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REVIEW ARTICLE

Optimizing Intraoperative Blood Management for One-Stage Bilateral Total Knee Arthroplasty

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Abstract *Background:* Effective blood management strategies are a major determinant of successful outcomes after one-stage bilateral total knee arthroplasty (BTKA). Proper patient selection with preoperative optimization and intra- and postoperative interventions can reduce transfusion risk and associated morbidity in these patients. *Questions/Purposes:* The purpose of this study was to evaluate intraoperative blood management modalities based on three keystone questions: (1) What is the role of the anesthesiologist?, (2) Which are the surgeon-dependent strategies?, and (3) Is there any place for pharmacologic interventions? *Methods:* We searched the established electronic literature database MEDLINE. After critical appraisal, 94 studies were deemed eligible from which to draw documented evidence. *Results:* A number of blood-conserving methods are currently implemented in patients undergoing one-stage BTKA. Among them, regional anesthesia, tourniquet use, and tourniquet deflation after wound closure, femoral canal sparing or femoral canal plugging, avoidance of drains, and tranexamic acid use were the intraoperative strategies with documented efficacy in blood conservation. *Conclusion:* Combined proper intraoperative anesthesiologic, surgical, and pharmacologic interventions reduce blood loss and need for transfusion in BTKA patients. However, contemporary relevant literature is lacking evidence-based guidelines.

Keywords bilateral total knee arthroplasty· intraoperative blood conserving

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Introduction

One-stage bilateral total knee arthroplasty (BTKA) performed using proper patient selection and perioperative care measures can successfully treat patients with bilateral end-stage degenerative or inflammatory disease of the knee [21, 36, 58]. The incidence of bilateral knee involvement is increased in the aging population; therefore, one-stage surgery may offer advantages, including a single hospitalization and reduced overall recovery time [65, 69]. Although some researchers have suggested that this approach is associated with modestly higher odds for major complications compared to unilateral total knee arthroplasty (UTKA) [27], others maintain that in patients with bilateral disease, one-stage BTKA can be performed safely, using appropriate selection criteria [69].

One-stage (or single-stage/same-day) BTKA is performed under the same session of anesthesia, with the two surgical procedures being simultaneously performed by two different surgical teams or sequentially, usually by the same

surgical team. Alternatively, two-stage (or staged) BTKA is performed during separate anesthetic sessions and during the same or different patient admissions, with varying time intervals between the two procedures.

One of the major concerns with BTKA, raised by its increased invasiveness, is blood loss and the subsequent need for transfusion. Recent studies show increased blood loss, transfusion rate, and allogeneic blood use in BTKA vs. UTKA [32, 69, 92]. Acute blood loss anemia results in prolonged hospital length of stay (LOS), complications related to blood transfusion (clerical errors, infections, immunologic reactions), and increased cost [48]. In order to minimize blood loss, many pharmacologic and nonpharmacologic approaches have been incorporated in contemporary practice.

We carried out a literature search to evaluate intraoperative blood management strategies in BTKA. Three questions were formulated in order to highlight the main fields of interest: (1) What is the role of the anesthesiologist?; (2) Which are the surgeon-dependent strategies?; and (3) Is there any place for pharmacologic interventions? Our main purpose was to document existing evidence (conflicting or not) and to define an optimal blood management protocol in these patients.

Methods

The electronic database MEDLINE (PubMed) was searched up to February 2016. Search keywords were as follows: "blood management," "blood conservation," "blood loss," "transfusion," "bilateral total knee arthroplasty," "bilateral total knee replacement," "BTKA," and "BTKR." These keywords were combined with the Boolean operators AND or OR. Only articles in English were included. The initial number of papers was 199. After reviewing abstracts and full-text articles, we excluded papers referring only to two-stage procedures and pre- or postoperative blood management strategies. The reference lists of all full-text articles were reviewed to identify any additional relevant studies. Finally, after critical appraisal, 94 studies were considered appropriate for this review.

Results

Anesthesiologist-Dependent Strategies

Anesthesia Technique

Same-day BTKA can be safely performed under regional anesthesia [74]. After examining a large sample of BTKA patients (15,687), Stundner et al. [11] found reduced odds of blood transfusion in patients receiving neuraxial anesthesia compared to general anesthesia. The etiology remains unknown. Potential mechanisms may include improved analgesia and decreased vascular tone and blood pressure in the lower extremities perioperatively. A similar association between regional anesthesia and lower blood transfusion rates in patients treated with BTKA was found by other investigators [94]. However, performance of BTKA under spinal anesthesia may be a significant risk factor for the development of postoperative hypotension compared with general anesthesia [73]. In another retrospective analysis of 221 patients undergoing same-day BTKA, peripheral nerve block anesthesia was associated with less blood transfusion compared to epidural anesthesia [64].

Another anesthesia-related strategy in blood management is hypotensive anesthesia. It consists of extensive epidural anesthesia, which results in sympathetic blockade and sustained hypotension [9]. It is associated with a documented decrease in intraoperative and postoperative blood loss and is well described in patients undergoing UTKA without tourniquet use [9, 35, 44]. However, there are no studies evaluating its efficacy in BTKA patients.

Body temperature is a modifiable factor that can be actively controlled intraoperatively. Hypothermia is common in joint arthroplasty patients and may result in platelet dysfunction and coagulation abnormalities [20]. Therefore, measures including warmed intravenous fluids, warm mattresses, and air warming seem to be important in patients undergoing same-day BTKA [29]; these measures, however, have not been evaluated in the literature.

Acute Normovolemic Hemodilution

Acute normovolemic hemodilution (ANH) is a blood preservation strategy that consists of removal of 1 to 3 units of blood shortly after induction of anesthesia, while normovolemia is maintained with crystalloid and/or colloid administration. The collected blood is then reinfused intra- or postoperatively, rendering this approach suitable for patients who, for various reasons, may refuse allogeneic blood products [48]. Overall blood loss is not affected, but hemodilution results in a loss of fewer red cells. This method may offer the additional advantage of potentially reducing the incidence of postoperative venous thromboembolism, due to lowered blood viscosity [9]. In UTKA, a study reported less postoperative allogeneic blood transfusion when ANH was implemented [63]. In patients undergoing BTKA, a prospective randomized trial showed no significant differences in allogeneic blood transfusion rate using ANH vs. preoperative autologous blood donation (PAD) [24]. Current evidence does not support its use in BTKA.

Surgeon-Dependent Strategies

Tourniquet Use

The use of a tourniquet is a common practice during TKA. The tourniquet reduces intraoperative blood loss while providing a bloodless surgical field for enhanced cement interdigitation and improved visualization, yielding decreased operative times [86]. However, its use is associated with increased local fibrinolytic activity (as a result of the postischemic release of tissue plasminogen activator) and reactive hyperemia after tourniquet release, which may lead to increased postoperative blood loss [17, 66]. In a recent level I therapeutic study, Dennis et al. [19] evaluated tourniquet use in patients undergoing BTKA. They used unilateral tourniquet application and found that the nontourniquet limbs had increased estimated intraoperative blood loss, albeit no difference was noted in total blood loss.

The timing of tourniquet deflation is an important parameter. In a randomized prospective study, the authors compared

tourniquet release and hemostasis before wound closure vs. tourniquet release after wound closure and compressive dressings in the same patients undergoing BTKA. They found no difference in perioperative blood loss [81]. In a recent meta-analysis of randomized controlled trials (RCTs) with patients undergoing UTKA, the authors concluded that tourniquet release for hemostasis before wound closure was not found to reduce total blood loss [91]. Moreover, a similar meta-analysis in UTKA showed that tourniquet release before wound closure significantly increased total, calculated, and postoperative blood loss [90]. To the best of our knowledge, tourniquet use and timing of tourniquet release have been only investigated in studies comparing the two knee procedures of the same patient undergoing BTKA and not different patients. As far as decision making is concerned, current evidence supports tourniquet release after wound closure.

Surgical Technique

Patient-specific instrumentation (PSI) has been recently introduced, aiming to optimize surgical technique. Among other advantages, proponents of the approach highlight the importance of avoiding intramedullary canal penetration during femoral preparation, which may reduce blood loss [72]. Rathod et al. [72] retrospectively evaluated blood loss and transfusion requirements in patients undergoing single-stage BTKA with and without PSI. The authors found a nonsignificant trend toward lower blood loss and lower number of units transfused in the PSI group. In terms of surgical approach and blood loss, a prospective randomized trial comparing subvastus and medial parapatellar approaches in patients undergoing BTKA did not find significant differences in blood loss between the groups [33].

Another technique adopted by orthopedic surgeons is computer-assisted surgery (CAS) [85]. Studies comparing this method vs. conventional instrumentation in UTKA showed conflicting results with respect to accuracy in mechanical axis reconstruction [1, 30, 31], blood loss, and operative times [1, 26, 78]. In a retrospective study of sequential BTKAs by Merz et al., who compared patients undergoing CAS and conventional surgery, the number of blood units transfused was significantly lower in the CAS group [59]. In summary, avoidance of the femoral intramedullary canal may account for the lower blood loss with the aforementioned techniques. From this standpoint, it is advocated to routinely plug the entry hole when using conventional cutting guides [45, 83].

The effect of implant type [posterior cruciate retaining (CR) vs. posterior stabilized (PS)] has been previously investigated in UTKA patients. While higher blood loss was found with PS implants [53], no significant difference in transfusion rates has been proven [15, 53]. Intuitively, the removal of additional bone in PS implants would lead to increased blood loss; this effect would be expected to be greater in BTKA. To date, however, there is no evidence supporting that the use of PS knees in BTKA increases blood loss or the need for subsequent transfusion.

Finally, surgical time in UTKA patients is an independent prognostic factor of perioperative blood loss [70] and allogeneic blood transfusion [62], further emphasizing the importance of shortening surgical time in BTKA patients. When comparing the first and second knees of sequential BTKAs, the second knee was associated with increased tourniquet time and postoperative drained blood amount. This could be attributed to several factors, including surgeon's fatigue and restricted operation field during the second operation [75]. A comparative study between sequential and staged BTKA showed increased total blood loss in sequential vs. staged BTKA, despite the shorter total operative and tourniquet time in the first group. However, similar transfusion rates were documented [49]. In another similar study, both actual and estimated blood loss per knee were similar, although the mean operative time per knee was significantly shorter for the sequential group compared to either of the staged TKA procedures [60]. Therefore, the effect of surgical time on BTKA blood loss has not been clarified in the literature yet.

Coagulation

The most common technique to control bleeding vessels is electrocoagulation. Monopolar electrocautery is universally used in TKA, especially by surgeons who either deflate the tourniquet before wound closure or do not use a tourniquet. Saline-coupled bipolar sealing is a novel technique and has been studied in UTKA [55, 56, 67, 68]. Kamath et al. evaluated its use in BTKA and concluded that it may be effective in reducing blood loss, but it comes with the downside of increased costs [38].

Drains

The use of drains in BTKA is a somewhat controversial issue. Although two studies showed advantageous blood management in BTKA patients without drains (Table 1), many surgeons, based on personal preference, are still using drains to prevent hematoma accumulation and related complications. In the UTKA field, recent literature does not support the routine use of postoperative suction drainage [71], since it is associated with increased estimated blood loss (EBL) and amount of allogeneic blood transfused [11]. A prospective RCT [6] comparing closed suction drains, reinfusion drains, and no drains found no differences in change in hemoglobin levels or transfusion rates. Drain clamping is used by some surgeons with the aim of reducing postoperative blood loss in UTKA through tamponade [4, 52, 89]. This approach may also be applied in patients undergoing BTKA, in case a drain is to be used.

Reinfusion Systems: Cell Saver

A reinfusion system may be used intra- or postoperatively in order to collect drained blood, which is subsequently reinfused, within 6 to 8 h. These systems combine the advantages of drains and PAD. Nonetheless, the risks of coagulopathy and contamination, as well as increased costs, have discouraged universal application [48, 57]. Moreover, topical hemostatic agents, when used intraoperatively, would be carried into systemic circulation along with reinfused blood. The volume of salvaged blood that is reinfused in BTKA patients may be considerable [25]. Two studies evaluated reinfusion systems in combination with PAD in patients undergoing bilateral knee replacement, but their efficacy as an independent approach was not evaluated [12, 13, 16]. In a retrospective study of one-stage BTKA patients, the unilateral use of a reinfusion device was not

Table 1 Evaluation of drain usage on blood management in one-stage BTKA patients

	Reference	
	Demirkale et al. [18]	Watanabe et al. [84]
Year	2014	2015
Type of study	Retrospective	Prospective
Study groups	T = 227 (drain on both knees) C = 255 (no drain)	T1 = 20 (drain on both knees) T2 = 22 (drain on one knee) C = 21 (no drain)
TXA use	No	INAI, 1 g at the end of operation through drain (T1, T2) or injection via a 18-gauge needle
Tourniquet use	T: pneumatic tourniquet with postdeflation hemostasis C: elastic tourniquet, removed after wound closure	Pneumatic tourniquet with post-deflation hemostasis in all patients
Type of drain	Closed suction drain	Closed suction drain
Drain clamping	No (personal communication with author)	For 1 h after TXA injection
Timing of drain removal	After 24 h (personal communication with author)	After 24 h
Results	Total blood units transfused T = 740; C = 278* Transfused blood units per patient (mean ± SD) T = 3.26 ± 0.71; C = 1.09 ± 0.81* Postoperative Hb in g/dL T = 9.2 ± 1.1; C = 7.5 ± 1.8*	Hb drop in POD1 in g/dL (mean ± SD) T1 = 2.2 ± 1.2; T2 = 2.2 ± 0.9; C = 1.5 ± 0.8* Number of cases with Hb drop > 3 g/dL T1 = 5 (25%); T2 = 3 (14%); C = 0 (0%) (T1* vs C)

BTKA bilateral total knee arthroplasty, *TXA* tranexamic acid, *T* treatment group, *C* control group, *INAI* intraarticular injection, *Hb* hemoglobin, *POD1* postoperative day 1, *SD* standard deviation
*$p < 0.05$ between T and C groups

associated with a reduction in allogeneic transfusion [41]. Yau et al. consider the routine use of an intraoperative blood-salvaging system justified for patients undergoing bilateral TKR because they are prone to having more intraoperative blood loss [88]. Even though these devices are incorporated in current practice, no definitive evidence supports their use.

Pharmacologic Interventions

Topical Hemostatic and Vasoconstrictive Agents

A variety of different hemostatic agents and techniques have been tested in BTKA, in an effort to reduce blood loss and the need for allogeneic transfusion. Nevertheless, none of these methods is accepted as a stand-alone approach. The use of bone wax to cover holes and uncovered osteotomy surfaces can be easily incorporated in routine practice [93]. Fibrin sealant is another hemostatic agent used topically. In one study, it was used unilaterally in patients undergoing BTKA, in combination with tourniquet use, tranexamic acid, and plugging of the femoral canal [79]. The authors found no difference in drain output between knees treated with and without fibrin sealant. Other agents have been sporadically tested, including a polysaccharide-based system [5] but lack universal acceptance and applicability.

Vasoconstrictive agents such as epinephrine or norepinephrine can be locally infused [23, 54] and/or infiltrated into periarticular tissues [7, 50, 54, 93]; they are low-cost agents, easily applied, and act by reducing the rebound increase in blood flow that occurs 20 to 30 min after tourniquet release in TKA [10]. Periarticular infiltration of epinephrine, usually combined with local anesthetics, morphine, antibiotics, steroids, or nonsteroidal anti-inflammatory drugs in solutions of various compositions (periarticular multimodal drug injection [PMDI]), is a common practice in BTKA [22, 46, 47, 82, 93] mainly for pain control; however, it has not yet been evaluated as an independent blood-conserving factor.

Antifibrinolytic Agents

Tranexamic acid (TXA), aprotinin, and ε-aminocaproic acid (EACA) are antifibrinolytic agents that have been used in TKA in order to reduce blood loss and transfusion requirements. TXA is a synthetic molecule that inhibits activation of plasminogen to plasmin, an enzyme that degrades fibrin clots, fibrinogen, and procoagulant factors V and VIII. At a higher concentration, TXA directly inhibits plasmin activity. Its plasma half-life is approximately 80 min [61], and maximum plasma levels are reached within 5 to 15 min. It diffuses rapidly into the synovial fluid and membrane, with therapeutic levels maintained for approximately 3 h [3]. TXA can be administered intravenously (IV) or topically. Topical application can have the form of intraarticular wash (before wound closure and usually 5 min before tourniquet release), periarticular soft tissue infiltration, or intraarticular injection after skin closure followed by drain clamping. The local infiltration technique can be combined with other local agents (PMDI) [93]. Even though its efficacy and safety are well established for BTKA [28, 87], there is great disparity throughout the literature regarding dosage, timing, and route of administration (Table 2).

The evidence for the use of aprotinin, a serine protease inhibitor, and EACA, an inhibitor of plasmin activation and fibrin binding for BTKA, is limited. EACA use has not been studied yet, and only one study has evaluated aprotinin for BTKA. Aprotinin (1 to 2 million units) infused over 30 min during closure of the knee operated first was used in 25 BTKA patients and was compared to a historical control group of 60 patients [43]. The authors reported significant reduction in early blood loss without adverse events. However, both aforementioned agents have been widely

Table 2 Dosage, route, and timing of TXA administration in one-stage BTKA patients

Reference	Type of study	Protocol of TXA administration			Main results
		Study groups	Route and dosage	Procedure	
Karam et al. [40]	Retrospective	T = 37 C = 50	IV, 20 mg/kg before incision, 1 dose	Sequential	Blood units transfused[a] T = 0.16 ± 0.50; C = 0.90 ± 1.07* Transfusion rate (%) T = 10.8 (4 patients); C = 50 (25 patients)* Hb drop on POD1 in g/dL[a] T = 3.58 ± 1.11; C = 4.64 ± 1.40* Hb drop on POD2 in g/dL[a] T = 4.50 ± 1.13; C = 5.34 ± 1.46*
Kim et al. [42]	RCT	T = 73 C = 73	IV, 10 mg/kg 30 min before tourniquet deflation for the 1st knee IV, 10 mg/kg 30 min before tourniquet deflation for the 2nd knee IV, 10 mg/kg 3 h after injection for the 2nd knee	Sequential	Blood units transfused[a] T = 1.5 ± 0.5; C = 1.4 ± 0.6 Transfusion rate (%) T = 6.8 (5 patients); C = 27.4 (20 patients)* Calculated total blood loss in mL[a] T = 1282.6 ± 308.5; C = 1379.6 ± 353.4 Drain output in mL[a] T = 61.0 ± 84.5; C = 162.4 ± 157.5*
Zhu et al. [95]	Retrospective	T = 45 C = 45	INAW, 1500 mg diluted in 100 mL N/S 0.9% 5 min of contact time before tourniquet deflation	Sequential	Blood units transfused[b] T = 1 (1–2); C = 1 (1–1.5) Transfusion rate (%) T = 37.8 (17 patients); C = 60.0 (27 patients)* Total blood loss in mL[b] T = 679 (543–850); C = 997 (740–1379)* Patients requiring > 1 blood unit (%) T = 8.9 (4 patients); C = 24.4 (11 patients)*
Bagsby et al. [8]	Retrospective	T = 46 C = 57	IV, 10 mg/kg 10 min before tourniquet deflation	Simultaneous	Blood units transfused intraoperatively[a] T = 0 ± 0; C = 0.07 ± 0.21* Blood units transfused postoperatively[a] T = 0.37 ± 0.88; C = 1.0 ± 1.04* Transfusion rate (%) T = 17.4 (8 patients); C = 57.9 (33 patients)* Estimated blood loss in mL[a] T = 229.89 ± 111.5; C = 222.81 ± 78.19
Karaaslan et al. [39]	RCT	T = 41 C = 40	IV bolus, 15 mg/kg 10 min before the 1st tourniquet inflation INAI, 3 g/100 mL after the 1st wound closure 10 min before tourniquet deflation (+ drain clamp for 2 h) IV infusion, 10 mg/kg/h continued for 3 h following completion on the 2nd side	Sequential	Blood units transfused[c] T = 0.00 (0.00–2.00); C = 0.00 (0.00–3.00) Transfusion rate (%) T = 10.1 (7 patients); C = 9.9 (13 patients) Total drain output in mL[c] T = 500.00 (190.00–1025.00); C = 900.00 (150.00–2625.00)* Hb drop 12 h postoperatively in g/dL[c] T = 2.10 (0.20–5.40); C = 3.10 (1.50–5.50)*
Hegde et al. [29]	Prospective	T1 = 30 T2 = 30 C = 30	T1 = IV, 1 g 20 min prior to tourniquet inflation T2 = INAI, 1 g after wound closure in each knee	Sequential	Blood units transfused[a] T1 = 0.63 ± 0.85; T2 = 0.23 ± 0.5; C = 1.1 ± 0.89* Postoperative Hb at 24 h in g/dL[a] T1 = 10.87 ± 1.15; T2 = 11.09 ± 1.3; C = 10.34 ± 1.84*
Jain et al. [34]	Prospective	T = 150	IV, 15 mg/kg after incision and then 10 mg/kg q 6 h for 12 h	Sequential	Authors evaluated only functional scores and safety of sequential BTKA
Dhillon et al. [20]	Retrospective	T = 52 C = 56	IV, 10 mg/kg just before the 1st tourniquet deflation IV, 10 mg/kg 3 h after the 1st dose	Sequential	Blood units transfused[a] T = 0.80 ± 0.90; C = 3.17 ± 0.81* Total drain output in mL[a] T = 274.62 ± 128.34; C = 809.64 ± 227.30* Postoperative Hb at 6 h in g/dL[a] T = 11.79 ± 1.96; C = 10.25 ± 1.40* Postoperative Hb at discharge in g/dL[a] T = 12.26 ± 1.45; C = 11.78 ± 1.33
Aggarwal et al. [2]	Prospective	T1 = 35 T2 = 35	T1 = IV, 15 mg/kg 30 min prior deflation of tourniquet and the same dose 2 h later irrespectively of the 2nd knee surgery T2 = INAW, 15 mg/kg in 100 mL N/S left for 10 min before suturing; drain clamped for 2 h; tourniquet deflation after dressing	Sequential	Total blood units transfused T1 = 7; T2 = 0* Total blood loss in mL[d] T1 = 1039 ± 483; T2 = 543 ± 264* Total drain output in mL (right/left)[d] T1 = 335 ± 144 / 307 ± 158; T2 = 168 ± 94 / 134 ± 67*
MacGillivray et al. [51]	Prospective Randomized	T1 = 20 T2 = 20 C = 20	T1 = IV, 10 mg/kg before the 1st tourniquet inflation and the same dose 3 h later T2 = IV, 15 mg/kg before tourniquet inflation and the same dose 3 h later	Simultaneous	Total blood units transfused T1 = 8; T2 = 18; C = 19 Transfusion rate (%) T1 = 20 (4 patients); T2 = 45 (9 patients); C = 50 (10 patients) Blood loss in mL[a] T1 = 678 ± 331; T2 = 462 ± 209; C = 918 ± 549 (*C vs T2) Allogeneic blood transfused in mL[a] T1 = 140 ± 197; T2 = 315 ± 223; C = 332 ± 290 Autotransfused blood in mL[a] T1 = 245 ± 262; T2 = 86 ± 150; C = 596 ± 493*

Table 2 (continued)

Reference	Type of study	Protocol of TXA administration			Main results
		Study groups	Route and dosage	Procedure	
Zhaohui et al. [93]	Prospective Randomized	T = 43 C = 47	Soft tissue administration, 5 mL (25 mg/mL) before and 10 mL after prosthesis installation (before tourniquet deflation) + 20 mL INAI, after closure of articular cavity; drain clamped for 4 h	Sequential	Blood units transfused[a] T = 0.3 ± 0.7; C = 1.8 ± 1.4* Transfusion rate (%) T = 14% (6 patients); C = 70% (33 patients)* Calculated total blood loss in mL[a] T = 693.0 ± 120.3; C = 953.2 ± 164.0* (*Results are not attributable only to TXA, since other blood strategies differed between T and C groups*)
Sepah et al. [76]	Retrospective	T = 15 C = 14	IV, 1 g before inflation IV, 1 g after deflation	Simultaneous	Mean blood units transfused T = 0.9; C = 2.6* Mean postoperative drain output in mL T = 1288; C = 2695* Mean postoperative Hb drop in g/dL T = 1.94; C = 2.21*
Kakar et al. [37]	RCT	T = 13 C = 13	IV, 10 mg/kg before the 1st tourniquet inflation and then 1 mg/kg/h until skin closure	Sequential	Total blood loss[a] T = 286 ± 83; C = 620 ± 75*
Shinde et al. [77]	RCT	T = 14 C = 14	IV, 10 mg/kg just before the 1st tourniquet deflation IV, 10 mg/kg 4 h after the 1st dose IV, 10 mg/kg 12 h after the 1st dose	Sequential	Mean blood units transfused T = 0.23; C = 2.42* Transfusion rate (%) T = 14% (2 patients); C = 100% (14 patients)* Intraoperative blood loss in mL[a] T = 282 ± 64; C = 425 ± 108* Postoperative blood loss in mL[a] T = 596 ± 235; C = 1349 ± 41* Postoperative Hb drop in g/dL[a] T = 2 ± 0.16; C = 3.89 ± 0.09*

BTKA bilateral total knee arthroplasty, *TXA* tranexamic acid, *T* treatment group, *C* control group, *RCT* randomized controlled trial, *Hb* hemoglobin, *INAI* intraarticular injection, *INAW* intraarticular wash, *IV* intravenous, *POD* postoperative day

*$p < 0.05$ between T and C groups

[a] Mean ± SD

[b] Mean (interquartile range)

[c] Median (range)

[d] Mean ± 2 standard error of mean (95% confidence interval)

abandoned, as TXA is a potent and cost-effective solution that is related with less allergenic reactions [51, 61].

Conclusion

Among many intraoperative techniques that assist in optimization of blood management in BTKA only a few are sufficiently supported by solid scientific evidence in the medical literature. A common practice in many studies was the unilateral application of blood management techniques in patients undergoing BTKA, using the other knee as a control. Presumably, any favorable outcomes can be generalized to bilateral surgery, especially since blood loss during the second sequential procedure is anticipated to be higher [14, 75]. Further studies are needed to determine the role of each modality in order to enhance the perioperative safety of BTKA. Among all evaluated techniques, we strongly believe that regional anesthesia, tourniquet application and postclosure deflation, femoral canal plugging or femoral canal sparing surgical techniques, TXA use (topical or IV), and drain avoidance should be the current standard protocol for all patients undergoing BTKA. TXA use seems to be a cost-effective blood-conserving method. However, the ideal dosage and route of administration is yet to be defined.

Compliance with Ethical Standards

Conflict of Interest: Vasileios Soranoglou, MD, PHD; Lazaros A. Poultsides, MD, PHD; Georgios K. Triantafyllopoulos, MD; Ivan De Martino, MD; and Stavros G. Memtsoudis, MD, PHD, declare that they have no conflict of interest. Thomas P. Sculco, MD, receives royalties from Exactech and serves as a board member of the Knee Society and an editorial board member of the *American Journal of Orthopedics* and *HSS Journal*.

Human/Animal Rights: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2013.

Informed Consent: N/A

Required Author Forms Disclosure forms provided by the authors are available with the online version of this article.

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