ORIGINAL ARTICLE

Effectiveness of Combined Intravenous and Periarticular Tranexamic Acid Compared to Intravenous Tranexamic Acid Alone for Decreasing Blood Loss in Simultaneous Bilateral Total Knee Arthroplasty

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Background: There are advantages of simultaneous bilateral total knee arthroplasty (TKA), including reduced leg length discrepancy (LLD), better gait balance, and affordability. However, the main issue is excessive blood loss. Systemic effects are lessened by peri-articular injection of tranexamic acid (PA-TXA). Compared to the intravenous method (IV-TXA), it is claimed to produce better results.

Objective: To evaluate the efficacy of IV-TXA + PA-TXA compared to IV-TXA alone in reducing blood loss during simultaneous bilateral TKA.

Materials and Methods: Between December 2022 and April 2024, 60 simultaneous bilateral TKA procedures were enrolled at Charoenkrung Pracharak Hospital. The control group, which was IV alone, and the study groups, which was IV-TXA plus PA-TXA, were randomly assigned, and postoperative follow-up was conducted to monitor 24 hours blood draining and total blood loss at 72 hours, blood transfusion, and complications over a 3-month period.

Results: The mean age was 68.28±6.97 years, and 95.0% of the participants were female. A body mass index (BMI) of 26.09±4.70 was the average. The data were evaluated by blood transfusion, complications, total blood loss at 72 hours, and 24-hour blood draining, respectively. Although there was no significant difference between the control and study groups (p=0.227 and 0.773, respectively), there was a decrease in 24-hour blood draining and total blood loss after 72 hours. The operating time and postoperative transfusion did not differ significantly. Neither group experienced infection or deep vein thrombosis (DVT).

Conclusion: Although not statistically significant, the combination of IV-TXA and PA-TXA appears to have lower total blood loss in simultaneous TKA as compared to the IV-TXA route alone.

Keywords: Total knee replacement; Bilateral total knee replacement; Tranexamic acid; Peri-articular injection; Intravenous tranexamic acid

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The primary treatment for patients with advanced osteoarthritis (OA) in their knees is total knee arthroplasty (TKA). Every year, the number and frequency of total knee replacements (TKAs) rise. It has been projected that TKA will rise 143% in the U.S. between 2015 and 2050[1]. It is commonly carried out in two separate or concurrent surgical procedures for bilateral lesions. Overall, the advantages of simultaneous bilateral TKA include lower costs, better gait balance, and higher patient satisfaction as a result of a reduced leg length discrepancy (LLD) issue following unilateral TKA[2]. Compared to unilateral TKA, simultaneous bilateral TKA does not result in an increase in postoperative problems. However, blood loss does increase in the absence of clinical symptoms[3]. Tourniquets, autologous blood transfusion, drain clamping[4], computer-assisted surgery, hypotensive anesthesia, intramedullary plugs, patient-specific instruments[5], and different medications[6] are strategies that have been developed to reduce blood loss during and after TKA.

The synthetic analogue of the amino acid lysine is called tranexamic acid (TXA). Through the reversible binding of four to five lysine receptor binding sites on plasminogen, TXA advertises itself as an antifibrinolytic drug. Thus, it inhibits the conversion of plasminogen to plasmin, stops the breakdown of

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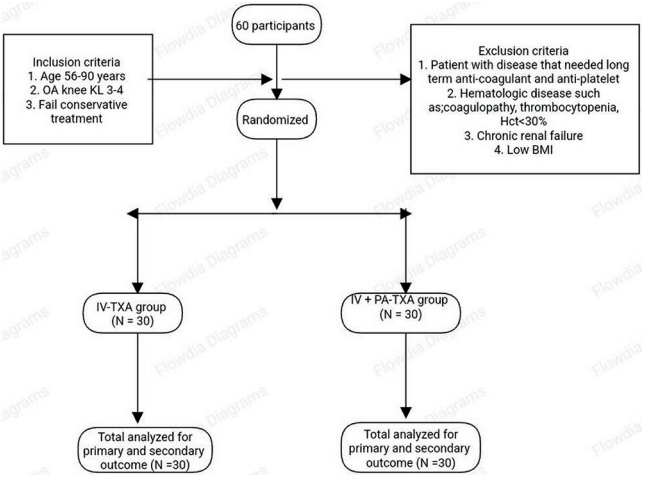

Figure 1. Flow diagram.

fibrin, and maintains the matrix structure of fibrin[7]. In surgical procedures, it is used to cure or prevent excessive blood loss. TXA rarely causes side effects. Seizures, color vision abnormalities, blood clots, and allergic reactions like anaphylaxis are examples of adverse effects. In recent years, TXA has become a well-established procedure for complete knee and hip replacements. It has been demonstrated that TXA administered intravenous (IV), intra-articular (IA), and peri-articular (PA) efficiently reduce postoperative blood loss in TKA[8,9].

TXA can be administered by a variety of methods, all of which have demonstrated promising outcomes. There is ongoing controversy over reports of merged routes of administration. For simultaneous bilateral TKA, combined IA plus IV routes of TXA produce better results than IV treatment alone[10]. According to research, there is no difference in the combined administered routes[11].

Due to the contentious outcomes of combined TXA routes, PA-TXA and IA-TXA have comparable effects in reducing blood loss, preventing systemic absorption, and mitigating the effects of TXA. In integrated routes, PA-TXA has been planned to replace IA-TXA. The purpose of the present study was to ascertain if the combined PA-TXA route with IV-TXA, as opposed to IV-TXA alone, significantly reduced blood loss in simultaneous TKA.

Materials and Methods

The Bangkok Metropolitan Administration Human Research Ethics Committees (BMAHREC) reviewed and authorized the present prospective randomized control trial (RCT) study (No. 116, TCTR Approval Number S019h/65). Between December 2022 and April 2024, 60 patients with severe OA based on Kellgren-Lawrence classification grading range III or IV with allowance for simultaneous bilateral TKA were informed and signed consent forms at Charoenkrung Pracharak Hospital. Computer-generated blocks of four randomizations were used to divide all subjects into two groups, study and control. The control group received a 40 mL PA injection of normal saline (IV-TXA + PA-NSS) along with a mean IV administration of 1 g TXA. Additionally, the study group was characterized as combined 1 g IV and 1 g PA TXA injections (IV-TXA + PA-TXA), which involved diluting 20 mL of TXA with NSS 20 mL to a concentration of 25 mg/mL[12] of TXA. The 56 to 90-year-old participants were assigned based on the inclusion criteria. The exclusion criteria were pulmonary embolism (PE), cerebrovascular disease such as stroke, seizure, and transient ischemic attack (TIA), abnormal coagulation, thrombocytopenia, tranexamic allergic drugs, anemia, high serum creatinine of more than 1.35 g/dL, low body mass index (BMI) of less than 18.5 kg/m², anticoagulant medication therapy, hormonal treatment, contraceptive drugs, and anemia. Severe difficult medical problems, intraoperative popliteal damage, and extended operating time of more than three hours were considered withdrawal issues (Figure 1).

Operative described details

All of the operations were done by a single surgeon who had completed over 100 TKA surgeries annually. In each instance, the anesthetic team used

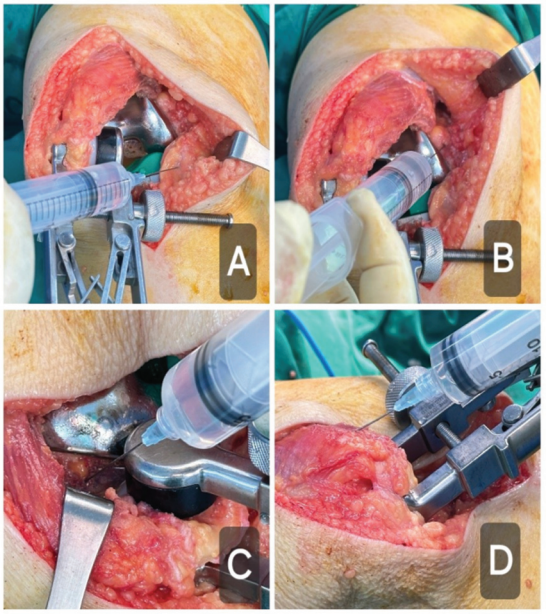

Figure 2. Injection at anterior capsule (A), medial gutter (B), lateral gutter (C), and Quidricep muscle (D).

spinal morphine anesthesia in conjunction with an adductor canal block for anesthesia. Two grams of fosfomicin were administered as a preventative antibiotic. No deep vein thrombosis (DVT) prevention medication was recommended. The first tourniquet was inflated to begin the operation, and the opposite tourniquet was deflated to conclude the operative time. The knees were simultaneously cleaned and prepared. During the procedure, a 400-mmHg tourniquet was applied, and it was deflated once the wound was closed. Following spinal block, a contained randomized allocated treatment was used to open the sealed packets. The procedure was conducted using the same surgical method. After the tourniquet was inflated, a midline incision approximately 12 cm in length was made, beginning 2 cm proximal to the superior pole of the patella and passing the midline of the patella, and finishing at the tubercle. The posterior cruciate ligament (PCL) was resected using the subvastus technique. Standard preparations were performed for the tibia as extramedullary guide and the femur as intramedullary guide. The conventional measured-resection technique was used to execute the TKAs. Flexion and extension gap balancing was done. Measurements were made of mechanical alignment. They employed primary cemented TKA (PCL sacrificed knee, Corentec, Lospa knee system). This procedure did not involve any revisions or additions to primary TKA. Electrocautery was used to denervate the patella, which then resurfaced in each knee. During the cement setting period, PA material, which was NSS for control, and TXA for study, was injected into the quadriceps muscle, medial and lateral gutters, and the capsule, but not in the posterior capsule, as depicted in Figure 2[9]. There was no injection of PA cocktail for postoperative pain control. Additionally, a drain was positioned prior to the skin and capsule being closed. For the first knee, an elastic bandage and Webril were used. An Esmarch bandage was used to pressure the opposing knee after the first knee's tourniquet had deflated. The second knee was put under the tourniquet. The second knee was the site of the identically performed surgery. Following surgery, both knees were placed in an elastic compression bandage. Both knees' Redivac drains were clamped for five hours after surgery. The Redivac drain would continue clamping for an additional three hours if more than 100 mL of blood per hour were drawn from it. Pain management and standard postoperative care were used. For an entire day, prophylactic IV fosfomycin was given.

Allogenic blood replacement would be administered if the serial hematocrit (Hct) was less than 30%, as transfusion trigger, or if there were clinical signs of hemodynamic instability such as unexplained tachycardia, hypotension, or oliguria that was not responsive to fluid replacement during the first 24 hours following the procedure[13]. To maintain normal urine production, of at least 0.5 to 1.5 cc/kg/hour, urine output was monitored every four hours. Clinical indicators of venous thromboembolism, including skin color changes, tightness in the calves, and swelling in the legs, were closely observed. On the first day, 80 mg of Acupan (Nefopam) and 50 mg of tramadol every six hours were administered IV to treat postoperative pain. On request, IV morphine and oral acetaminophen were administered. In the initial days following surgery, no NSAID was prescribed. On the participants' desire, IV morphine would be prescribed following the first operating day. The drain and Foley's catheter were taken out on the first postoperative day. Active range-of-motion exercises and walking with a walker were part of the postoperative rehabilitation program. The range of motion on the continuous passive motion machine and early ambulation had been initiated.

To determine total blood volume loss and screen for DVT, hemoglobin levels and plasma D-dimer were measured on the day of admission and the third postoperative day[14]. Allogenic blood replacement would be administered on the third postoperative day

if the hemoglobin level was below 6 g/dL. During the stay in the inpatient unit, there was close monitoring for DVT such as leg pain, warmth, swelling, cramping, and changing skin color, and wound infection looking at the skin surrounding the wound for redness, sore, warmth, swelling, and fluid leakage from the wound. This monitoring continued in the outpatient department at 2 weeks, 6 weeks, and 3 months after surgery. If the patient exhibited clinical symptoms of DVT, computed tomography angiography and Doppler ultrasonography would be used.

Hemoglobin concentration, the amount of postoperative 24 hours blood draining, and the need for a blood transfusion were the primary outcome measures. The author measured clinically diagnosed DVT, knee flexion after discharge, pain using a visual analogue scale (VAS) with 0 for no pain and 10 for the worst awful pain, local soft tissue consequences for skin infection and necrosis, and length of hospital stay as secondary outcomes. Two nurses recorded the VAS. Two experienced interns recorded knee flexion on the day of discharge.

Following the removal of the Redivac drain the amount of blood that drained from the draining bottle during the first 24 hours following surgery was measured.

The approach of Nadler et al. and Wu et al.[15,16] were used to calculate the total blood volume loss 72 hours following surgery.

$$\text{Blood volume (L)} = K_1 + (HT \times K_2) + (Wt \times K_3)$$

$$Hgb_{loss} = \text{blood volume} \times (Hgb_{adm} - Hgb_{fin}) + Hgb_{trans}$$

$$\text{Blood loss (mL)} = 1{,}000 \times (Hgb_{loss} / Hgb_{adm})$$

HT=height $(m)^3$, Wt=weight (kg), K_1=0.604 in male, 0.183 in female, K_2=0.367 in male, 0.356 in female, K_3=0.032 in male, 0.033 in female, Hgb_{loss}=hemoglobin loss (g/L), Hgb_{adm}=hemoglobin on admission (g/L), Hgb_{fin}=hemoglobin at 72 hours (g/L), Hgb_{trans}=transfusion hemoglobin (g/L), pack red cell (PRC) one unit contains hemoglobin 1 g/dL (according to Thai Red Cross Society).

The average score between two nurse records was calculated using the VAS. Using a goniometer, the knee flexion on the day of discharge was calculated as the average of two trained intern records. All participants were required to flex both knees at least 90 degrees on the day of discharge. The pain score on the VAS was below 5. There were no infections or other issues discovered.

Statistical analysis

IBM SPSS Statistics, version 26.0 (IBM Corp., Armonk, NY, USA) was used to express the data. The demographic information was shown as mean±standard deviation (SD), median, percent, and number. Prior to use parametric statistics, continuous data were assessed for normal distribution using the Kolmogorov-Smirnov test. An unpaired t-test for normally distributed data or Mann-Whitney U test for non-normally distributed data were used to assess the differences in continuous data between the two clusters. The categorical variables of both groups were compared using either Fisher's exact or Pearson's chi-square test. The p-values below 0.05 were regarded as significant.

The sample size (n) for each group was determined using the two independent population means, as stated in Tsukada & Wakui[11] and Rosner[17] article. The present study focus was on α=0.05 and β=0.20 (test power=80). The Tsukada & Wakui study[11] defined u1 and u2 as respectively the combined mean and standard deviation of operative blood loss under bilateral TKA performed concurrently with only IV-TXA and operative blood loss under IA injection and IV-TXA (1,638±400 versus 1,201±374 mL). Patients who received simultaneous bilateral TKA were randomly assigned in a 1:1 ratio to either the study or control group in our single-center, double-blind, clinical RCT. The authors calculated that each group would have a total of 14. To guarantee there was enough data, the author did, however, provide an average of 100% of the samples. As a result, each group had thirty participants.

Results

Demographic information such as age, gender, BMI, underlying disease, pre-operative hemoglobin, pre-surgical D-dimer, operating time, and hospital stay did not substantially differ between the two groups of 60 patients, which included 57 females and three males, who had simultaneous bilateral TKA in the present study (p>0.05), as displayed in Table 1.

As shown in Table 2 and Figure 3-5, there were no statistically significant differences between the two groups' postoperative 24 hours blood draining and total blood loss at 72 hours (p=0.227 and 0.773, respectively). This was also true for the PRC transfusion and hemoglobin change at day 3 (p=0.140 and 0.943, respectively). Both groups showed no signs of postoperative infection or DVT.

There were no statistically significant differences in the flexion mobility of the right and left knees on the day of discharge or the VAS score on the first and third postoperative days, respectively,

Table 1. The demographic data of the control and study groups

Variable	Total sample	IV + PA-TXA group	IV-TXA group	p-value	Effect size d
Age (year); mean±SD	68.28±6.97	67.80±6.82	68.77±7.20	0.595[a]	0.14
Female; n (%)	57 (95.0)	27 (90.0)	30 (100.0)	0.237[b]	
BMI; mean±SD	26.09±4.70	26.10±4.13	26.07±5.28	0.983[a]	0.01
Normal (<23 kg/m^2); n (%)	17 (28.3)	8 (26.7)	9 (30.0)	0.774[c]	
Over (≥23 kg/m^2); n (%)	43 (71.7)	22 (73.3)	21 (70.0)		
Underlying; n (%)					
Hypertension	51 (85.0)	27 (90.0)	24 (80.0)	0.472[b]	
Diabetes	17 (28.3)	9 (30.0)	8 (26.7)	0.774[c]	
Dyslipidemia	43 (71.7)	24 (80.0)	19 (63.3)	0.152[c]	
Other	11 (18.3)	7 (23.3)	4 (13.3)	0.317[c]	
Pre-operative Hb (g/dL); mean±SD	12.50±1.15	12.50±1.10	12.50±1.21	>0.999[a]	0.00
Pre-operative D-dimer (µg/dL); median (Q1, Q3)	0 (0, 0.66)	0 (0, 0.73)	0 (0, 0.62)	0.320[d]	0.32
Operative time (minute); mean±SD	96.40±11.62	95.17±10.51	97.63±12.69	0.415[a]	0.21
Hospital stay (day); median (Q1, Q3)	7 (7, 9)	7.50 (7, 9)	7 (6.75, 9.75)	0.784[d]	0.21

IV=intravenous; PA=peri-articular; TXA=tranexamic acid; BMI=body mass index; Hb=hemoglobin; SD=standard deviation
a: Student t-test, b: Fisher' exact test, c: Chi-square test, d: Mann-Whitney U test, * Statistically significant

Table 2. Compare to the combination IV and PA-TXA acid and IV TXA acid alone in simultaneous bilateral TKA with regard to 24 hours of blood draining, total blood loss at 72 hours, Hb at 3rd day, blood transfusion, D-dimer at day 3, pain score at 1 and 3, and knee motion at discharge day

Variable	IV + PA-TXA group (n=30)	IV-TXA group (n=30)	p-value	Effect size d
Redivac 24 hours; mean±SD	377.17±187.07	436.83±191.20	0.227[a]	0.32
Total blood loss 72 hours (mL); mean±SD	679.84±420.71	649.66±386.44	0.773[a]	0.07
Hb (g/dL) at day 3; mean±SD	10.27±0.89	10.25±0.91	0.943[a]	0.02
PRC (mL); median (Q1, Q3)	95.50 (0, 308.75)	235.5 (0, 426.50)	0.140[d]	0.38
D-dimer (µg/dL) at day 3; median (Q1, Q3)	2.95 (1.95, 4.86)	2.63 (1.83, 3.49)	0.098[d]	0.50
Pain score at day 1; mean±SD	3.27±0.64	3.47±0.78	0.281[a]	0.28
Pain score at day 3; median (Q1, Q3)	2 (2, 3)	2 (2, 3)	0.830[d]	0.25
Knee motion RT; median (Q1, Q3)	110 (100, 110)	100 (98.75, 110)	0.207[d]	0.33
Knee motion LT; median (Q1, Q3)	107.5 (100, 110)	100 (100, 110)	0.133[d]	0.39

IV=intravenous; PA=peri-articular; TXA=tranexamic acid; Hb=hemoglobin; PRC=pack red cell; RT=right; LT=left; SD=standard deviation
a: Student t-test, d: Mann-Whitney U test, * Statistically significant

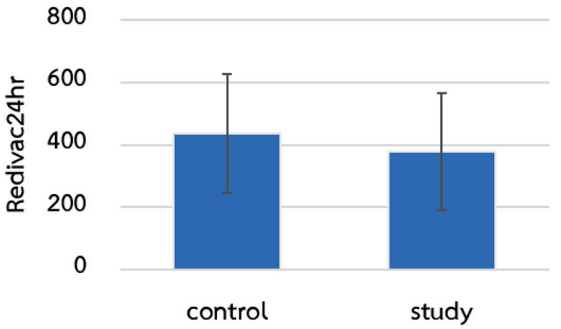

Figure 3. Postoperative 24 hours blood draining of control vs. study groups.

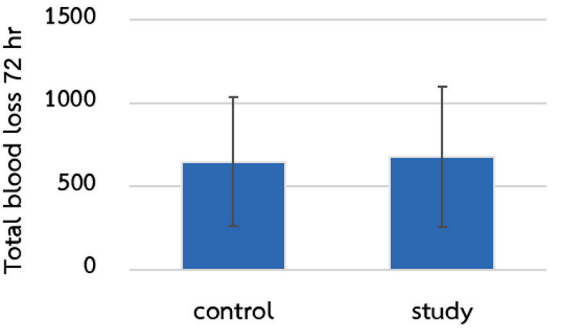

Figure 4. Postoperative blood loss at 72 hours of control vs. study groups.

with respect to the aggressive management of pain in the first few postoperative periods of both groups and secondary outcome results (p=0.207, 0.133, 0.281, and 0.830, respectively). There was no statistically

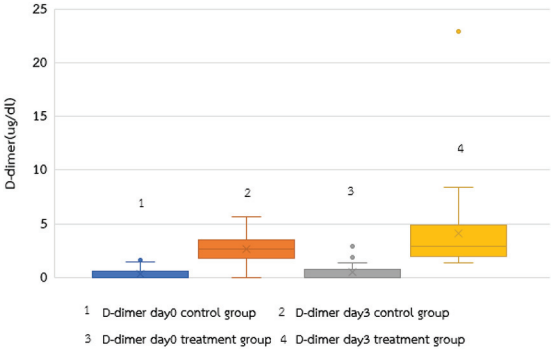

Figure 5. Plasma D-dimer at 24 and 72 hours of control vs. study groups.

significant difference in the operative time results between the two groups using the identical operative maneuver (p=0.415).

Discussion

IV-TXA is currently commonly used to reduce bleeding during a variety of surgical procedures, including TKA. Surgeons have expressed concern about the possibility of venous thromboembolic events. It has been demonstrated that topical TXA applications, such as IA and PA routes, are beneficial without causing negative side effects[9,10]. Because the PA-TXA route exhibits a lower plasma TXA level than IA-TXA of 1.8 times at two hours after administration, with the same results and a lessened systemic effect[18], it has become more widely used. In studies, combined IV and IA-TXA had superior effects than IV-TXA alone[10,11]. The combined route of IV and IA-TXA, compared with only IA or IV-TXA alone, offered lower total blood loss (p<0.001), lower postoperative blood draining (p=0.009), and lower hemoglobin drop (p<0.001) than IV alone, according to the updated meta-analysis by Ling et al., which examined the safety and efficacy of combined IV and IA-TXA in TKA in 2022 with 1,306 patients in ten RCTs. However, no significant results were found regarding the rate of transfusion (p=0.137) and DVT[19] (p=0.293). Furthermore, only one person in the IV-TXA group had PE[19].

However, Meshram et al. had mixed results that were split into four groups, simultaneous bilateral TKA with IA-TXA only, simultaneous bilateral TKA with combined IV-TXA and IA-TXA), staged TKA with IA-TXA alone, and staged TKA with combined IV-TXA and IA-TXA[20]. It showed no benefit for combined routes. Lastly, they recommended that the IA-TXA method be used alone for routine TKA to prevent systemic impact issues.

In line with PA-TXA, which recently asserted a different administrative route. The combined group of PA-TXA + IV-TXA or IA-TXA, had a higher rank than the IV-TXA or IA-TXA group in terms of hemoglobin change (p<0.0001), according to Fan et al.'s systematic review and meta-analysis of ten research pertaining to PA-TXA routes[21].

Therefore, at various doses, the author's goal in the present study was to compare the safety and effectiveness of combined IV-TXA and PA-TXA to IV-TXA alone. Topical TXA and combination routes should have a ceiling effect of no more than 2 g[8].

There is no discernible difference (p>0.05) between these two groups' demographic distributions in age, gender, BMI, underlying disease, hemoglobin at day 0, D-dimer at day 0, and operative time. Ninety-five percent of participants were female. The primary underlying conditions were hypertension, dyslipidemia, and diabetes mellitus, respectively. The total blood loss in the IV-TXA and combination groups of IV-TXA + PA-TXA, was 649.66±386.44 mL and 679.84±420.71 mL, respectively, according to the author's simultaneous bilateral TKA in the present study. According to the literature review, the average calculated blood loss during unilateral TKA without the use of TXA was 1,346±671 mL[22,23]. The calculated blood loss in each group was smaller than the average calculated blood loss.

Studies showed that topical TXA with drainage clamping might lessen blood loss in the 24 hours of drainage[24-26] when more than one route application is used. The present study found that the combination route PA-TXA + IV-TXA and IV-TXA resulted in less blood loss, although there was no significant difference at 377.17±187.07 versus 436.83±191.20 (p=0.227). The median volume of transfused PRC was only 95.5 mL in the PA-TXA + IV-TXA group, compared to 235.5 mL in the IV-TXA group. This was in addition to lowering the blood transfusion, although there was no discernible difference (p=0.140).

Regarding a D-dimer blood test, which quantifies a chemical released in the blood as a clot disintegrates. Normally, D-dimer is either undetectable or just very weakly detectable unless our body is producing and dissolving large blood clots. DVT, PE, disseminated intravascular coagulation (DIC), and stroke are among the blood clotting disorders that can be identified by the D-dimer test. The D-dimer test is extremely sensitive at more than 95% in acute DVT or PE, according to prior studies. It typically has

Table 3. Features and complications in RCTs comparing the IV-TXA route alone with the combination TXA routes

Study	Group	Unilateral/ bilateral	Total dose	Age (year)	Sex (M/F)	DVT (N)	Pulmonary embolism (N)	Wound infection (N)
Huang et al.[31], 2014, China, N (92:92)	G1: IV 1.5 g + IA 1.5 g G2: IV 3 g	Unilateral	3 g 3 g	65.4±8.7 64.7±9.5	37/55 30/62	G1=0 G2=1	G1=0 G2=0	G1=6 G2=8
Jain et al.[32], 2015, India, N (59:60)	G1: IV 15 mg/kg once + 10 mg/kg twice + IA 2 g G2: IV 15 mg/kg once + 10 mg/kg twice	Unilateral	>4 g <3.5 g	68.3±8.6 70±6.5	20/39 24/36	G1=0 G2=1	G1=0 G2=0	NA NA
Nielsen et al.[10], 2016, Denmark, N (30:30)	G1: IV1.5 g + IA 3 g G2: IV 1 g	Unilateral	4 g 1 g	65.5±7.8 63.2±8.6	13/17 15/15	G1=0 G2=0	G1=0 G2=0	NA NA
Iseki et al.[33], 2018, Japan, N (75:70)	G1: IV 1 g + IA 1 g + IV 1 g G2: IV 1 g twice	Unilateral	3 g 2 g	77±7 75±8	18/57 17/60	G1=0 G2=0	G1=0 G2=0	NA NA
Adravanti et al.[34], 2018, Italy, N (50:50)	G1: IV 1 g three times + IA 3 g G2: IV 1 g three times	Unilateral	6 g 3 g	69.5±8.3 70.9±9.6	25/75	G1=0 G2=0	G1=0 G2=0	G1=0 G2=0
Tsukada et al.[11], 2019, Japan, N (43:34)	G1: IV 1 g twice + IA 1 g/knee G2: IV 1 g twice	Bilateral	4 g 2 g	75±6 77±6	10/33 6/28	G1=0 G2=0	G1=0 G2=0	G1=1 G2=0
The present study, 2024, Thailand, N (30:30)	G1: IV 1 g + PA 1 g G2: IV 1 g	Bilateral	2 g 1 g	67.8±6.8 68.77±7.2	3/27 0/30	G1=0 G2=0	G1=0 G2=0	G1=0 G2=0

M=male; F=female; DVT=deep vein thrombosis; IV=intravenous; IA=intra-articular; PA=peri-articular; NA=not available

a cut-off value of 50 µg/dL, which is reasonable for ruling out acute venous thromboembolism, especially in individuals with low or moderate clinical probability[15]. The majority of research revealed no rise in DVT incidence along any path[27,28].

No participant in the author's study had clinical PE or DVT. On postoperative day three, D-dimer was slightly higher than on day zero at 2.95 versus 2.63 µg/dL. D-dimer levels, however, fell short of the threshold. On day three, there was no discernible difference in D-dimer between the combined group and the IV-TXA route alone at 2.95 versus 2.63 µg/dL (p=0.098). Increased periprosthetic joint infection (PJI) is linked to blood transfusions during TKA. Administering TXA lowers the incidence of PJI and the blood transfusion rate by about 50%[29]. Studies showed that TXA had no benefit over PJI[30] and blood transfusion. The present study also showed no infection incidence. In contrast to the IV-TXA group alone, the author examined the literature on combined IV-TXA and IA-TXA, including the current investigation, as indicated in Table 3.

In contrast to the IV-TXA group alone, this is the first time the author had used the PA-TXA administration method in conjunction with IV-TXA for simultaneous bilateral TKA. A literature review indicated that the combined sorts PA-TXA + IV-TXA or IA-TXA were superior to the IV-TXA or IA-TXA group in terms of hemoglobin change[20], which was likely that the present study employed the combined PA-TXA route instead of the IV-TXA route. According to the data, 95% of the patients were female, and their average age was 68.28±6.97 years. There was no statistically significant difference (p=0.773, 0.14, and 0.415) between the combined IV-TXA and PA-TXA groups and the IV-TXA alone groups in terms of blood volume loss at 72 hours, PRC supplement, and operating time. No DVT or PE was presented.

The author's study, which revealed that combined IV-TXA and PA-TXA routes were more successful than IV-TXA alone in simultaneous bilateral TKA, has the strength that, after evaluating the literature, no comparable publications were found in Thailand. However, the small number of participants constituted the study's weakness. In simultaneous bilateral TKA with a large population, more prospective RCT involving PA-TXA pathways have to be encouraged.

Conclusion

In summary, the difference between IV+PA-TXA and IV-TXA alone was not statistically significant in terms of total blood loss or blood transfusion. More extensive and well-designed research is required.

What is already known on this topic?

Any method of applying TXA could lessen the overall amount of blood lost during TKA. In research, dual routes of TXA treatment showed greater benefits for lowering total blood loss; however, articles have reported conflicting results.

What does this study add?

In comparison to IV-TXA alone in simultaneous bilateral TKA, this study is the first to be published in Thailand on the combined TXA routes, which are PA-TXA plus IV-TXA. Because of the advantages of lower costs and less LLD following unilateral TKA, the author chose the simultaneous bilateral TKA procedure. The decreased systemic effects of

the PA injection method also led to its adoption. Lastly, the author discovered that, although there was no discernible difference, the combination TXA, which is PA-TXA plus IV-TXA, could lower overall blood loss when compared to the IV route alone. The utilization of combined PA-TXA with alternative administration routes in simultaneous bilateral TKA involving bigger populations should be examined in future prospective RCTs.

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Conflicts of interest

No conflicts of interest are disclosed by the author.

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