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Benefits of Limited Use of a Tourniquet Combined With Intravenous Tranexamic Acid During Total Knee Arthroplasty

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Background: Blood loss during total knee arthroplasty (TKA) may require blood transfusions that are associated with increased risk, morbidity, and cost. Multiple techniques exist to reduce blood loss in TKA, including the use of a tourniquet and tranexamic acid (TXA). While multiple studies suggest that TXA is effective in reducing blood loss, the use of a tourniquet is more controversial. We studied the combined effect of TXA with a limited-use tourniquet on blood loss and complications in the setting of primary TKA.

Methods: A retrospective review of a prospectively gathered arthroplasty database from a single institution was performed. We compared our limited-use cohort data with the published results of randomized controlled trials evaluating the effectiveness of tourniquets used during the entire TKA procedure.

Results: Fifty-one procedures from our institution's database met the inclusion criteria. TXA (administered in a single 15-mg/kg dose) with limited tourniquet use (a mean duration of 26.3 minutes) resulted in an average intraoperative estimated blood loss of 94.7 mL. The mean decrease in hemoglobin from the preprocedure baseline to postoperative day 1 was 2.6 $\pm$ 0.9 g/dL ($P<0.001$), and only 2 of the 51 procedures required a blood transfusion. When compared to recent randomized controlled trials, the 51 procedures demonstrated lower levels of blood loss, similar operative time, and no increase in morbidity or mortality.

Conclusion: Our study results suggest that using TXA in combination with a tourniquet during the cementation portion only of a TKA provides a reasonable operative time and low intraoperative blood loss without increasing perioperative morbidity or complications.

Keywords: *Arthroplasty–replacement–knee, blood transfusion, tourniquets, tranexamic acid*

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INTRODUCTION

Total knee arthroplasty (TKA) is among the most commonly performed elective procedures in the United States.[1] Its prevalence has increased dramatically during the past several decades because of increases in obesity, the size of the aging population, and utilization.[1] The desire to stay active among members of the modern population may be responsible for the rise in per capita utilization. TKA may be associated with significant blood loss for which blood transfusion might be necessary.[2] Transfusion rates as high as 60% have been reported.[1] Allogeneic blood transfusion, despite current testing parameters, carries significant potential risks[1,3,4] and costs.[1,5] Risks include mismatch attributable to clerical error, infection, and immunologic reactions caused by the transfusion or contaminants.[1,3,4] Costs associated with TKA-related intraoperative blood loss and allogeneic transfusions include the costs of the blood units, of longer hospital stays, and of readmissions for transfusion-related complications.[1,5]

A pneumatic tourniquet is commonly used during TKA to reduce intraoperative blood loss and to improve visualization.[1,2,6-8] The pneumatic tourniquet has also been shown to reduce operative time and to improve cement interdigitation.[2,6-8] A 2009 survey of the members of the American Association of Hip and Knee Surgeons reported that 95% used a tourniquet during TKA.[9] However, the clinical role of the tourniquet in TKA remains controversial[2,8,10,11] because of the potential deleterious effects of prolonged pneumatic tourniquet use[2,8,11-19] that can be devastating.[1,2,8,11,12,17-32] Intraoperatively, the use of a tourniquet during trial reduction and patellofemoral tracking has been associated with an increased risk of lateral release, secondary to a tethered quadriceps mechanism.[2,13-15] Postoperatively, limb pain,[2] swelling,[12] stiffness,[8,19] delay of muscle-power recovery,[12] subcutaneous limb fat necrosis,[2,16] and wound hematoma leading to persistent wound drainage and subsequent increased infection risk[2,31] have all been reported. Less common complications associated with prolonged pneumatic tourniquet use during TKA include nerve palsy mediated or modulated by compression neuropraxia,[8,11,20,21,32,33] compartment syndrome,[12,33] rhabdomyolysis,[2,8,24] renal failure,[8,24] direct vascular injury,[11,22,26-28] deep vein thrombosis (DVT),[2,8,11,25,27,30] pulmonary embolism (PE),[1,8,11,23,25,29] acute pulmonary edema, and cardiac arrest immediately following tourniquet release.[8,17-19] Last, prolonged tourniquet use during TKA may interfere with postoperative functional recovery and affect overall patient knee range of motion and clinical success.[8,11,17-19]

While some studies have shown that a tourniquet is effective in reducing intraoperative blood loss,[30,34,35] others have failed to demonstrate this benefit.[10,36,37]

Tranexamic acid (TXA), a synthetic lysine analogue and competitive inhibitor of plasminogen at its lysine-binding site for fibrin,[38,39] has been used successfully in numerous nonorthopedic surgical procedures to decrease blood loss.[40-48] In the United States, initial interest in the use of TXA in the field of joint arthroplasty focused on primary and revision total hip arthroplasty[46,47,49-51] because of the high potential for blood loss during these procedures. After demonstrating a significant decrease in blood loss and need for blood transfusion[46,47,51] with primary and revision total hip arthroplasty procedures, TXA became commonly used in TKA.[52,53]

The literature is largely unclear regarding best-practice use of the pneumonic tourniquet and TXA.[9,34-37,46-48,51-58] Consequently, the goal of this investigation was to determine whether the limited use of a pneumatic tourniquet in conjunction with the use of TXA would alter operative time, intraoperative blood loss, transfusion rate, and complication rates when compared with the use of a pneumatic tourniquet throughout the procedure.

METHODS

Patients

After Institutional Review Board approval was obtained, a search of the prospectively gathered arthroplasty database was conducted at the participating institution. All adult patients who underwent routine primary unilateral TKA (current procedural terminology [CPT] code 27447) by the senior author (A.D.R.) between April 30, 2013, and December 8, 2014, for osteoarthritis (OA) or rheumatoid arthritis (RA) were identified for inclusion in this retrospective cohort study. Patients who had undergone revision TKA, distal third femoral replacement TKA, or same-setting bilateral TKA; patients requiring computer assist or other electronic devices; and patients who had undergone previous intraarticular or periarticular open reduction and internal fixation were not included. Our search revealed a total of 70 patients.

Patients having preoperative gross deformities, severe contractures, or constrained TKA—a total of 21 patients—were excluded. A total of 51 knees, 29 right and 22 left, in 49 patients met the inclusion criteria. Two patients received bilateral knee arthroplasty in separate procedures.

All patients had their TKA performed by the senior author (A.D.R.) under general anesthesia and received a single dose of TXA, 15 mg/kg intravenously. All of the procedures were done through a midline skin incision and medial parapatellar arthrotomy. Tourniquet use was limited to the period of cementation. In all patients, the tourniquet was inflated after the extremity was exsanguinated, just prior to cementation, and deflated when the bone cement had cured. Intraoperative blood loss was estimated by addition of the volume of blood noted on the sponges to the volume collected in the suction canisters and subtraction of the amount of irrigation fluid used. Suction drains, cell savers, and autologous blood were not used. To further characterize postprocedural blood loss, hemoglobin levels were measured preprocedure and on postoperative day (POD) 1.

Data Collection

We individually reviewed patient medical records and operative reports. Data collected for the study included the anesthesia technique, TXA dose and route of administration, tourniquet inflation duration and pressure, operative time (from incision to completion of wound closure), intraoperative blood loss, hemoglobin levels (preoperatively and on POD 1), length of stay, and number of units of packed red blood cells transfused. All complications were noted, including surgical-site infections, delayed wound healing, readmission within 30 days for surgical complications, DVT, and PE. Patients were screened for DVT and PE only if clinically indicated.

Historical Control Selection

Electronic databases (PubMed, MEDLINE, and Embase) were searched by 2 independent researchers (Y.A.M. and A.D.R.) to identify studies published from January 2009 to June 2015. The keywords used in the search were total knee arthroplasty or total knee replacement and blood loss, tourniquet, and randomized controlled trial (RCT). Reference lists of the relevant papers were thoroughly searched for any further relevant studies. Only studies including a minimum of 25 patients in each arm were included. Eight RCTs that included the use of a tourniquet met the inclusion criteria and were included in the analysis from which root studies were reviewed and raw data were extracted.

Statistical Analysis

The statistical program SPSS v.19 (IBM) was used to analyze the data. Basic descriptive statistics are reported as means $\pm$ SD in addition to the median, minimal, and maximal values for continuous variables, and proportions and frequencies are reported for categorical variables. Paired *t* tests were used to examine changes in hemoglobin levels at POD 1 compared to preprocedure hemoglobin level. A P value <0.05 was used to determine statistical significance.

RESULTS

Patient demographics and comorbidities are described in Table 1. The average age of the patients at time of surgery

Table 1. Patient Demographics and Comorbidities

Demographic Variable	Mean	SD	Median	Min	Max
Age, years	65	9	63	50	83
BMI, kg/m^2	35	6	35	21	47
American Society of Anesthesiologists physical status classification	3	not determined	3	2	4
Length of stay, days	2	not determined	2	2	4
Comorbidity	**n**	**%**			
Obese (BMI >30 kg/m^2)	40	81.6			
Coronary artery disease	15	30.6			
Cerebral vascular accident/Temporary ischemic attack	2	4.1			
Diabetes mellitus, type 2	15	30.6			
Osteoarthritis	50	98.0			
Rheumatoid arthritis	1	2.0			
Peripheral artery disease/Peripheral vascular disease	1	2.0			

BMI, body mass index; Max, maximum; Min, minimum.

was 65 ± 9 years (range, 50-83 years). A total of 51 procedures/knees in 49 patients (20 males and 29 females) were included in the investigation. The majority of procedures (50 of 51) were for the treatment of OA, with 1 procedure related to RA. We examined the demographics of our patient cohort in relation to published comparison studies that included patients for whom the tourniquet was inflated throughout the procedure, from incision to wound closure (Table 2).[18,33,37,58-62] The patient characteristics in the published studies were comparable to the patient characteristics in our cohort.

Data on the mean duration of procedure and tourniquet inflation time for our study cohort are presented in Table 3. Our operative variables and results were also comparable to published controls (Tables 4 and 5). Our mean duration of procedure was 116 minutes, which is within the range reported in the historical comparison studies (70.0-120.8 minutes). Our mean intraoperative estimated blood loss, a less precise measure, was 94.7 mL ± 48.5 mL, and this value is lower than the blood loss reported in all of the published RCTs used for comparison, except for the study published by Tai et al[62] who reported a mean intraoperative blood loss of 25.6 ± 30.9 mL (Table 5).

In our cohort, the mean decrease in hemoglobin from the preprocedure baseline to POD 1 was 2.8 g/dL ± 0.9 g/dL with hemoglobin levels at POD 1 (11.5 g/dL ± 1.4 g/dL) significantly decreased in comparison to baseline values (14.1 g/dL ± 1.2 g/dL, $P<0.001$) (Figure). Hemoglobin values on discharge were not significantly different than those measured on POD 1. The mean hemoglobin drop in the published comparison studies ranged from 1.9-3.4 mg/dL. This change is similar to the mean hemoglobin drop of 2.8 mg/dL noted in our study on POD 1; however, the timing of these published levels varied in some instances beyond POD 1.

Of our 51 procedures, only 2 (3.9%) required blood transfusions during the perioperative period, with each patient receiving 2 units each. No surgical-site infections were reported in our patient cohort. One patient developed a PE after surgery. No patients required readmission for

Table 2. Demographics of Patients Receiving Limited Tourniquet Use Plus Tranexamic Acid During Total Knee Arthroplasty in Relation to Historical Comparison Studies

Study	Number of Patients/Knees	Female/Male Ratio	Mean Age, Years	Mean BMI, kg/m^2	Mean ASA
Current study	49 (51 knees)	29F / 20M	65 ± 9	35 ± 6	3
Tarwala et al, 2014[33]	35 (39 knees)	22F / 13M	66.1 ± 9.8	29.9 ± 5.3	NR
Ejaz et al, 2014[59]	33 (33 knees)	15F / 18M	68	25	1.34
Fan et al, 2014[58]	30 (30 knees)	23F / 7M	65.4 ± 7.1	27.2 ± 2.7	1
Chen et al, 2014[60]	32 (32 knees)	25F / 7M	72.5 ± 6.9	26.3 ± 5.9	NR
Mittal et al, 2012[61]	32 (32 knees)	23F / 9M	66.6	32.6	NR
Tai et al, 2012[62]	36 (36 knees)	27F / 9M	72.1 ± 6.9	28.6 ± 4.5	NR
Ledin et al, 2012[18]	25 (25 knees)	15F / 10M	70	29	1.5
Li et al, 2009[37]	40 (40 knees)	29F / 11M	71 ± 6	27.3 ± 6.3	NR

ASA, American Society of Anesthesiologists physical status classification; BMI, body mass index; NR, not recorded.
Note: SDs were not provided for the Ejaz, Mittal, and Ledin studies.

Table 3. Procedure Characteristics

	Mean	SD	Median	Min	Max
Duration of procedure, minutes	116	11.5	113	95	145
Pressure of tourniquet, mmHg	273.5	25.2	250	250	300
Tourniquet inflation time, minutes	26.3	3.7	26	17	37

Max, maximum; Min, minimum.

surgery-related postoperative complications or surgical revision.

DISCUSSION

The results of this investigation revealed that the use of TXA in combination with a tourniquet for only cementation provided reasonable operative time and low intraoperative blood loss without increasing perioperative morbidity or complications.

Our study findings concur with findings published by Tarwala et al[33] in that the use of limited tourniquet along with TXA in the performance of TKA is as effective as using a tourniquet throughout the entire procedure as it relates to operative time, intraoperative blood loss, and need for blood transfusion. Two metaanalyses of randomized studies comparing tourniquet use throughout an entire case vs no tourniquet at all found differences only in total blood loss.[2,63] More recently, 2 studies comparing the use of a tourniquet just for cementation of the implants with tourniquet use during the entire operation found no important clinical differences between the 2 methods.[33,58]

Our study has several limitations. First, it is a retrospective review. Second, we reviewed only 51 knee operations all performed by a single surgeon. Third, the majority of our patients were obese; therefore, our results may not be applicable to all populations. Finally, the study has no true control group to provide baseline blood loss levels for TKA without a tourniquet and without TXA.

From 1999-2009, the reported number of TKA cases performed annually in the United States doubled.[64] Such an increase may be at least partially attributed to rising obesity rates, as well as to improved imaging and longer life expectancy.[65,66] Increasing numbers of patients who require TKA and the high economic burden of this procedure will require techniques such as we have described for surgical and anesthetic management.[67-72]

Table 4. Procedure Characteristics in Our Study Cohort in Relation to Historical Comparison Studies

Study	Anesthesia	TXA Used	Mean Duration of Operation, minutes	Mean Tourniquet Duration, minutes	Mean Tourniquet Pressure, mmHg	Time of Tourniquet Release	Cementation	Hemovac Drain
Current study	General	Yes	116 ± 11.5	26.3 ± 3.7	273 ± 25	After prosthesis insertion	Cement	None
Tarwala et al, 2014[33]	Hybrid	Yes	86 ± 22	43	250	After prosthesis insertion	Cement	Yes
Ejaz et al, 2014[59]	Spinal	Yes	70	NR	250	After dressing bandage	Cement	NR
Fan et al, 2014[58]	19 General; 11 Spinal	No	120.8 ± 8	75 ± 14	Varied with patient SBP	After prosthesis insertion	NR	Yes
Chen et al, 2014[60]	General	No	78.2 ± 11.3	78.2 ± 11.3	SBP + 100 mmHg	After dressing bandage	NR	Yes
Mittal et al, 2012[61]	18 General; 16 Spinal	No	103	76.4	300	After prosthesis insertion	Cement	Yes
Tai et al, 2012[62]	NR	No	72.0 ± 8.4	52.5 ± 10.0	SBP + 100 mmHg	After joint capsule closed	Cement	None
Ledin et al, 2012[18]	Spinal	No	85	NR	275	NR	Cement	Yes
Li et al, 2009[37]	Hybrid	NR	73 ± 19	NR	SBP + 100 mmHg	After dressing bandage	NR	None

NR, not recorded; SBP, systolic blood pressure; TXA, tranexamic acid.
Note: SDs were not provided for the Ejaz, Mittal, and Ledin studies.

Table 5. Complications in Our Study Cohort in Relation to Historical Comparison Studies

Study	Mean Intraoperative Blood Loss, mL	Mean Postoperative Hemoglobin Decrease, g/dL	Number of Procedures Requiring Blood Transfusion	Venous Thromboembolism Prophylaxis	Number of Patients With DVT or PE
Current study	94.7 ± 48.5	2.8 ± 0.9	2 (3.9%)	Coumadin + Mechanical	1 DVT (2.0%)
Tarwala et al, 2014[33]	144 ± 53	3.4	NR (predonated packed red blood cells)	Aspirin + Mechanical	None
Ejaz et al, 2014[59]	140	NR	0	Rivaroxaban	2 DVT (6%)
Fan et al, 2014[58]	NR	3.4	NR	Low molecular weight heparin + Mechanical	6 DVT (20%)
Chen et al, 2014[60]	213.8 ± 87.4	1.9	1 (3.9%)	Rivaroxaban	17 Asymptomatic DVT (53%)
Mittal et al, 2012[61]	NR	NR	2 (3.9%)	Low molecular weight heparin + Mechanical	1 DVT (3%)
Tai et al, 2012[62]	25.6 ± 30.9	2.6	2 (3.9%)	None	None
Ledin et al, 2012[18]	317	NR	4 (3.9%)	Low molecular weight heparin	NR
Li et al, 2009[37]	317 ± 72	NR	NR	Low molecular weight heparin + Mechanical	NR

ASA, American Society of Anesthesiologists physical status classification system; DVT, deep vein thrombosis; NR, not recorded; PE, pulmonary embolism.
Note: SDs were not provided for the Ejaz, Mittal, and Ledin studies.

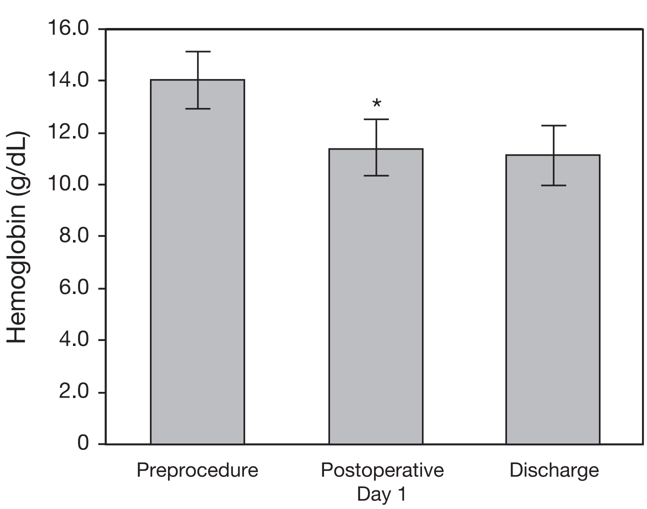

Figure 1. Mean hemoglobin preprocedure, on postoperative day 1, and on discharge. *The mean decrease in hemoglobin from the preprocedure baseline to postoperative day 1 was 2.6 ± 0.9 g/dL (*P*<0.001).

CONCLUSION

Our investigation results demonstrate that using TXA in combination with a tourniquet for only cementation provides reasonable operative time and low intraoperative blood loss without increasing perioperative morbidity or complications.

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