TOURNIQUETLESS TOTAL KNEE ARTHROPLASTY WITH MODERN PERIOPERATIVE PROTOCOLS DECREASES PAIN AND OPIOID CONSUMPTION IN FEMALES

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Abstract

Introduction: This study examined whether a modern TKA protocol without a tourniquet results in less patient-reported pain and in-hospital opioid consumption compared to TKA with a tourniquet.

Methods: A retrospective study of 203 primary unilateral cemented TKAs consecutively performed with or without tourniquet was performed. Identical perioperative pain and blood loss protocols were used in all cases. In tourniquetless TKAs, the tourniquet was not inflated at any time and sterile CO_2 gas compression maximized cement interdigitation.

Results: After exclusions for scientific confounds, 184 TKAs (93 with tourniquet; 91 tourniquetless) were analyzed. Controlling for multiple covariates, females with a tourniquet reported significantly more pain ($p = 0.002$) and opioid consumption ($p < 0.001$) the first 24 hours following surgery compared to females without a tourniquet. There were no differences in pain ($p = 0.192$) or amount of opioids consumed ($p = 0.203$) among males with and without a tourniquet. Tourniquet use resulted in a significant reduction in blood loss for both females ($p \leq 0.040$) and males ($p \leq 0.020$), although the total blood savings of approximately 200 milliliters is of unknown clinical significance.

Conclusion: Avoiding tourniquet use during TKA for females may be a relatively risk-free adjunct to minimize opioid consumption during hospitalization. Further study is warranted to elucidate the factors accounting for different outcomes in females and males.

Keywords: total knee arthroplasty, tourniquet, tourniquetless, pain, opioids, blood loss

Introduction

Pneumatic tourniquets are commonly used in total knee arthroplasty (TKA) to reduce intraoperative blood loss, enhance operative visualization, provide a cleaner field for cement penetration and fixation, and increase operative efficiency. The use of tourniquets during TKA has been a subject of debate in the scientific literature due to risks and benefits associated with their use. Systematic reviews and meta-analyses of randomized controlled trials (RCTs) show high similarity in results. Pooled analyses of 634 knees, [1] 493 patients, [2] 859 patients, [3] and 689 knees [4] all showed significantly less intraoperative blood loss in tourniquet groups, although two of these studies showed no difference in calculated ("true" or "actual") blood loss. [1, 4] Three of these reviews reported no statistically significant differences in the incidence of deep vein thrombosis and/or pulmonary embolism, [1-3] although two reviews [1, 4] showed a greater likelihood of thrombotic events in general in tourniquet groups. Wound problems, [1] minor complications, [2] and surgical site infection [3] were all more likely when a tourniquet was used. Two systematic reviews and meta-analyses of RCTs comparing tourniquet release before and after wound closure comprised of 670 knees [5] and 1170 patients [6] reported that complications were lower when tourniquets were released prior to wound closure. Further, several studies have demonstrated that tourniquets result in greater pain in the immediate postoperative period after TKA.[7-12] Some studies additionally have noted either an increase [7, 12] or no difference in [11] analgesia consumption in relation to this increased pain.

In recent years, misuse and abuse of narcotic prescriptions has risen to the forefront as an urgent and grave concern. In 2011, the Executive Office of the President of the United States identified prescription drug abuse as the nations' fastest growing drug problem and issued a strong call for action. [13] Surgical specialties including orthopedics, the fifth highest opioid

prescribing specialty group in the U.S. in 2012, prescribed 9.8% of all U.S. opioid prescriptions in that year.[14] In an evaluation of half of all prescriptions issued nationwide in 2009, orthopedic surgeons prescribed 7.7% (6.1 million) of all opioid prescriptions, fourth behind primary care and internal medicine physicians and dentists.[15] In step with many other professional organizations, the American Academy of Orthopaedic Surgeons addressed the nations' call to action by issuing a statement on "opioid use, misuse, and abuse in orthopedics," providing recommendations for addressing excessive and inappropriate opioid consumption in orthopedic patients. [16] Subsequently, several studies have identified preoperative opioid use, age, and sex, among other factors, as strong predictors of continued opioid use after TKA. [17-19] In this study, we examined the effect of tourniquet use on pain and opioid consumption in the early postoperative period following TKA performed with modern perioperative pain protocols. Blood loss in tourniquet and non-tourniquet TKAs is presented as a secondary outcome.

Methods

Study Sample

A retrospective study of 203 primary unilateral cemented TKAs consecutively performed at a single academic institution between January 2016 and March 2017 was conducted with Institutional Review Board approval. Inclusion criteria included unilateral cemented TKA secondary to primary osteoarthritis, traumatic osteoarthritis, or inflammatory arthritis. To maintain scientific validity of the study by minimizing confounding variables, patients who took antiplatelet medications except aspirin (n = 8), had a clotting disorder (n = 6), unplanned tourniquet disruption (n = 4), or preexisting periarticular hardware (n = 1) were excluded. The final analysis sample consisted of 184 TKAs, 93 of which included the use of a tourniquet and 91

of which did not. The consecutive series of surgeries performed with a tourniquet was immediately followed by the consecutive series of cases performed without a tourniquet. To maximize the effect of limb ischemia time on the outcome variables, the tourniquetless knee group did not have a tourniquet inflated at any time including during cementation of components. Carbon dioxide compression gas (CarboJet® CO_2 Bone Preparation System, Kinamed Incorporated, Camarillo, CA) was used in tourniquetless knees to optimize cement penetration.

Surgical Procedure

Surgeries were performed by a single fellowship-trained arthroplasty surgeon. A median parapatellar approach was used for all procedures. Standard coronal plane femoral bone cuts were made with computer-aided navigation (Stryker Navigation, Kalamazoo, MI) and tibial cuts were performed with an extramedullary cutting guide. The same cruciate retaining knee implant was used in all cases (EMPOWR 3D Knee™, DJO Surgical, Vista, CA). Surgeries were performed with standardized light general anesthesia, low-dose intrathecal/single-shot spinal injection of 25 mcg fentanyl and 4.5 mg bupivacaine, and a periarticualar injection of 0.2% (200mg) ropivacaine, 0.5 mg epinephrine, 80 mcg clonidine and 30 mcg ketorolac to equal 101.3 mL total volume immediately following component fixation. Dosing was identical in all patients, except that ketorolac was removed for patients with renal insufficiency. Multimodal perioperative pain protocols were used in all cases and consisted of preoperative oxycodone, Lyrica, Celebrex (or ketorolac if sulfa allergic) and oral Tylenol 24 hours prior to surgery. Postoperative protocols were identical with the addition of oxycontin if under 70 years of age, and tramadol if 70 or older. The same modern perioperative pain control, clinical, and rehabilitation protocols were used for all patients.

Prior to closure of the arthrotomy, a medium hemovac drain was placed in all knees and one gram of topical tranexamic acid was applied to the site. When tourniquets were used, the tourniquet was inflated to a pressure of 250 mm Hg from surgical incision until the postoperative sterile dressing was applied. A pad was applied between the skin and the tourniquet cuff to protect the skin.

Measurements

Patient sex, age in years, body mass index (BMI), American Society of Anesthesiologists Physical Status (ASA-PS) classification, procedure time in minutes, tourniquet use (yes/no), tourniquet (limb ischemia) time in minutes, hospital length of stay (LOS) in days, and preoperative presence of lumbar spine disease, fibromyalgia or systemic lupus erythematosus, depression (controlled or uncontrolled with medications), and narcotic use (none, scheduled, or pro re nata) were retrieved from the electronic medical record (EMR). Patients reported current narcotic use to a perioperative internal medicine specialist whose practice focuses exclusively on medical assessment and optimization prior to and following total joint arthroplasty.

Primary outcomes of pain and opioid consumption during the first 24 hours after surgery were retrieved from the EMR. Patient-reported pain scores recorded by nursing staff on a 10 point scale (ranging from none to severe) every four hours were averaged to derive an overall pain score during the first 24 hours following surgery. Narcotics consumed during the first 24 hours after surgery were recorded and standardized to morphine milligram equivalents using a previously published methodology. [20]

Secondary outcomes related to blood loss also were retrieved from the EMR. Blood loss was evaluated via four metrics: (1) change in preoperative to postoperative day one hemoglobin levels in g/dL, (2) calculated total blood loss in liters, (3) total hemovac drain output in

milliliters, and (4) average drain output per hour to account for the variable time drains were in situ. The change in hemoglobin was calculated by subtracting postoperative day one hemoglobin levels from hemoglobin levels obtained at the preoperative medical clearance appointment within thirty days of the index procedure. Total blood loss was calculated using established methodology [21] by multiplying estimated blood volume (EBV) by the change in hemoglobin divided by the average hemoglobin level. EBV was calculated by taking into account the height, weight, and sex of the patient. To determine the estimated blood loss assuming slow or steady blood loss with standard maintenance intravascular fluids, the change in hematocrit, or hemoglobin, over a given time interval has been found to be ideal to determine intraoperative blood loss.[21] However, the formula for intraoperative blood loss has since been modified to better serve the purpose of estimating perioperative blood loss after TKA.[22, 23] Drain output was measured from placement until discontinuation. The use of the last recorded time point of drain output was used to standardize drain output per hour because drain output was not always recorded at the time of discontinuation on the day after surgery. Drain hours were rounded to the nearest fifteen minutes.

All data points used in this study were prospectively collected and entered into the EMR by non-study clinical personnel. Data points were extracted from the EMR without alteration or conversion. Because tourniquet time was collected for the study, data collection was not blinded to study group.

Data Analysis

Minitab 17 (State College, PA) was used for statistical analysis. Dixon's *r*22 ratio was used to test continuous variables for statistical outliers. After outliers were identified and removed (total of three data points), Anderson Darling tests were used to evaluate whether

continuous variables were normally distributed. Student's t-test (t) and Pearson's correlation coefficient (r) were used to compare means of normally distributed continuous variables. Mann Whitney (W) tests and Spearman's rank correlation (rho) were used to compare medians of non-normally distributed continuous variables. Chi-Square (X^2) with Fishers *p* for 2 x 2 tables was used to analyze categorical variables. An alpha level of 0.05 was used to determine statistical significance.

Results

The average age of patients in the tourniquet (67.7, range 33-91 years) and no tourniquet (67.0, range 47-85 years) groups was not statistically different (t = 0.58, $p = 0.561$). Median BMI in kg/m^2 also did not differ in the two groups (32.7 [Q1, Q3 = 28.2, 38.5] vs. 34.2 [Q1, Q3 = 28.7, 39.7], respectively, W = 8618.0, $p = 0.580$). There were significantly more females in the tourniquet group (55.9%) compared to the no tourniquet group (44.1%) ($X^2 = 5.945$, $p = 0.019$). Consequently, outcome analyses were performed separately for females and males.

Sample demographics and covariates are presented separately based on sex and tourniquet use (yes/no) in Table 1. Preoperative depression was 1.6 times higher in female patients for whom a tourniquet was not used compared to those for whom a tourniquet was used ($p = 0.047$). Depression in all patients in both groups was controlled by medication. Age, BMI, procedure time, LOS, and the prevalence of lumbar spine disease, fibromyalgia or systemic lupus erythematosus, and preoperative narcotic use did not statistically differ among females in the two groups ($p \geq 0.578$). Among male patients, mean age was higher by 4.6 years ($p = 0.046$) and median procedure time was 7.9 minutes shorter ($p = 0.023$) in the tourniquet group. None of the other demographic characteristics statistically differentiated males with and without tourniquet use ($p \geq 0.146$).

Patient-reported pain and opioid consumption are provided separately for females and males and tourniquet use in Table 2. Females who had a tourniquet reported more postoperative pain (median pain score of 2.7 vs. 1.9, $p = 0.002$) and greater opioid consumption (median morphine milligram equivalents of 42.8 vs. 18.8, $p < 0.001$) in the first 24 hours following surgery compared to females without a tourniquet. The presence of depression did not affect median pain scores in the first 24 hours in females with a tourniquet (2.6 vs. 2.7, W = 2017.0, $p = 0.245$) or those without a tourniquet (1.9 vs. 1.8, W = 1013.5, $p = 0.923$). Median morphine milligram equivalents consumed in the first 24 hours by females with a tourniquet (40.4 vs. 45.6, W = 1954.0, $p = 0.250$) and those without a tourniquet (22.8 vs. 14.3, W = 1078.0, $p = 0.291$) also did not differ based on the presence of depression (no vs. yes). Time to first opioid did not differ in females with and without a tourniquet (p = 0.525).

There were no differences in self-reported pain ($p = 0.192$), time to first opioid ($p = 0.119$) and amount of opioids consumed ($p = 0.203$) among males with and without a tourniquet (Table 2).

For both females and males, respectively, tourniquet use was associated with significantly lower decreases in mean delta Hgb (-2.4 vs. -3.0 g/dL, t = 4.15, $p < 0.001$ and -1.7 vs. -2.8 g/dL, t = 3.34, $p = 0.003$); less mean total blood loss (-0.9 vs. -1.1 liters, t = 3.69, $p < 0.001$ and -0.8 vs. -1.3 liters, t = 2.69, $p = 0.013$); mean total drain output (220 vs. 265 ml, t = 2.08, $p = 0.040$ and 274 vs. 426 ml, t = 2.72, $p = 0.009$); and mean drain output per hour (13.7 vs. 17.3 ml, t = 2.70, $p = 0.008$ and 15.9 vs. 23.4 ml, t = 2.43, $p = 0.020$).

Discussion

Pain after primary TKA can be substantial and has been shown to increase continued opioid use and dependence in previously opioid-naïve [24] and opioid-experienced [25, 26]

patients. Several studies have observed that tourniquets result in greater pain in the immediate postoperative period, [7-12] with two of those studies [7, 12] showing increased analgesia consumption as a result and one showing no differences in analgesia consumption. [11] None of these studies examined pain and analgesia consumption separately for females and males, and modern perioperative protocols including TXA were not used. More recently, however, evidence of sex differences in knee pain both prior to [27, 28] and after TKA [29, 30] indicating greater pain in females has been reported.

We observed no differences in median pain (1.9 vs. 2.3 on a 10 point scale, $p = 0.192$) or opioid consumption (37.1 vs. 39.9 morphine milligram equivalents, $p = 0.203$) during the first 24 hours after TKA in male patients with and without a tourniquet, respectively. This may be related to existing observations that male patients with symptomatic knee osteoarthritis (OA) have significantly higher thresholds for mechanically-, heat-, and cold-induced pain at the knee than females, [27] and that pain scores adjusted for covariates are significantly lower in males at all levels of OA as measured by the Kellgren and Lawrence System. [28] In addition, consistent with our observations, men reported significantly less pain than women 24 to 36 hours and 24 to 48 hours after TKA, although tourniquet use was not addressed. [29] Unlike our findings, however, the latter study did not find a concomitant sex difference in opioid consumption.

In contrast, we found that female patients with and without tourniquets reported higher median pain (2.7 vs. 1.9, $p = 0.002$) and opioid consumption (42.8 vs. 18.8 morphine milligram equivalents, $p < 0.001$) in the same period of time. It is noteworthy that median pain scores among females with and without tourniquets were higher than median pain scores in males with and without tourniquets. More importantly, the difference in morphine milligram equivalents

consumed by female patients with and without tourniquets is equivalent to the difference between 80 mg compared to 35 mg of hydrocodone daily.

With respect to blood loss, consistent with existing literature, tourniquet use resulted in a statistically significant reduction in blood loss for both female ($p \leq 0.040$) and male ($p \leq 0.020$) patients, although the total blood savings of approximately 200 milliliters is of unknown clinical significance, especially in non-anemic patients.

Our primary findings suggest that, barring contraindications, switching to tourniquetless TKA for females may reduce opioid analgesia in the postoperative period in this specific demographic without dramatically increasing blood loss or adding additional operative time (Table 1). Reduced opioid use in the postoperative period is likely to reduce unwanted opioid-related side effects such as constipation, potential for immunosuppression, urinary retention, sedation, and the increased medication load required to reduce these side effects [31] and may lessen the likelihood of chronic opioid dependence. [32] In addition, undesirable consequences associated with tourniquet use including pain, parasthesias, muscle weakness and rare, but devastating vascular injury, would be eliminated.

Limitations of our study include its retrospective design, the unavailability of inpatient pain scores and opioid use beyond the first 24 hours following TKA, and limited data on preoperative narcotic use. We were unable to provide data on inpatient pain and opioid consumption beyond 24 hours because most patients were discharged on postoperative day one resulting in a small number of data points beyond 24 hours. We were able to control for patient narcotic use immediately prior to surgery, but did not have data on long-term narcotic use or dependence. It is a strength of our study that TKAs were performed by a single surgeon at a single academic institution using modern perioperative pain protocols.

232 In light of national and profession-specific calls to action to address the opioid crisis in
233 America, avoiding tourniquet use during TKA for females may be a relatively risk-free way to
234 decrease opioid consumption during hospitalization. Further study is warranted to elucidate the
235 factors accounting for different outcomes in females and males.
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Table 1: Sample Demographics and Covariates

	FEMALES				**MALES**			
	Tourniquet	**No Tourniquet**	**Statistic**	***p***	**Tourniquet**	**No Tourniquet**	**Statistic**	***p***
N	**76**	**60**			**17**	**31**		
Mean (Range) Age in Years	66.9 (33-91)	67.2 (47-85)	t = 0.20	0.844	71.3 (61-83)	66.7 (47-83)	t = 2.05	**0.046**
Mean (Range) BMI (kg/m2)	33.5 (20-47)	33.8 (21-48)	t = 0.27	0.788	33.5 (24-45)	34.4 (23-50)	t = 0.44	0.664
Median (Q1, Q3) Female/Mean (Range) Male Procedure Time in Minutes	74.0 (69:80)	74.5 (67:82)	W = 4158.5	0.833	77.3 (61-96)	85.2 (69-106)	t = 2.40	**0.023**
Median (Q1, Q3) Limb Ischemia Time in Minutes	70.0 (65:75)	0.0	*	*	70.0 (65:80)	0.0	*	*
Median (Q1, Q3) Length of Stay in Days	1 (1:1)	1 (1:1)	W = 4044.0	0.702	1 (1:1.5)	1 (1:1)	W = 733.5	0.396
% with Lumbar Spine Disease	18.4	15.0	X^2 = 0.279	0.651	41.2	22.6	X^2 = 1.838	0.201
% with Fibromyalgia or Systemic Lupus Erythematosus	7.9	6.7	X^2 = 0.074	1.000	0.0	0.0	--	--
% with Depression	27.6	45.0	X^2 = 4.429	**0.047**	0.0	16.1	X^2 = 3.061	0.146
% with Uncontrolled Depression	0.0		**	**	--	0.0	**	**
% with Preoperative Narcotic Use								
None	65.8	71.7	X^2 = 0.647	0.724	64.7	67.7	X^2 = 0.065	0.968
Scheduled	6.6	6.6			11.8	9.7		
PRN	27.6	21.7			25.5	22.6		

*Could not be tested because all values were the same for the no tourniquet group
**X2 invalid due to low cell counts

Table 2: Inpatient Pain and Opioid Use Outcomes								
	FEMALES				**MALES**			
	Tourniquet	**No Tourniquet**	**Statistic**	***p***	**Tourniquet**	**No Tourniquet**	**Statistic**	***p***
PAIN								
Median (Q1, Q3) Pain in First 24 Hours	2.7 (1.8, 3.6)	1.9 (1.1, 2.7)	W = 3408.0	**0.002**	1.9 (0.8, 2.7)	2.3 (1.7, 3.3)	W = 820.5	0.192
OPIOID USE								
Median (Q1, Q3) Time to First Opioid in Minutes	193 (123, 323)	183 (106, 343)	W = 3840.0	0.525	260 (178, 331)	172 (108, 268)	W = 661.5	0.119
Median (Q1, Q3) Amount of Opioids in First 24 Hours in Morphine Milligram Equivalents	42.8 (28.5, 64.8)	18.8 (11.4, 34.2)	W = 2885.5	< **0.001**	37.1 (24.2, 57.0)	39.9 (34.2, 68.4)	W = 819.0	0.203