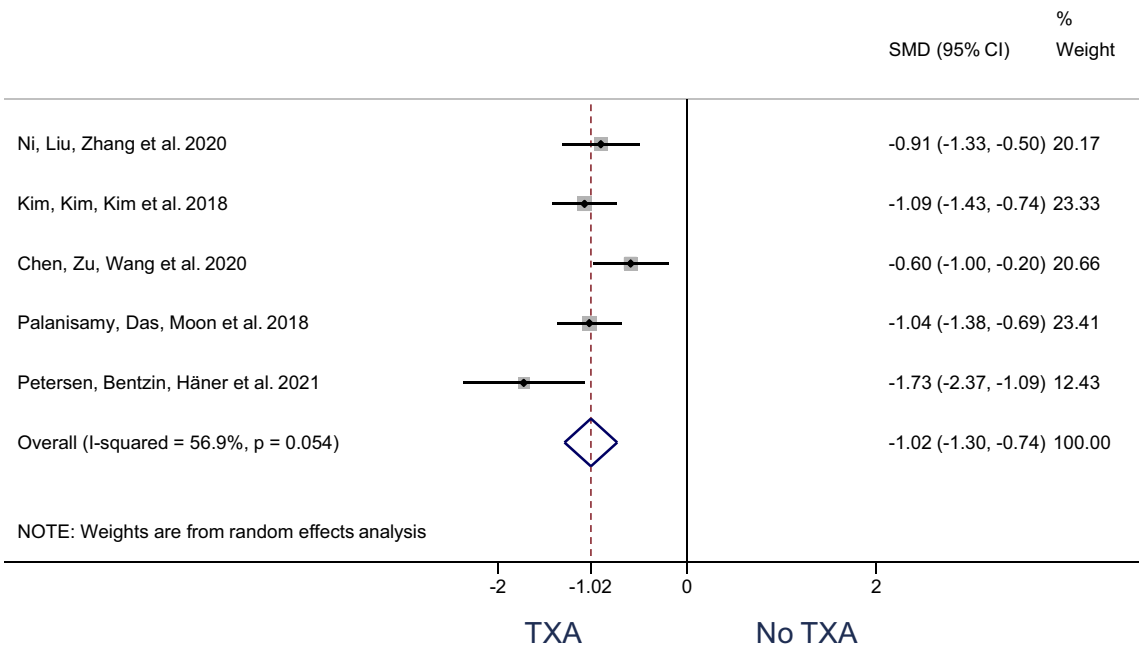

Fig. 2 Hb decrease (standardized mean difference)

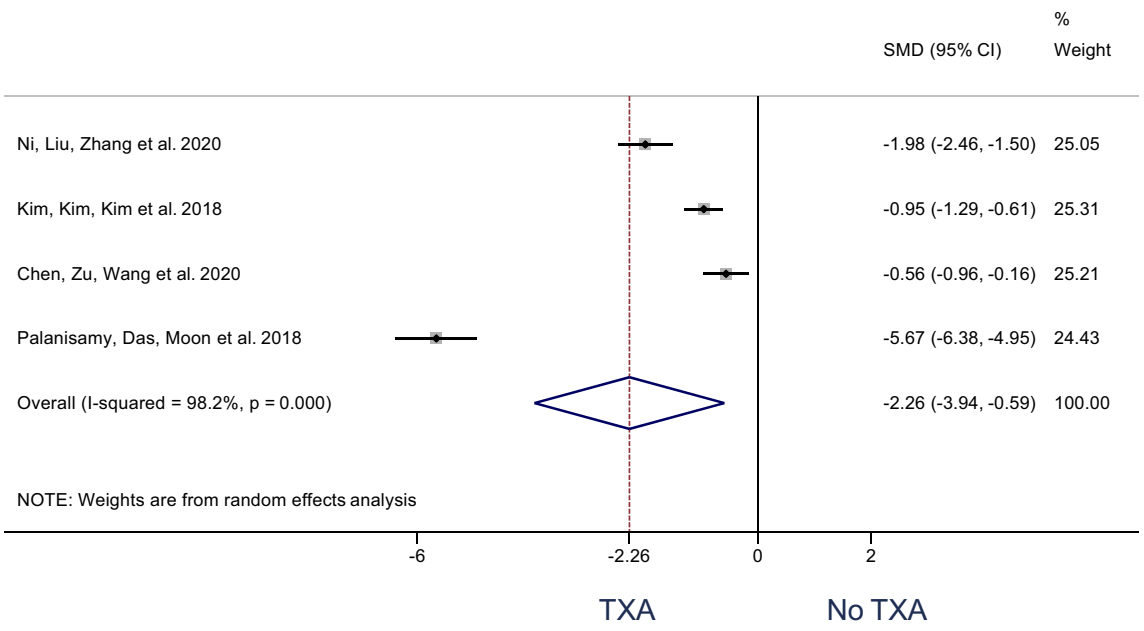

Fig. 3 Blood loss (standardized mean difference)

Adverse effects

In none of the included studies a thromboembolic event was noted, neither in the TXA group nor in the non TXA group (Table 4).

Blood transfusions had to be given more frequently in non TXA group (4 times vs. 0 times). This difference was statistically significant (OR 3.53, *p* value: 0.000, Fig. 5).

Wound complications were less frequently observed in the TXA group compared to the non TXA group (2

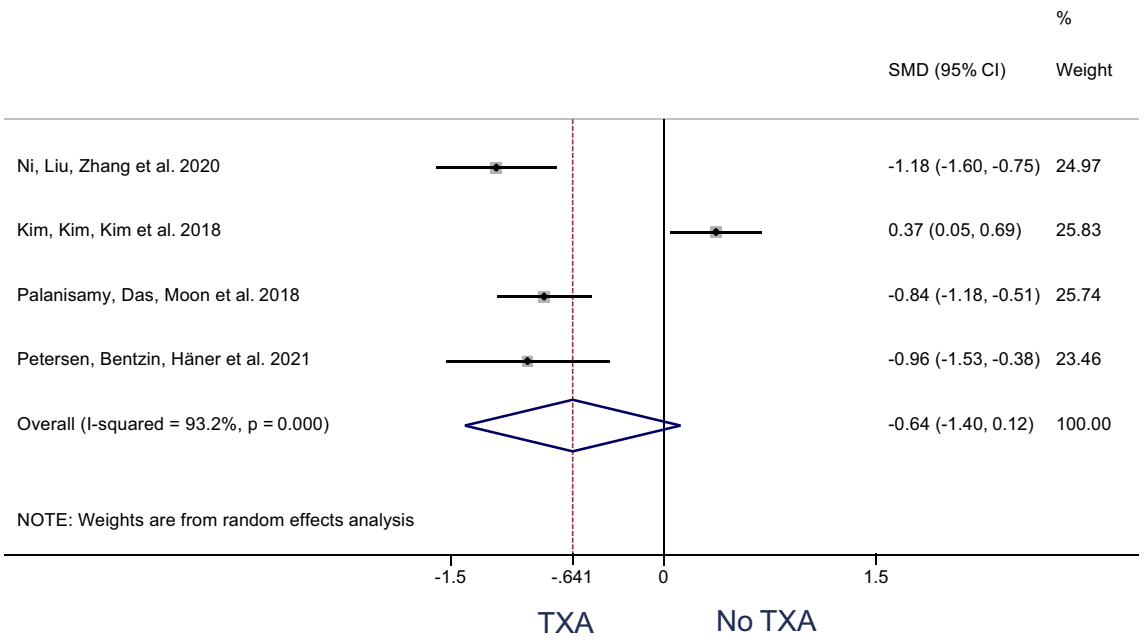

Fig. 4 Drainage volume (standardized mean difference)

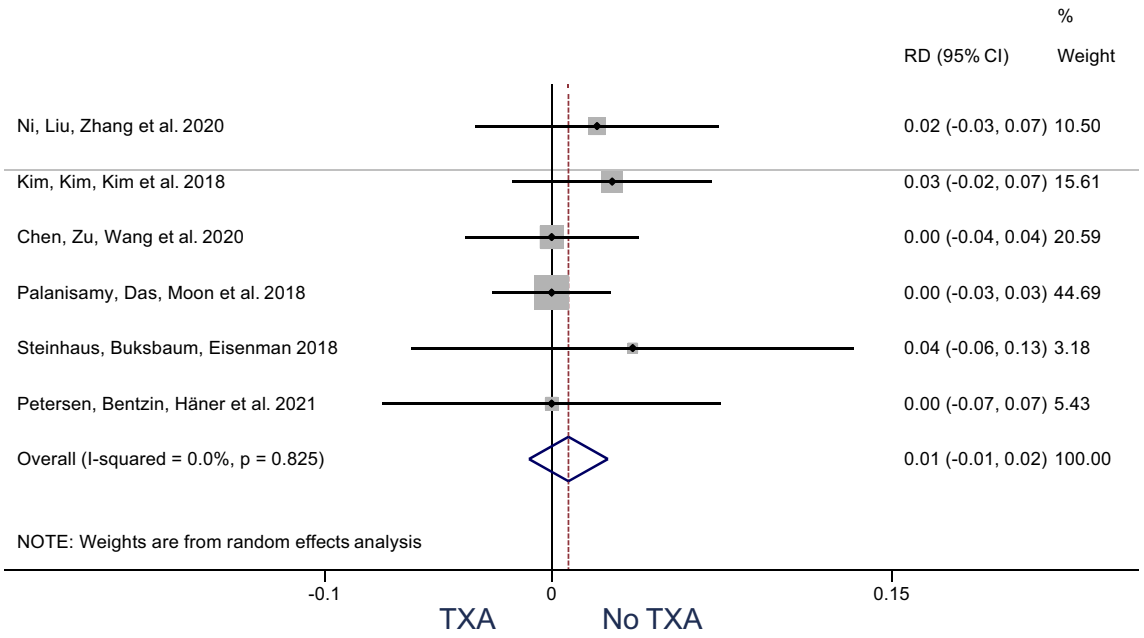

Fig. 5 Risk difference for blood transfusion

vs. 11, Fig. 6, Table 5). This difference was also statistically significant (OR: 1.9, *p* value: 0.05). In one study a hemathrosis had to be aspirated in the TXA group [19].

Other outcome criteria

Two studies examined pain as measured on a visual analogue scale (VAS) for the assessment of pain [17, 19]. In both studies mean VAS for pain at the first postoperative

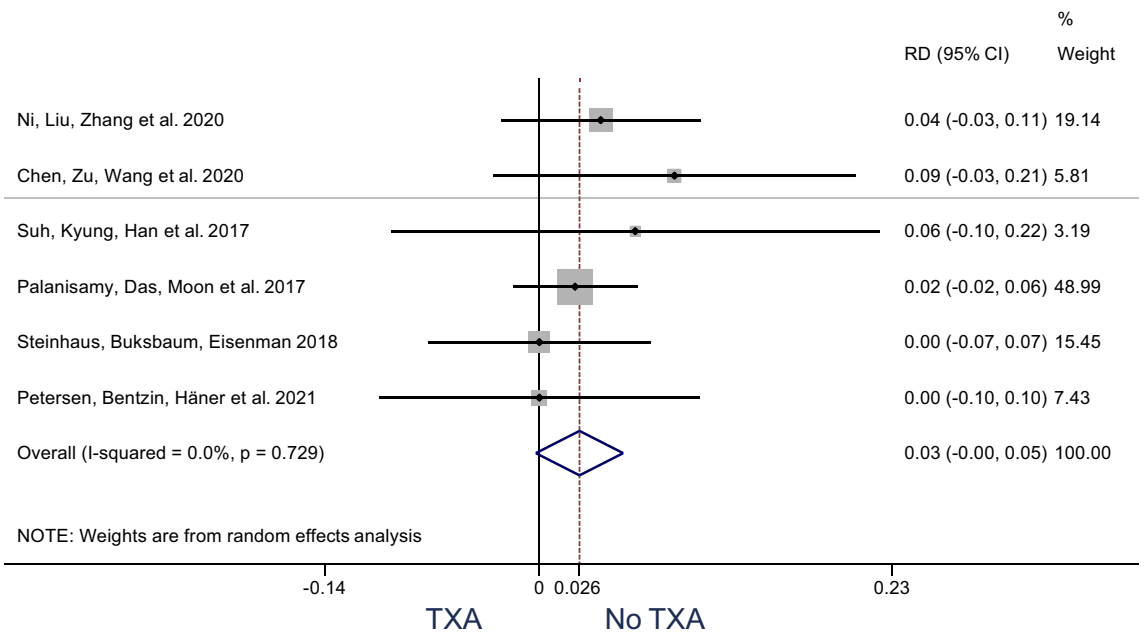

Fig. 6 Risk difference for wound complications/hematoma

day was significantly lower in the TXA group in comparison to the non TXA group. In one study range of motion was significantly higher in the TXA group in comparison to the non TXA group and intraarticular effusion and calf diameter were significantly less in the TXA group [19].

Discussion

The results of the present systematic review support our hypothesis stated at the end of the introduction. The most important findings of the present study were, that the use of TXA when performing an osteotomy around the knee reduces Hb decrease and blood loss. Both factors may be responsible for the reduced rate of blood transfusions and wound complications in the TXA group. In none of both treatment groups thromboembolic events were noted.

The clinical benefit of the use of TXA in osteotomies around the knee has been questioned, as previous studies could not show a difference in the transfusion rate or wound complications between the two treatment groups [10]. This may be due to the fact that the number of cases in previous studies was too low to detect a significant difference in the transfusion rates [2, 7, 16, 17, 19, 23, 24] The present meta-analysis is the first study to show an effect of tranexamic acid on complication rates such as transfusions and wound complications in osteotomies around the knee. Due to pooling of data of the previous studies the number of cases was large enough to calculate statistical significance. The meta-analysis showed that an osteotomy close to the knee results in a transfusion rate of 1.3% in the control group without administration of TXA and 0% in the TXA group. In an earlier meta-analysis that included only 5 studies, no significant difference in the transfusion rates after osteotomies near the knee joint with and without TXA could be found [9].

In total knee arthroplasty, the effect of tranexamic acid on the transfusion rate and wound complications has already been demonstrated in a small number of cases [5, 26]. This may be because both complications occur more often after total knee arthroplasty, either due to the patients or procedural characteristics [5]. In knee arthroplasty, transfusion rates of approx. 25% are reported [5]. These transfusion rates could be reduced significantly through the use of TXA [5, 26]. Therefore, the clinical benefit of TXA in knee arthroplasty appears to be greater with regard to the risk of transfusion. Nevertheless, the authors of the present study believe that even a reduction of a transfusion rate of 1.3% to 0% represents a clinical benefit.

An increased rate of wound complications after knee arthroplasty has been described in obese patients [27]. There are no direct comparisons of patients with osteotomy or knee arthroplasty in the literature. However, it can be assumed that the BMI of typical knee prosthesis patients is higher than that of patients after osteotomy.

However, the reduction of transfusions or wound complication is not the only advantage of the administration of TXA. Postoperative hematoma can also lead to pain, discomfort and a reduced range of motion. Interestingly, only two studies. examined postoperative pain as additional

Table 5 Adverse events of studies comparing the administration of tranexamic acid (TXA) in patients with osteotomy around the knee

References	Thromembolic events		Blood transfusions		Wound complications or hematoma	
	TXA group	Non TXA group	TXA group	Non TXA group	TXA group	Non TXA group
Ni, Liu, Zhang et al. [16]	Not specifically mentioned	Not specifically mentioned	Not mentioned	One patient	No wound complications	One wound hematoma (treated by paracentesis and pressure dressing), one superficial wound infection (surgical debridement)
Kim, Kim, Kim et al. [7]	No symptomatic DVT or events happened	No symptomatic DVT or events happened	No transfusion occurred	Two patients	Not reported	Not reported
Chen, Zu, Wang et al. [2]	/	/	No transfusion occurred	No transfusion occurred	Two hematoma, one infection	Five hematoma, two infections
Suh, Kyung, Han et al. [24]	/	/	/	/	No wound complications	One extensive hematoma requiring additional surgery
Steinhaus, Buksbaum, Eisenman [23]	No symptomatic DVT or events happened	No symptomatic DVT or events happened	No patient	One patient	No wound complications	No wound complications
Palanisamy, Das, Moon et al. [17]	No symptomatic DVT or events happened	No symptomatic DVT or events happened	No transfusion occurred	No transfusion occurred	No wound complications	One superficial wound infection (treated with meticulous wound care and IV antibiotics) and one wound hematoma (treated by surgical drainage)
Petersen, Bentzin, Häner et al. [19]	No symptomatic DVT or events happened	No symptomatic DVT or events happened	No transfusion occurred	No transfusion occurred	One hematom (aspiration)	One hematom (surgical debridement)
Average value	0	0	0	4	3	11

outcome measure [17, 19]. In both studies, pain measured with a visual analog scale (VAS) at the first postoperative day was significantly lower in the TXA group [17, 19]. In one study postoperative range of motion was higher in the TXA group whereas calf diameter and intraarticular effusion were less in the TXA group [19]. However, there was no difference in PROMs at 1 year after surgery [19].

Possible side effects of TXA such as deep venous thrombosis or pulmonary embolism have not been observed in the present review. This observation is in accordance with other studies about the application of TXA in total knee arthroplasty [5, 14, 26] In none of these studies a higher rate of deep venous thrombosis or pulmonary embolism in the TXA group have been described [5, 14, 26].

As every study, the present systematic review has some limitations. One limitation could be that only one of the included studies randomized patients to the different treatment groups. It has been criticized that non-randomized trials may suggest causal relationship but cannot prove them definitively. However, in a recent Cochrane review the differences between randomized and non-randomized trials were not as significant as previously believed [1]. A well-known pitfall of randomized controlled trials for example is selection bias [18]. Therefore, the results of these trials cannot be transferred to a real-world scenario. In addition, the advancing regulations have made RCT a time-consuming and costly project.

A second limitation of the present study is that the occurrence of deep venous thrombosis was not examined with Doppler ultrasound in the included trials. The diagnosis has been made by clinical examination such as the Wells Score which is a reliable diagnostic tool for detecting clinically relevant thromboses [25].

A third limitation is that only one study examined the effect of TXA for femoral osteotomies. There is definitely need for further studies about the effect of TXA on the outcome of femoral osteotomies.

The last limitation is that the dosage protocols and administration (i.v. or topical) varied among the different studies [2, 7, 16, 17, 23, 24]. For this reason, the optimal dosage and administration route of TXA in osteotomies around the knee is not clear.

Despite these limitations, the results of the present systematic review prove the clinical benefit of systemic TXA application in osteotomies around the knee. The results demonstrate that the application of TXA reduces the postoperative Hb decrease, blood loss, transfusions and wound complications.

Conclusion

The results of the present study show that the use of TXA reduces hemoglobin fall, blood loss and drainage volume. These positive effects could be responsible for the lower rate of side effects after administration of TXA in knee osteotomy. In our opinion, the administration of TXA should be an integral part in knee osteotomy.

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Declarations

Conflict of interest The authors declare no conflict of interest.

Ethical approval The present study was registered prospectively (www.crd.york.ac.uk/PROSPERO; no.: CRD42021229624).

References

1. Anglemyer A, Horvath HT, Bero L (2014) Healthcare outcomes assessed with observational study designs compared with those assessed in randomized trials. Cochrane Database Syst Rev. https://doi.org/10.1002/14651858.MR000034.pub2
2. Chen DS, Zhu JW, Wang TF et al (2020) Tranexamic acid is beneficial to patients undergoing open-wedge high tibial osteotomy. Biomed Res Int. https://doi.org/10.1155/2020/2514207
3. Deeks JJ, Dinnes J, D'Amico R et al (2003) Evaluating non-randomised intervention studies. Health Technol Assess (Rockv). https://doi.org/10.3310/hta7270
4. Floerkemeier S, Staubli AE, Schroeter S et al (2014) Does obesity and nicotine abuse influence the outcome and complication rate after open-wedge high tibial osteotomy? A retrospective evaluation of five hundred and thirty three patients. Int Orthop 38:55–60. https://doi.org/10.1007/s00264-013-2082-3
5. Goldstein M, Feldmann C, Wulf H, Wiesmann T (2017) Tranexamic acid prophylaxis in hip and knee joint replacement. Dtsch Arztebl Int 114:824–830. https://doi.org/10.3238/arztebl.2017.0824
6. Kehlet H, Thienpont E (2013) Fast-track knee arthroplasty - status and future challenges. Knee. https://doi.org/10.1016/S0968-0160(13)70006-1
7. Kang-Il K, Kim HJ, Kim GB, Bae SH (2018) Tranexamic acid is effective for blood management in open-wedge high tibial osteotomy. Orthop Traumatol Surg Res 104:1003–1007. https://doi.org/10.1016/j.otsr.2018.07.019
8. Li S, Lu Q, Guo X et al (2020) Intravenous combined with topical tranexamic acid administration has no additional benefits compared with intravenous administration alone in high tibial osteotomy: a retrospective case-control study. Orthop Surg. https://doi.org/10.1111/os.12652
9. Ma J, Lu H, Chen X et al (2021) The efficacy and safety of tranexamic acid in high tibial osteotomy: a systematic review and meta-analysis. J Orthop Surg Res 16:373. https://doi.org/10.1186/s13018-021-02512-4
10. Maak TG (2018) CORR insights®: intravenous tranexamic acid reduces postoperative blood loss after high tibial osteotomy. Clin Orthop Relat Res 476:2155–2156. https://doi.org/10.1097/CORR.0000000000000447
11. Maher CG, Sherrington C, Herbert RD et al (2003) Reliability of the PEDro scale for rating quality of randomized controlled trials. Phys Ther 83:713–721. https://doi.org/10.1093/ptj/83.8.713
12. Martin R, Birmingham TB, Willits K et al (2014) Adverse event rates and classifications in medial opening wedge high tibial

osteotomy. Am J Sports Med 42:1118–1126. https://doi.org/10.1177/0363546514525929
13. Melvin JS, Stryker LS, Sierra RJ (2015) Tranexamic acid in hip and knee arthroplasty. J Am Acad Orthop Surg 23:732–740. https://doi.org/10.5435/JAAOS-D-14-00223
14. Moráis S, Ortega-Andreu M, Rodríguez-Merchán EC et al (2014) Blood transfusion after primary total knee arthroplasty can be significantly minimised through a multimodal blood-loss prevention approach. Int Orthop 38:347–354. https://doi.org/10.1007/s00264-013-2188-7
15. Nadler SB, Hidalgo JH, Bloch T (1962) Prediction of blood volume in normal human adults. Surgery 51:224–232. https://doi.org/10.5555/URI:PII:0039606062901666
16. Ni J, Liu J, Zhang J et al (2020) Tranexamic acid is beneficial for blood management of high tibial osteotomy: a randomized controlled study. Arch Orthop Trauma Surg. https://doi.org/10.1007/s00402-020-03558-5
17. Palanisamy JV, Das S, Moon KH et al (2018) Intravenous tranexamic acid reduces postoperative blood loss after high tibial osteotomy. Clin Orthop Relat Res 476:2148–2154. https://doi.org/10.1097/CORR.0000000000000378
18. Petersen W, Achtnich A, Lattermann C, Kopf S (2015) The treatment of non-traumatic meniscus lesions. Dtsch Aerzteblatt Online. https://doi.org/10.3238/arztebl.2015.0705
19. Petersen W, Bentzin M, Bierke S et al (2021) Use of tranexamic acid in medial open wedge high tibial osteotomy. Arch Orthop Trauma Surg. https://doi.org/10.1007/s00402-021-04219-x
20. Petersen W, Bierke S, Häner M (2020) Osteotomy near the knee joint in unicompartmental knee osteoarthritis: what is the current situation? Arthroskopie 33:244–255. https://doi.org/10.1007/s00142-020-00378-y
21. Petersen W, Metzlaff S (2016) Open wedge high tibial osteotomy (HTO) versus mobile bearing unicondylar medial joint replacement: five years results. Arch Orthop Trauma Surg 136:983–989. https://doi.org/10.1007/s00402-016-2465-1
22. Sidhu R, Moatshe G, Firth A et al (2020) Low rates of serious complications but high rates of hardware removal after high tibial osteotomy with Tomofix locking plate. Knee Surgery Sport Traumatol Arthrosc. https://doi.org/10.1007/s00167-020-06199-8
23. Steinhaus ME, Buksbaum J, Eisenman A et al (2020) Tranexamic acid reduces postoperative blood loss in distal femoral osteotomy. J Knee Surg 33:440–444. https://doi.org/10.1055/s-0039-1678540
24. Suh DW, Kyung BS, Han SB et al (2018) Efficacy of tranexamic acid for hemostasis in patients undergoing high tibial osteotomy. J Knee Surg 31:50–55. https://doi.org/10.1055/s-0037-1600091
25. Wells PS, Hirsh J, Anderson DR et al (1995) Accuracy of clinical assessment of deep-vein thrombosis. Lancet 345:1326–1330. https://doi.org/10.1016/S0140-6736(95)92535-X
26. Winther SB, Foss OA, Wik TS et al (2015) 1-year follow-up of 920 hip and knee arthroplasty patients after implementing fast-track: good outcomes in a Norwegian university hospital. Acta Orthop 86:78–85. https://doi.org/10.3109/17453674.2014.957089
27. Yu S, Siow M, Odeh K et al (2018) Periarticular soft tissue envelope size and postoperative wound complications following total knee arthroplasty. J Arthroplasty 33:S249–S252. https://doi.org/10.1016/j.arth.2018.02.046