Prevention of post-operative anaemia in hip and knee arthroplasty – a systematic review

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ABSTRACT

INTRODUCTION: Patient blood management strategies for total hip and knee arthroplasty are controversial. They range from pre-operative haemoglobin optimisation to intra- and post-operative interventions. The aim of this study was to assess the various treatment modalities with respect to blood loss, haemoglobin levels and blood transfusions.

METHODS: The analysis was based on the principles of a systematic review. The literature was searched in PubMed for the period from 2004 to November 2014. The articles were reviewed with respect to blood loss, post-operative haemoglobin drop, blood transfusions and length of hospital stay. The papers were evidence-graded. Non-randomised clinical studies and papers not concerning total hip or knee arthroplasty were excluded as were studies lacking a control group. Sub-analyses were performed for tranexamic acid, tourniquet and fibrin use.

RESULTS: A total of 49 studies were found eligible which is equivalent to a total of 4,752 patients. Tranexamic acid administered either orally, topically, intravenously or in combination decreased blood loss, increased the post-operative haemoglobin level, decreased the number of patients receiving blood transfusions and minimised the length of stay. A similar result was found for fibrin spray in total hip arthroplasty. However, for total knee arthroplasty, the outcome was blurred. Tourniquet use was uniformly not significant in the measured parameters.

CONCLUSIONS: Tranexamic acid is useful in managing anaemia and blood loss. Fibrin sealant also has this potential, but is not more potent than tranexamic acid. Tourniquet use is not advantageous.

During primary hip (THA) and knee (TKA) arthroplasty, the mean calculated visible and invisible blood loss is approx. 1,500 ml, which is followed by a mean drop of haemoglobin (Hgb) of approximately 3 g/dl. This may lead to allogeneic blood transfusion in up to 69% of patients depending on the transfusion threshold [1]. Orthopaedic surgery is the leading surgical indication for transfusion, accounting for about 10% of all red blood cell (RBC) units transfused. Patients with preoperative anaemia are more likely to receive perioperative blood transfusions in the orthopaedic setting than non-anaemic patients [2]. Several patient blood management techniques have been investigated in an attempt to minimise both blood loss and blood transfusions [3]. Some of the intraoperative strategies include antifibrinolytics such as tranexamic acid (TXA) [4], the use of fibrin sealant [5] and tourniquet [6].

These strategies may all reduce the need for transfusions in THA and TKA. This systematic review was undertaken to perform a critical analysis of these intraoperative modalities. The primary outcomes were blood loss and Hgb drop, and the secondary outcomes were number of patients transfused and length of hospital stay (LOS).

METHODS

Search strategy

A systematic search was conducted in the PubMed database. It was performed based on a protocol developed and reported in line with the recommendations in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. For consistent information retrieval, the following basic search strings based on medical subject headings (MeSH) terminology were used: “Arthroplasty Replacement” OR “Arthroplasty” OR “Arthroplasty Replacement Knee” OR “Arthroplasty Replacement Hip”. In addition, search results on selected patient blood management interventions were obtained by combining the basic search strings with the following MeSH terms: “Fibrin”, “Tourniquet” and “Tranexamic Acid.”

The search was limited to the past ten years (2004 to 25 November 2014) in order to include studies reflecting only contemporary principles of total joint arthroplasty (TJA). Additional, relevant studies not identified from the electronic search were sought by manual

SYSTEMATIC REVIEW

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KEY POINTS

With an average blood loss of 1,500 ml and a haemoglobin drop of 3 g/dl following primary hip or knee replacement, several patient blood management techniques have been investigated.

This review investigates the published randomised controlled trials and meta-analyses (n = 49; 4,752 patients in total) on tranexamic acid, fibrin and the use of a tourniquet.

The authors conclude that tranexamic acid taken either orally, topically, intravenously or in combination is useful in managing anaemia and blood loss. Fibrin sealant also has this potential, but it is not more potent than tranexamic acid. Tourniquet-use is not beneficial.

searches of bibliographies of relevant identified articles and by consultation with clinical experts in the field.

Study exclusion criteria

Only randomised controlled trials (RCTs) with a control group (or the contralateral joint used as control) published in Danish and English were included. All included studies were at least evidence-graded as level 1– or better (**Table 1**). Only original articles were included. Thus, reviews, meta-analyses and case reports were excluded. Papers on hip fractures or arthroplasty anywhere besides the hip and the knee were excluded.

RESULTS

If possible and to ensure clarity (see methods above), results are reported separately for each treatment modality. From a pool of 159 potentially relevant studies, 49 studies were included with a total of 4,752 patients (**Figure 1**). Results from the literature are summarised in Table 1. Included studies are listed summarising main outcomes and with graded evidence according to Harbour & Miller, 2001 as outlined in **Table 2**.

Tranexamic acid

A total of 27 clinical, controlled trials were identified (Ta-

TABLE 1

Summary of included studies and outcomes.

Reference, year	TJA	Treatment	Patients, n	Blood loss difference with treatment, ml	Hgb difference post-operatively, g/dl	Patients receiving blood transfusion, difference%	LOS difference, days	Grade of evidence
TXA group								
[11], 2004	TKA	TXA, IV + oral	80	–222 (TXA long) –239 (TXA short) –106 (TXA oral)	–	–45 (TXA long) –50 (TXA short) –40 (TXA oral)	–	1++
[31], 2005	THA	TXA, IV	21	–297	+0.70	–[a]	–	1–
[12], 2005	THA	TXA, IV	100	–330	–	–20	–	1++
[24], 2005	THA	TXA, IV	39	–310	–	NS	–	1++
[7], 2006	TKA	TXA, IV	29	NS	–	NS	–	1++
[4], 2006	TKA	TXA, IV	127	–689	+0.90	–30.8	–	1++
[13], 2007	THA	TXA, IV	40	–237	+0.60	–25	–	1–
[14], 2008	TKA	TXA, IV	95	–443	+0.50	–13.5	–	1+
[9], 2009	THA	TXA, IV	36	–311	NS	–18.7	–	1–
[15], 2010	THA	TXA, IV	64	–375	+0.66	–38	–2.5	1–
[25], 2010	THA	TXA, IV	42	–150	+0.90	NS	NS	1++
[26], 2010	TKA	TXA, topical	124	–315 (1.5 g) –402 (3 g)	+1.40 (1.5 g) +1.50 (3 g)	NS	NS	1++
[16], 2011	TKA	TXA, IV	60	–240 (10 mg/kg) –456 (15 mg/kg)	NS	–30 (10 mg/kg) –5 (15 mg/kg)	–	1++
[8], 2011	TKA	TXA, topical	100	NS	+0.80	–	–	1–
[17], 2011	TKA	TXA, IV + oral	100	–481.27	+1.21	–34	–	1+
[27], 2012	TKA	TXA, IV + topical	206	–409[c]	–	NS	NS	1++
[18], 2012	TKA	TXA, IV + topical	150	–305 (IV) –407 (topical)	+0.40 (IV) +0.20 (topical)	–60 (IV) –74 (topical)	–	1+
[28], 2012	TKA	TXA, topical	50	–553.4	+1.09	NS	–	1–
[19], 2012	TKA	TXA, IV	151	–187 (1 × IV) –236 (2 × IV)[d]	+0.90	–18.2 (1 × IV) –15.9 (2 × IV)[d]	NS	1++
[20], 2013	THA	TXA, topical	161	–129	+0.84	–19.6	–1	1++
[21], 2013	TKA	TXA, topical	157	–168	+0.83	–15.4	–1.2	1++
[22], 2013	TKA	TXA, topical	135	–89.5 (250 mg) –112 (500 mg)	+0.70	–9 (250 mg) –22 (500 mg)	–	1++
[29], 2013	TKA	TXA, topical	101	–352.90	+0.90	NS	NS	1+
[33], 2013	TKA	TXA, oral	53	–224.8	–	–[a]	–	1++
[10], 2014	TKA, THA	TXA, IV	98	–650	NS	–75.5	–	1++
[23], 2014	THA, TKA	TXA, topical	100	–	+0.61 (THA) +0.50 (TKA)	–5.7	NS	1+
[30], 2014	TKA	TXA, IV + topical	200	–384 (IV) –117 (joint irrigated) –687 (inj. into drain)	+1.90 (IV) +0.30 (joint irrigated) +0.60 (inj. into drain)	NS	–	1–

CONTINUES

ble 1) investigating the use of oral, intravenous (IV) or intra-articular TXA in TKA and THA. Two studies demonstrated a non-significant reduction of blood loss after TXA administration [7, 8], and three studies showed a non-significant reduction of the post-operative Hgb drop [8-10]. The remaining studies showed a significant reduction of blood loss volume and Hgb drop compared with a control group. The overall picture for the transfusion rate was not uniform. While some studies illustrated a significant reduction in the number of patients receiving blood transfusions [4, 9-23], eight studies showed no significant difference from the control group [7, 24-30]. Eight studies had included the LOS, and three of these showed a reduction [15, 20, 21]. None of the studies found a significant increase in adverse events to be associated with TXA use (although the studies were not powered to show this). Looking at topically administered TXA, a study on TKA demonstrated that 2 g of topical TXA only resulted in a decrease in blood volume immediately after surgery, while the overall post-operative blood loss volume was not significantly reduced. The study did, however, show an increase in the post-operative Hgb level compared with the control group [8]. Another study showed a decrease in the Hgb drop and a reduction in the number of patients needing transfusions in the TXA-administered groups [23]. An additional study compared 1.5 g and 3 g of TXA with a control group and showed that while the blood loss reduction and Hgb-drop was significantly lower than in the control group, it was not significantly different between the two study groups [26].

Thus, no definite dosage of topical TXA can be pro-

TABLE 1, CONTINUED

Summary of included studies and outcomes.

Reference, year	TJA	Treatment	Patients, n	Blood loss difference with treatment, ml	Hgb difference post-operatively, g/dl	Patients receiving blood transfusion, difference%	LOS difference, days	Grade of evidence
Tourniquet group								
[32], 2008	TKA	Tourniquet	80	+181	–	–	–	1–
[6], 2010	TKA	Tourniquet	60	NS	–	–	–	1+
[34], 2010	TKA	Tourniquet	84	NS	NS	NS	–	1–
[35], 2012	TKA	Tourniquet	50	–54	–	–	–	1–
[37], 2012	TKA	Tourniquet	72	–120	–1.10	NS	NS	1+
[36], 2014	TKA	Tourniquet	70	–140	–	NS	–	1++
Fibrin group								
[5], 2006	THA	Fibrin	80	NS	NS	NS	NS	1–
[38], 2006	THA	Fibrin	100	–230	+0.50	–[a]	–	1–
[46], 2006	TKA	Fibrin	165	–	+2.40	–19.2	–1.4	1–
[50], 2007	TKA	Fibrin, TXA	150	–225 (fibrin) –190 (TXA)	–0.52 (fibrin) –0.45 (TXA)	–8 (fibrin) –12 (TXA)	–1.04 (fibrin) –0.76 (TXA)	1++
[39], 2011	THA	Fibrin, TXA	66	–380 (fibrin) –270 (TXA)	–	–	–	1++
[42], 2012	TKA	Fibrin	196	NS	+0.52	NS	NS	1++
[52], 2012	TKA	Fibrin	90	–586.7 (10 ml) –400 (5 ml)	–1.20 (10 ml) –1.10 (5 ml)	–39.7 (10 ml) –30 (5 ml)	–4.4 (10 ml) –3.6 (5 ml)	1+
[47], 2012	TKA	Fibrin, TXA	66	–374 (fibrin) NS (TXA)	–	–	–	1++
[48], 2012	TKA	Fibrin	24	–337.9	NS	NS	NS	1–
[40]e, 2013	THA	Fibrin	95	–368	–	–	–	1+
[41], 2013	THA	Fibrin	70	NS	+0.9	–23.8	NS	1++
[43], 2013	TKA	Fibrin	24	NS	–	–	NS	1++
[51], 2013	TKA	Fibrin, TXA	172	NS (fibrin) –523 (TXA)	NS	NS (fibrin) –23.7 (TXA)	NS	1++
[44], 2014	TKA	Fibrin	200	NS	–0.37	NS	–	1++
[49], 2014	TKA	Fibrin	70	–340	NS	–25.72	–	1+
[45], 2014	TKA	Fibrin	62	NS	NS	NS	NS	1++

Hgb = haemoglobin; IV = intravenous; LOS = length of hospital stay; NS = not significant between treatment and control group; THA = total hip arthroplasty; TJA = total joint arthroplasty; TKA = total knee arthroplasty; TXA = tranexamic acid.

a) No blood transfusions given in this study.

b) Converted from graph in the article.

c) Greatest blood reduction in the group receiving TXA in 3 doses (pre-, intra-, post-operatively) compared to control.

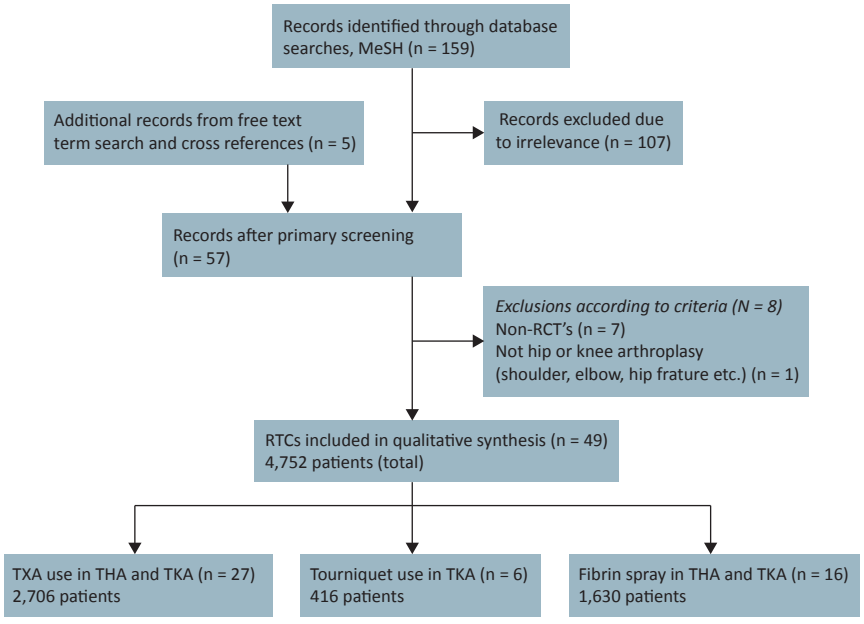
d) IV transfusion given once or twice, respectively.

e) Bipolar sealer not included.

FIGURE 1

Flow diagram of the study selection.

MeSH = medical subject headings; RCTs = randomised controlled trials; THA = total hip arthroplasty; TKA = total knee arthroplasty; TXA = tranexamic acid.



posed. However, throughout the range of administering from 250 mg to 3 g, there was a coherent decrease in blood loss and a higher post-operative Hgb [20-22, 28, 29].

Studies consistently showed a decrease in blood loss volume upon administration of intravenous (IV) TXA, and some either showed a lower value or a non-significant difference from the control group concerning the Hgb drop and the transfusion rates [4, 9, 10, 12-16, 24, 25, 31].

TABLE 2

Evidence grading according to Harbour & Miller, 2001 (Harbour R, Miller J. A new system for grading recommendations in evidence based guidelines. BMJ 2001;323:334-6).

Level of evidence	
1++	High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1-	Meta-analyses, systematic reviews or RCTs, or RCTs with a high risk of bias
2++	High quality systematic reviews of case-control or cohort studies High quality case-control or cohort studies with a very low risk of confounding, bias, or chance and high probability that the relationship is casual
2+	Well conducted case-control or cohort studies with a low risk of confounding, bias, or chance and a moderate probability that the relationship is casual
2-	Case-control or cohort studies with a high risk of confounding, bias, or chance and a significant risk that the relationship is not casual
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

RCTs = randomised controlled trials.

To investigate the composition of an optimal administration regime, studies comparing administration forms were examined. Two studies compared IV to topical administration of TXA. One of the studies found the topical TXA administration to be more efficient in reducing blood loss and transfusion rates than IV administration [22].

Yet, the Hgb drop was lowest in the IV group [18]. Supporting this finding, another study reported a similar result, but failed to show a significant difference in the number of patients requiring transfusions [32]. Another study examined five regimens (four IV, one local) with a placebo group.

The four IV regimens included 1) an intraoperative dose (IO) given before tourniquet deflation, 2) an additional preoperative dose (POIO), 3) an additional post-operative dose (IOPO), 4) all three doses (POIOPO), and 5) a single local application (LA). Total blood loss was significantly reduced in the POIO, POIOPO and LA groups, but the POIOPO group had the least total blood loss [27].

To support multiple-regime use of TXA, a study reported the effect of IV TXA up to 3 h post-operatively followed by oral TXA for five days. This showed a lower mean post-operative volume of drained blood, a lower Hgb drop and a lower number of transfused patients in the TXA group than in the control subjects [17]. To further establish the oral use, an oral dosage of 1 g 2 h before surgery which was continued every 6 h for 18 h

after surgery was shown to reduce the blood volume significantly in another study [33].

Tourniquet

Tourniquet during TKA can be used in three different ways: no tourniquet, limited use only during cementing or use throughout the whole operation. Six RCTs were included in this review, five of which concluded that tourniquet use is not beneficial in TKA surgery [6, 32, 34-36]. Opposing tourniquet use, some studies concluded that TKA without the use of tourniquet resulted in faster recovery in terms of better functional outcome [32, 36], less post-operative pain [35-37] and improved knee range of motion (ROM) [35, 36]. Although intraoperative bleeding was more pronounced in the non-tourniquet group, calculated blood loss, post-operative visible and hidden bleeding were significantly more pronounced in the tourniquet group. Overall, there was no significant difference in the total amount of blood loss and Hgb between the two groups. The hidden loss as a percentage of calculated total blood loss was 56% in the tourniquet group and 42% in the non-tourniquet group [36].

Reinforcing these results, a study investigated three techniques: no tourniquet, a tourniquet used and deflated for haemostasis once all components had been inserted and, lastly, a tourniquet deflated after wound closure and application of a compressive dressing. The difference in mean blood loss between these groups was not significant. The only significant outcome was a mean increase of 35.5 min. in the duration of surgery without tourniquet use compared with the other two groups. Hence, eliminating tourniquets in TKA had no effect on blood loss [34].

However, a study supporting the use of tourniquet showed that the tourniquet group had smaller decreases in Hgb, less calculated blood loss and smaller increases in C-reactive protein and creatinine phosphokinase than the non-tourniquet group. There were no significant differences in terms of swelling, rehabilitation progress or LOS. Thus, the study showed tourniquet use to be effective for reducing blood loss and avoiding excessive post-operative inflammation and muscle damage. The use of a tourniquet was related to slightly more post-operative pain, but did not affect post-operative recovery [37].

Fibrin

A total of 16 RCTs were included in this review, five in THA and the remainder in TKA.

Fibrin sealant used in THA failed to reduce blood loss during surgery and wound drainage volume compared with the control group in one study. Likewise, no statistically significant differences were found between groups regarding transfusions, Hgb-drop and LOS [5]. Conversely, the remaining four studies in THA showed a significant decrease in blood loss, a slightly improved Hgb level post-operatively and fewer patients receiving post-operative blood transfusions [38-41].

Four studies found the drain output in knees treated with fibrin sealant and placebo to be similar [42-45]. Nonetheless, this was in contradiction to six studies showing a significant decrease in blood loss post-operative TKA and a reduction in the number of patients receiving blood transfusions and LOS [46-50].

Four studies were identified comparing fibrin sealant to TXA. Two of these showed fibrin to be as potent as TXA in TKA and THA. Thus, the reduction in blood loss, Hgb drop, number of patients transfused and LOS in the topical fibrin spray group was not significantly different from that achieved in the TXA group [39, 50]. One study showed that fibrin is more effective in lowering the total blood loss than TXA [47]. However, the last study concluded that TXA is more potent in reducing blood loss and the transfusion rate [51].

DISCUSSION

As aging progresses in our population, the number of patients who will need THA or TKA may increase significantly in years to come. However, in arthroplasty surgery, considerable blood loss remains a major problem, which may lead to a need for allogeneic blood transfusion. Such transfusion of allogeneic erythrocytes is not free of adverse events, and it has been associated with transmission of infectious diseases, increased post-operative bacterial infection, immune sensitisation, transfusion-related acute lung injury, intravascular haemolysis, transfusion-induced coagulopathy, renal failure, admission to intensive care and even death. Also, health economics disfavour blood transfusion on the grounds of reduced supply of blood components and high costs of blood preservation. Apart from diagnosing and treating preoperative anaemia, blood management strategies include preventing loss of blood intra- and post-operatively, which could otherwise potentially lead to post-operative anaemia and blood transfusion.

The present systematic review identified several clinically important patient blood management regimes to lower the post-operative anaemia rate in patients undergoing THA and TKA. Systematic reviews have the advantage of being reproducible while preventing study selection bias. Conversely, they are limited by the publication bias itself and by the quality of MeSH term coding.

This review found that TXA use in oral, IV and topical form was safe and involved no signs of adverse events. All three forms of TXA use reduce the need of blood transfusion and blood loss and have the potential to reduce the Hgb drop post-operatively and to lower

LOS. These results are comparable to those found in six meta-analyses in which TXA reduced the total blood loss by a mean 305-570 ml, significantly ameliorated post-operative Hgb decrease and reduced the transfusion rate. None of the meta-analyses pooling safety data demonstrated a significant risk of deep venous thrombosis or pulmonary embolism associated with TXA use [53-60].

TXA is a synthetic derivative of the amino acid lysine and a competitive inhibitor of plasminogen activation that interferes with fibrinolysis, which explains why TXA can decrease bleeding.

Conflicting reports have been published about the administration form and doses of TXA. Strengthening our results, a multiple-dose regimen is recommended since a single-dose regimen does not fully cover the bleeding peak period: most of the external blood loss occurs in the first few hours post-operatively; however, a single IV dose of TXA of 10 mg/kg can only maintain such a plasma concentration for approximately 3 h. Our results suggest that a minimum of two doses is required for optimal reduction of blood transfusions [27].

The meta-analyses involved only examined the use of IV TXA. Our analysis showed that oral and topical use could also significantly reduce blood loss and transfusion rates. One could justify intra-articular TXA use since the IV and oral form are distributed throughout the body fluids, thereby reducing its therapeutic concentration in the joint. In contrast, topically applied TXA is distributed predominantly within the joint, whereby a higher therapeutic concentration is achieved at the bleeding site. This effectively limits blood loss with little or no systemic absorption and subsequent risk of systemic side effects [20]. Conversely, one could also argue in favour of the oral use since it is simple and does not require specific infusion equipment [11, 33].

Another treatment modality in TKA surgery is the use of a tourniquet. Several studies support that tourniquet use has no effect on blood loss and that it does, in fact, increase the volume of hidden blood loss and causes more pain to the patient. Yet, a single study included did show that tourniquet use is effective in reducing blood loss and helps avoid excessive post-operative inflammation and muscle damage [37].

Supporting the tourniquet-free surgery modality, three meta-analyses support the results reported in the present systematic review. Overall, there is consensus that tourniquet-free surgery reduces intraoperative blood loss, but the post-operative blood loss and the transfusion rate are not significantly different from those achieved in surgery performed without a tourniquet. This phenomenon suggests that TKA involves some blood loss that goes unrecognised in the routine assessment of either intraoperative blood loss or the post-operative drainage amount. This is especially so when using a tourniquet during the operation, which confirms a substantial, hidden blood loss. According to the meta-analyses, there were more complications (thrombosis, wound complications) in the tourniquet than in the non-tourniquet group. This is in line with current theory: The formation of thrombi is associated with the triad of venous stasis, endothelial injury and hypercoagulability. A tourniquet can cause venous stasis, endothelial damage via direct trauma and possibly damage to calcified blood vessels.

Post-operative ROM in the tourniquet group was 10° lower than that in the non-tourniquet group in the early stage (≤ 10 days after surgery). There was no statistically significant difference in LOS between the tourniquet and non-tourniquet group [61-63]. Conversely, one meta-analysis showed decreased total and intraoperative blood losses when applying a tourniquet. This analysis also showed that although there is a temporary loss of function in the compressed thigh muscles, no difference was observed in long-term flexion. The authors concluded that a benefit is associated with tourniquet use. However, this study did not investigate the rate of transfusion between the two groups [64]. One of our included studies found that a tourniquet-free approach increased the duration of surgery by 35.5 min. [34]. This is contrary to the results of a meta-analysis which showed a mere difference of 4.57 min. between tourniquet and non-tourniquet groups [63].

As far as fibrin sealants are concerned, the main components are fibrinogen, factor XIII, thrombin, and antifibrinolytic agents such as aprotinin or TXA. Fibrin sealants achieve their local haemostatic effects by reproducing the last step of the coagulation cascade, thereby facilitating formation of a stable fibrin clot and subsequent haemostasis [65]. The use of fibrin remains controversial. In our review, five studies showed that both fibrin and thrombin-based sealants had no significant effect on blood loss, transfusion requirement or LOS. Conversely, ten studies showed a significant effect of fibrin sealants when compared with controls. These positive results are supported by a meta-analysis showing that fibrin sealant is safe and efficient for blood loss, Hgb level, ROM, LOS and complications [65]. No meta-analysis including the use of fibrin in THA was found. However, the cost of fibrin sealant also warrants discussion. The beneficial effects of fibrin sealant use are associated with decreased rates of red blood cell transfusion. But as our review showed, the potency of fibrin is similar or even less than that of TXA. The latter is the more inexpensive option. Hence, considering the health economic perspective, fibrin use cannot be justified.

Based on a crude calculation, our results showed a similar effect in terms of our primary and secondary out-

comes in both TKA and THA when using TXA. When comparing TKA and THA patients receiving fibrin, the results were also overall similar, except for the post-operative Hgb levels. In the fibrin group, Hgb levels were higher in THA patients than in TKA patients.

There is a need to develop and evaluate more large-scale RCTs to understand some of the unanswered questions related to safety and effectiveness of tourniquet use and to evaluate if tourniquet-free surgery could potentially lead to increased component loosening over time (although two studies evaluating this with radiostereometric analysis found the quality of cementation to be unaffected by tourniquet use [35, 66]), which administration form and dose of TXA is the most efficient, and if it can replace the use of fibrin sealant. There is also a need to investigate if there is a difference in outcome between the various blood management techniques in THA and TKA, respectively.

CONCLUSIONS

The available evidence supports the safety of using TXA in THA and TKA. Tourniquet and fibrin use should be avoided and restricted, respectively, since their effects are ambiguous.

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CONFLICTS OF INTEREST: Disclosure forms provided by the authors are available with the full text of this article at www.danmedj.dk

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