

ARTHROPLASTY

Percutaneous intra-articular tranexamic acid following total knee arthroplasty without drainage to reduce blood loss

Gericke E¹ , De Beer J² , Deacon M³ , Marais LC⁴ 

¹ MBChB; Orthopaedic Registrar, Department of Orthopaedic Surgery, University of KwaZulu-Natal; King Edward Hospital, Durban, South Africa

² MBChB, HDip(Ortho), FC Ortho(SA); Specialist Orthopaedic Surgeon, Gateway Private Hospital and Alberlito Hospital, Durban, South Africa

³ MBChB, MMed(HDip(Ortho), FC Ortho(SA); Specialist Orthopaedic Surgeon, Gateway Private Hospital and Alberlito Hospital, Durban, South Africa

⁴ MBChB, FC Orth SA, MMed(Ortho), PhD; Head of Department of Orthopaedic Surgery, University of KwaZulu-Natal, Nelson R Mandela School of Clinical Medicine, Durban, South Africa

Corresponding author: Dr E Gericke, PO Box 177, Winklespruit, 4145; tel: 083 276 8703; email: bertusgericke@gmail.com

Abstract

Background: Administration of tranexamic acid (TXA) peri-operatively is a well-recognised strategy used by orthopaedic surgeons to reduce blood loss during total knee arthroplasty (TKA). Furthermore, not using a drain has been advocated to be a safe and effective way to further reduce blood loss. The main aim of this study is to assess the effect of a combination of these two strategies on total blood loss associated with TKA.

Methods: This is a retrospective study conducted on a single surgeon's data gathered over a two-year period. This study compares the blood loss in two groups of patients. The control group received no antifibrinolytic agents and a drain was inserted, while the study group received TXA and the drain was omitted.

Results: A total of 109 patients were included in the analysis, with 86 patients in the study group and 23 patients in the control group. The two groups were compared in terms of pre-operative haemoglobin, American Society of Anesthesiologists (ASA) score and body mass index (BMI). The mean age of the study group was lower than that of the control group (64±8 years vs 68±9 years; p=0.03). The mean total blood loss was lower in the study group compared to the control group (mean difference 171.8 ml; 95% CI 31.2–312.2; p=0.01). Duration of hospital stay was also reduced in the study group (2.4 days vs 3.1 days; p=0.003). There was, however, no difference in the functional outcome according to the Knee injury and Osteoarthritis Outcome Score (KOOS).

Conclusion: These findings are in accordance with previous studies, indicating that intra-articular administration of TXA and omission of negative pressure drainage may be associated with a reduction in blood loss following TKA. Larger, well-designed studies are required to determine the optimal TXA administration strategy.

Level of evidence: Level 4

Keywords: total knee arthroplasty, tranexamic acid, intra-articular, blood loss

Citation: Gericke E, De Beer J, Deacon M, Marais LC. Percutaneous intra-articular tranexamic acid following total knee arthroplasty without drainage to reduce blood loss. SA Orthop J 2020;19(2):74-78. <http://dx.doi.org/10.17159/2309-8309/2020/v19n2a3>

Editor: Dr Michael Held, University of Cape Town, South Africa

Received: June 2019

Accepted: November 2019

Published: May 2020

Copyright: © 2020 Gericke E. This is an open-access article distributed under the terms of the Creative Commons Attribution Licence, which permits unrestricted use, distribution and reproduction in any medium, provided the original author and source are credited.

Funding: No funding was received for the purposes of performing this study.

Conflict of interest: All authors confirm they have no conflicts of interest to declare with regard to this article.

Introduction

Blood loss is a common and challenging complication in total knee arthroplasty (TKA), which has been reported as ranging from 700 ml to 1 700 ml.^{1,2} Substantial blood loss could lead to allogeneic blood transfusion, which in itself may be associated with complications and risks to the patient. Disease transmission, immunological reaction and increased risk of peri-prosthetic joint infection are some of the unwanted consequences that have been described.³⁻⁵ Blood loss could also lead to an increase in duration of hospital stay, delayed rehabilitation, an increase in morbidity and increased overall cost per patient.³

Blood loss can be attributed to numerous intra-operative, but also post-operative factors. Some of the intra-operative factors are the actual surgical intervention itself, the surgical technique and the specific haemostatic measures that were taken during surgery. Post-operative blood loss mainly involves a disproportional fibrinolytic activity. The increase in fibrinolytic activity relates to tissue damage caused by surgery, but may also be associated with the use of a pneumatic tourniquet which causes release of tissue plasminogen activator from the vascular endothelium.^{5,6} Furthermore, the use of a drain contributes to increased post-operative blood loss, and it is postulated that it could be due to the loss of tamponade effect.⁷

Multiple strategies have been proposed to reduce blood loss following TKA, which can be divided into pre-, intra- and post-operative strategies.⁸ Administration of tranexamic acid (TXA) peri-operatively is one of the strategies used to reduce blood loss during TKA. This approach has been researched extensively, and numerous studies on the topic have recently been published.^{4,6} Furthermore, not using a drain has been advocated to be a safe and effective way to further reduce blood loss.^{1,9,10}

The main aim of this study is to assess the effect of the combination of these two strategies, namely, injecting TXA intra-articularly and omitting negative pressure draining post-operatively, on total blood loss associated with TKA.

Patients and methods

A retrospective cohort study was conducted on a single surgeon's data gathered over a two-year period, from January 2016 to December 2017. All patients who had primary cemented unilateral TKA (posterior-cruciate substituting) were included in the study. Procedure-related exclusion criteria were: primary complex or revision TKA, simultaneous bilateral TKA, and TKA combined with other surgical procedure in the same setting. Patient-related exclusion criteria were: patients allergic to TXA, inflammatory arthritis as the primary reason for TKA, pre-operative anaemia that required pre-op transfusion, history of thromboembolic event, and inability to cease all anticoagulants with exception of low-dose aspirin before surgery.

A total of 109 patients were included in the study after the exclusion criteria were met. The surgeon changed his blood loss management protocol within the month of May 2016 from not using antifibrinolytic agents and inserting a drain, to the use of intra-articular TXA and omitting a drain. This study compares the two groups of patients. The study group contained 86 patients who received percutaneous intra-articular TXA and no suction drain, and the control group included 23 patients who received no TXA but had suction drains inserted.

Data was extracted from patient records. Patients' demographic profiles and general medical health data were collected, which included: age, sex, weight, height, body mass index (BMI), on which side the replacement was done, pre-operative haemoglobin (Hb) levels and ASA class (American Society of Anesthesiologists

Classification).¹¹ Furthermore, surgical time, duration of hospital stay and Knee injury and Osteoarthritis Outcome Score (KOOS)¹² scores were collected. KOOS scores were calculated pre-operatively and six weeks post-operatively. However, not all KOOS scores were complete in all patient records. Only 65 out of 86 patient records in the study group had pre-operative and post-operative KOOS scores, and 18 out of 23 patient records in the control group had pre-operative and post-operative KOOS scores. Complications during the hospital stay, wound and soft tissue condition, and thromboembolism events were also monitored.

Patients were given either general anaesthesia with a femoral nerve block or a spinal according to anaesthetist recommendation or patient request. All patients received intravenous prophylactic antibiotics prior to surgery and two further doses post-operatively. A first-generation cephalosporin was used unless contraindicated. A standard midline skin incision with medial para-patellar approach was used with tourniquet inflation only prior to cementing. Tourniquet inflation continued for the remaining duration of the surgery until a compressive dressing was applied. The patella was not resurfaced and only debrided from osteophytes if needed. Axial alignment was achieved with an extramedullary guide for the tibia and an intramedullary rod guide for the femur. Once bony cuts were made, standard soft tissue balancing was used to achieve sagittal and coronal balancing. The posterior cruciate ligament was resected in all patients and a posterior-cruciate substituting (PS) implant was used. All components were fixed with cement. In the study group 2 g (two ampules of 10 ml each, 1 000 mg/10 ml) TXA was injected percutaneously and intra-articularly immediately after skin closure prior to tourniquet deflation. This was similar to the method used by Wang *et al.*¹ although a higher dose of TXA was used in this study. In the control group, a 3 mm closed-circuit portable vacuum drain was inserted and no TXA was given to the patient. The drain was removed the next day.

The implants used were either the Persona[®] (PS) or the Vanguard[®] (PS) knee system, both from Zimmer Biomet (Warsaw, Indiana, USA). The only variation to implants used was one patient from the study group that received a Unity knee[™] (Corin Cirencetser, USA). Forty-six patients received a Persona[®] implant, 39 patients received the Vanguard[®] implant and one patient received a Unity[™] implant in the study group. One patient received the Persona[®] implant and 22 patients received the Vanguard[®] implant in the control group.

Post-operatively all patients in the two study groups were given the same thrombo-prophylactic regimen. A low molecular weight heparin (LMWH) was given post-operatively and continued until discharge. Thereafter the LMWH was discontinued and a low-dose aspirin (Ecotrin[®] 81 mg; Mercury Pharma) was given for a month at home. The LMWH used was 40 mg enoxaparin sodium (Clexane[®] injection; Sanofi-Aventis, South Africa [Pty] Ltd) subcutaneously as a single dose in the morning.

Rehabilitation started on the first post-operative day and discharge criteria were: patient could mobilise independently to the bathroom and back, could climb stairs with assistance, could achieve knee flexion of at least 90 degrees, and pain was well controlled. Once discharged, patients were followed up after two weeks to assess the wound and range of movement. Further follow-up was at six weeks for assessment of mobility, range of movement and radiological evaluation. Thereafter patients were assessed at 6- to 12-month intervals, at the surgeon's discretion.

The measurements indicating degree of blood loss included: pre-operative Hb levels, post-operative Hb levels on day 1 post-operatively and total blood volume loss. The latter was calculated with the formula described by Nader *et al.*¹³ and Sehat *et al.*¹⁴ It is based on the Hb decrease adjusted for the weight, height and sex of the patient.

Formula:

$$\begin{aligned} \text{Total blood loss (ml)} &= 100 \times \text{Hb}_{\text{loss}}/\text{Hb}_i \\ \text{Hb}_{\text{loss}} &= \text{BV} \times 10 \times (\text{Hb}_i - \text{Hb}_e) \\ \text{BV (L)} &= \text{estimated total body blood volume in litres} \\ &= 0.3669 \times \text{H}^3 + 0.03219 \times \text{W} + 0.6041 \text{ (men)} \\ &= 0.3561 \times \text{H}^3 + 0.03308 \times \text{W} + 0.1833 \text{ (women)} \end{aligned}$$

where H is the patient's height (m); W is the body mass (kg); Hb_i is haemoglobin concentration prior to surgery (g/dL), and Hb_e is haemoglobin concentration post-operatively (g/dL).

Statistical analyses were performed using STATA Statistics/Data Analysis software, version 15.0 (StataCorp LLC, 4905 Lakeway Drive, College Station, Texas, 77845, USA). Continuous variables were reported as mean (\pm SD) or median (with interquartile range) and categorical variables as number and percentages, unless otherwise stated. The two-sided t-test with equal variances was used to analyse parametric data. The two-sample Wilcoxon rank-sum (Mann-Whitney) test was used for non-parametric data. The Fisher's exact or chi-squared test was used for categorical data comparisons. A difference of $p \leq 0.05$ was considered to be significant.

Results

The baseline characteristics of the two groups are depicted in *Table I*. The mean age of the study (TXA) group was lower than that of the control group (64 \pm 8 years vs 68 \pm 9 years; 95% confidence interval [CI] 60.4–67.4 vs 66.7–70.7; $p=0.03$).

The comparison between the outcome measures in the study group and the control group is summarised in *Table II*. The mean blood loss in the TXA group was 776.8 \pm 308.9 ml. The mean total blood loss was lower in the study group in comparison to the control group (mean difference 171.8 ml; 95% CI 31.2–312.2; $p=0.01$). Duration of hospital stay was also shorter in the study group compared to the control group (2.42 days vs 3.13 days, $p<0.01$). There was no significant difference in the pre-operative and post-operative (at six weeks post-operatively) KOOS scores of the study group and control group (24.8 \pm 2.2 vs 24.5 \pm 4.7).

Two patients in the study group had minor post-operative swelling of the knee which resolved uneventfully, two patients had

minor oozing of the wound necessitating dressing change on post-operative day 1 and two patients had decreased range of movement, of which one had to receive manipulation under anaesthesia later. One patient from the control group had swelling of the knee. This patient's swelling was more significant and Doppler ultrasound was done to exclude thrombosis.

Discussion

This study aimed to investigate the impact of the use of intra-articular TXA injection without the use of negative drainage on peri-operative blood loss following uncomplicated unilateral knee replacement. Our findings suggest that intra-articular TXA may reduce total blood loss.

TXA is a synthetic antifibrinolytic, preventing the formation of plasmin by blocking the conversion of plasminogen to plasmin.¹⁵ At higher concentration, TXA acts directly to inhibit plasminogen and binding of plasmin to fibrin.⁶ The end result is the inhibition of fibrin degradation and breakdown of clots. Benoni *et al.* was first to describe the benefit of using TXA in TKA in 1995.¹⁶ Numerous randomised controlled trials^{1,5,17,18} and meta-analyses^{19,20} have since been published; however, there is no consensus on the method of administration and dose required for optimal effect with the least number of possible side effects and complications.

There are five methods of TXA administration described in TKA to reduce blood loss which can be used either individually or in combination, namely: oral,^{20,21} topical,^{18,22} intravenous,^{3,22} intra-capsular³ and intra-articular.^{1,22-24} Earlier studies focused on intravenous injections, although there were some concerns about thromboembolic complications.^{23,25} It is also generally accepted that only a small percentage of TXA reaches the target location.^{1,26} Chen *et al.* compared intra-articular with intravenous administration of TXA in TKA and found no difference in blood loss.¹⁷ Similar studies have been conducted comparing the other different methods of TXA administration with similar results.^{3,22,23} The preferred method of TXA administration remains controversial and has not yet been defined. However, topical intra-articular TXA may have a theoretical advantage in that it is applied directly when and where it is needed to control bleeding.²⁷

Different methods of intra-articular administration of TXA have also been described. Some authors inject the TXA once after

Table I: Summary of patients' profiles

Variable	Study group (n=86)	Control group (n=23)	p-value
Age	64.0 \pm 8.2	68.7 \pm 9.3	0.0303
Sex (male/female)	26/60	7/16	
BMI	31.3 \pm 7.1	31.6 \pm 1.33	0.8334
Pre-op Hb (g/dl)	13.56 \pm 1.26	13.92 \pm 1.46	0.5113
ASA score	2.14 \pm 0.61	2.22 \pm 0.95	0.6360
TKA side (Rt/Lt)	13/10	46/40	

Table II: Summary of results

Variable	Study group (n=86)	Control group (n=23)	p-value
Post-op Hb (g/dl)	11.38 \pm 0.14	11.16 \pm 0.31	0.2376
BV loss ml	776.84 \pm 33.31	948.60 \pm 56.90	0.0170
Days in hospital	2.42	3.13	0.0037
	Study group (n=65)	Control group (n=18)	
KOOS pre-op	35.27 \pm 1.51	31.94 \pm 14.23	0.3264
Koos post-op	68.08 \pm 1.79	63.33 \pm 3.72	0.3264
Diff in KOOS	24.80 \pm 2.20	24.56 \pm 4.72	0.9621

completion of fascial closure to prevent leakage.²⁴ Injecting the TXA percutaneously immediately after the skin has been closed has also been described.¹ Other studies described injecting TXA through the drain and clamping the drain for some period afterwards.⁴ In this study, TXA was administered percutaneously following skin closure as per the surgeon's discretion.

The use of a drain in TKA has also come into question in numerous studies;^{8,9,10} it is postulated that the tamponade effect is lost with a drain and this could lead to post-operative blood loss.⁷ Wang et al. confirmed the efficacy of TKA without using drainage in terms of blood loss.¹ Other studies also reported the safety of non-drainage in TKA.^{9,10} The method we used was injecting the TXA percutaneously immediately after the skin was closed and before deflation of the tourniquet.

Wang et al. published a double-blind, randomised, placebo-controlled trial; comparing 30 patients who had a 500 mg TXA intra-articular injection immediately after skin closure without drainage, and 30 patients with saline intra-articular injections immediately after skin closure. Findings showed a significant reduction of mean blood loss of 560.55 ml (999.22 ml vs 1 559.77 ml; $p < 0.01$) between the groups at day 5 post-operatively.¹ An earlier study by Wong et al. (2010), which was one of the first publications to evaluate the benefit of topical TXA administration without the use of a drain, also showed reduction of blood loss (1 208 ml TXA 3 g vs 1 295 ml TXA 1.5 g vs 1 610 ml placebo).¹⁸ Craik et al. and Yang et al. also used intra-articular TXA without a surgical drain and they had similar results.^{24,28} The findings in our study were similar to previously mentioned studies.^{1,18,24,28} We noted a significant reduction in blood loss of 171.76 ml (776.8 ml vs 948.60 ml; $p < 0.01$). The duration of hospital stay was also reduced (2.42 days vs 3.13 days; $p = 0.003$). There was, however, no difference in the functional outcome according to the KOOS scores.

There are several shortcomings to this study. It was a retrospective study and selection bias could not be excluded. The difference in age between the two groups is notable. The study did not identify which one of the two changes in treatment, namely administering TXA or omitting a drain, were responsible for the reduction of blood loss, nor did it identify the degree of independent contribution each one of the treatments made. The use of LMWH as thromboprophylaxis deserves mention as it may have contributed to an increased blood loss in both groups.²⁹ The sample size was small, especially in the control group, and it was not sufficiently powered to assess thromboembolic events and wound complications. Similarly, the low event rate prevents drawing any conclusions in terms of allogenic blood transfusion rates. Furthermore, post-operative blood tests were done the next day and not at a fixed time interval, and no further blood test comparisons were conducted after that. Follow-up of the patients was insufficient, as can be seen in the incomplete KOOS scores: only 65 out of 86 in the study and 18 out of 23 control group were complete.

Despite the large number of publications on the topic of TXA in arthroplasty, it appears that some controversy remains in terms of the optimal strategy. Future research including randomised controlled studies and meta-analysis are needed to assess the most appropriate dose, route and most effective method for TXA administration.

Conclusion

These findings are in accordance with other studies, indicating that intra-articular administration of TXA and omission of negative pressure drainage may be associated with a reduction in blood loss following TKA. Larger, well-designed studies are required to determine the optimal TXA administration strategy.

Ethics statement

This study received prior approval from a Level 1 Ethics committee (ref BRE311/17). The authors declare that this submission is in accordance with the principles laid down by the Responsible Research Publication Position Statements as developed at the 2nd World Conference on Research Integrity in Singapore, 2010.

Declaration

The authors declare authorship of this article and that they have followed sound scientific research practice. This research is original and does not transgress plagiarism policies.

Author contributions

GE contributed to the conception and design of the work; the literature review; developed the study protocol and submitted the study for ethics approval; the acquisition, analysis and interpretation of the data for the work; drafting the work and submitting the final version to be published.

DBJ was the primary surgeon in all the cases, contributed in the gathering of patient data and revised the article critically for important intellectual content.

DM contributed to the conception and design of the work, and the developing of the study protocol; and revised the article critically for important intellectual content.

MLC revised the article critically for important intellectual content, compiling the statistics and final approval of the version to be submitted to the journal.

ORCID

Gericke E  <https://orcid.org/0000-0002-7613-9266>

De Beer J  <https://orcid.org/0000-0002-2692-4717>

Deacon M  <https://orcid.org/0000-0002-1100-1370>

Marais LC  <https://orcid.org/0000-0002-1120-8419>

References

- Wang CG, Sun ZH, Liu J, Cao JG, Li ZJ. Safety and efficacy of intra-articular tranexamic acid injection without drainage on blood loss in total knee arthroplasty: A randomized clinical trial. *Int J Surg*. 2015;**20**:1-7.
- Sehat KR, Evans R, Newman JH. How much blood is really lost in total knee arthroplasty? Correct blood loss management should take hidden loss into account. *Knee*. 2000;**7**(3):151-55.
- May JH, Rieser GR, Williams CG, et al. The assessment of blood loss during total knee arthroplasty when comparing intravenous vs intracapsular administration of tranexamic acid. *J Arthroplasty*. 2016;**31**(11):2452-57.
- Ishida K, Tsumura N, Kitagawa A, et al. Intra-articular injection of tranexamic acid reduces not only blood loss but also knee joint swelling after total knee arthroplasty. *Int Orthop*. 2011;**35**(11):1639-45.
- Orpen NM, Little C, Walker G, Crawford EJ. Tranexamic acid reduces early post-operative blood loss after total knee arthroplasty: a prospective randomised controlled trial of 29 patients. *Knee*. 2006;**13**(2):106-10.
- Jansen AJ, Andreica S, Claeys M, et al. Use of tranexamic acid for an effective blood conservation strategy after total knee arthroplasty. *Br J Anaesth*. 1999;**83**(4):596-601.
- Goes RFD, Silva AFD, Lyra FS, et al. Prospective randomized study after the use of drains in total knee arthroplasty with implant. *Rev Bras Ortop*. 2013;**48**(3):257-62.
- Harwin SF, Kapadia BH, Issa K, Mont MA. Blood management strategies in total knee arthroplasty. *J Knee Surg*. 2013;**26**(6):371-72.
- Demirkale I, Tecimel O, Sesen H, et al. Non- drainage decreases blood transfusion need and infection rate in bilateral total knee arthroplasty. *J Arthroplasty*. 2013;**29**(5):993-97.
- Zhang QD, Guo WS, Zhang Q, et al. Comparison between closed suction drainage and nondrainage in total knee arthroplasty: a meta-analysis. *J Arthroplasty*. 2011;**26**(8):1265-72.
- Saklad M. Grading of patients for surgical procedures. *Anesthesiology*. 1941;**2**:281-84.
- Roos EM, Lohmander LS. The Knee injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis. *Health Qual Life Outcomes*. 2003;**1**(1):64.
- Nader SB, Hidalgo JU, Blouch T. Prediction of blood volume in normal human adults. *Surgery*. 1962;**51**:224-32.

14. Sehat KR, Evans RL, Newman JH. Hidden blood loss following hip and knee arthroplasty. Correct blood loss should take hidden loss into account. *J Bone Joint Surg Br.* 2004;**86**(4):561-65.
15. Dunn CJ, Goa KL. Tranexamic acid. A review of its use in surgery and other indications. *Drugs.* 1999;**57**:1005-1032.
16. Benoni G, Carlsson A, Petersson C, Fredin H. Does tranexamic acid reduce blood loss in knee arthroplasty? *Am J Knee Surg.* 1995;**8**(3):88-92.
17. Chen JY, Chin PL, Moo IH, et al. Intravenous versus intra-articular tranexamic acid in total knee arthroplasty: A double-blinded randomised controlled noninferiority trial. *Knee.* 2016;**23**(1):152-56.
18. Wong J, Abrishami A, El Beheiry H, et al. Topical application of tranexamic acid reduces postoperative blood loss in total knee arthroplasty: a randomized, controlled trial. *J Bone Joint Surg.* 2010;**92**(15):2503-13.
19. Panteli M, Papakostidis C, Dahabreh Z, Giannoudis PV. Topical tranexamic acid in the total knee replacement: a systematic review and meta-analysis. *Knee.* 2013;**20**(5):300-309.
20. Lee QJ, Ching WY, Wong YC. Blood sparing efficacy of oral tranexamic acid in primary total knee arthroplasty: a randomized controlled trial. *Knee Surg Relat Res.* 2017;**29**:57-62.
21. Fillingham YA, Kayupov E, Plummer DR, Moric M, Gerlinger TL, Della Valle CJ. The James A. Rand Young Investigator's Award: A randomized controlled trial of oral and intravenous tranexamic acid in total knee arthroplasty: The same efficacy at lower cost? *J Arthroplasty.* 2016;**31**(9):S26-S30.
22. Lee SY, Chong S, Balasubramanian D, Na YG, Kim TK. What is the ideal route of tranexamic acid in TKA? A randomized controlled trial. *Clin Orthop Related Res.* 2017;**475**:1987-96.
23. Tanaka N, Sakahashi H, Sato E, et al. Timing of the administration of tranexamic acid for maximum reduction in blood loss in arthroplasty of the knee. *J Bone Joint Surg Br.* 2001;**83**(5):702-705.
24. Yang Y, Lv YM, Ding PJ, Li J, Z Ying-Ze. The reduction in blood loss with intra-articular injection of tranexamic acid in unilateral total knee arthroplasty without operative drains: a randomized controlled trial. *Eur J Orthop Surg Traumatol.* 2015;**25**:135-39.
25. Konig G, Hamlin BR, Waters JH. Topical tranexamic acid reduces blood loss and transfusion rates in total hip and total knee arthroplasty. *J Arthroplasty.* 2013;**28**(9):473-76.
26. 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.
27. Moskal JT, Capps SG. Intra-articular tranexamic acid in primary total knee arthroplasty: meta-analysis. *J Knee Surg.* 2018;**31**(1):56-67.
28. Craik JD, Ei Shafie SA, Kidd AG, Twyman RS. Can local administration of tranexamic acid during total knee arthroplasty reduce blood loss and transfusion requirements in the absence of surgical drains? *Eur J Orthop Surg Traumatol.* 2014;**24**(3):379-84.
29. Xia ZN, Zhou Q, Zhu W, Weng XS. Low molecular weight heparin for the prevention of deep venous thrombosis after total knee arthroplasty: A systemic review and meta-analysis. *Int J Surg.* 2018;**54**:265-75. ■