Title:
Impact of Tourniquet Use on Functional Outcomes and Complications after TKA
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OVERVIEW

Background information:

Functional recovery after total knee arthroplasty (TKA) has seen dramatic improvement over the past 20 years through advances in surgical technique, implant design, perioperative pain management strategies, and physical therapy protocols. Tourniquet use during TKA, however, remains controversial due to conflicting reports in the literature on these benefits and risks of its use. Reported advantages of tourniquet use include improved visualization of the surgical field and decreased intraoperative blood loss. (Austin, 2019) Reported disadvantages of tourniquet use include increased postoperative pain and slower functional recovery as a direct result of the pressure of the tourniquet on the thigh during the procedure. (Ejaz 2014, Harsten 2015)

Traditionally with tourniquet use during TKA, the limb is exsanguinated and the tourniquet is raised to a fixed, pressure at the beginning of the case, typically 250mmHg to 350mmHg, and let down after closure. A novel tourniquet design that adjusts the tourniquet pressure in real-time based on intraoperative patient blood pressure measurements. This design may allow for the tourniquet to be inflated at a lower mean pressure while still maintaining efficacy.

A prospective study comparing total blood loss, pain and functional recovery after TKA using this novel tourniquet design, design (Zimmer A.T.S.® 4000TS Automatic Tourniquet System, with disposable contour cuffs) and TKA without tourniquet would further the current literature. Total blood loss will be calculated by previously validated methods. Pain and functional recovery will be closely monitored throughout the postoperative period using a patient wearable activity tracker (FitBit Inspire HR) and a smartphone-based patient engagement platform with integrated digital

surveys paired with smart-brace based home PT assessments (FocusMotion).Pain and functional recovery will be closely monitored throughout the postoperative period using a patient wearable activity tracker (FitBit Inspire HR) and a smartphone-based patient engagement platform with integrated digital surveys paired with smart-brace based home PT assessments (FocusMotion). Applying this technology to the proposed study can help identify problematic pain that is not appreciable during admission; given the fact that markers of inflammation and myocyte damage increase over time until at least post-operative day 3, it is possible that TKAs performed under tourniquet may have pain and narcotic requirements not appreciated with short-stay admissions (Huang 2014). The proposed study will further the literature on pain and narcotic use in the early time period after TKA, and will help identify if tourniquet has an effect on these variables.

Furthermore, sleep quality is a component of functional recovery and is correlated with pain. Knee osteoarthritis affects general quality of life by increasing sleep disturbance and nighttime wakening, and this is correlated with the pre-operative radiographic severity of disease (Sasaki, 2014). Sleep quality is affected in the immediate post-operative period after TKA as well, but improves by 3-6 months post-operatively (Chen, 2016). The proposed study would be the largest prospective study investigating the effect of TKA on pain and sleep quality, as well as being the first to investigate tourniquet use as a factor affecting sleep quality and pain. The proposed study would be the first to collect both subjective and objective data on the subject, using validated survey measurements as well as the data collected by the Fitbit Inspire HR device.

Research objectives:

The purpose of this study is to determine the effect of novel pressure-regulating tourniquet use on pain, functional recovery, sleep and total blood loss following total knee arthroplasty.

Specific Aim 1: Our primary aim is to determine the effect of tourniquet use on pain after TKA. Pain levels and oral analgesic requirements will be assessed daily using the FocusMotion remote patient monitoring platform.

Specific Aim 2: Secondary aim to determine the effect of tourniquet use on functional recovery after TKA. To do so, we will using a combination of standardized clinical assessments performed by physical therapy preoperatively and at 3 months postoperatively, as well as assessments with patient reported outcome surveys and functional assessments at regular intervals using the FocusMotion remote patient monitoring and virtual physical therapy platform.

Specific Aim 3: The third aim is to investigate sleep quality in the post-operative period after TKA with and without tourniquet use. We will apply both subjective measurements using the Pittsburgh Sleep Quality Index (PSQI) as well as sleep quality data as collected by the Fitbit HR.

Specific Aim 4: The fourth aim is to determine the effect of tourniquet use on total calculated blood loss after total knee arthroplasty. Hemoglobin dilution will be utilized to determine calculated blood loss using a validated methodology.

Potential Contribution: This study would give us a better understanding of the effect of a pressure auto-regulating tourniquet on pain, functional recovery sleep, and blood loss after total knee arthroplasty.

METHODS

Timeline: 3 years (2 year of prospective enrollment, 3 months years of follow-up for all participants, approx. 9 months of data analysis)

Inclusion/Exclusion criteria: The Principal Investigator (PI) will independently review all cases to confirm study eligibility for each patient. The following inclusion and exclusion criteria will be used to determine patient eligibility.

Inclusion criteria:

1. Age 18 and up
2. Primary unilateral TKA
3. BMI<45
4. Primary diagnosis of osteoarthritis
5. Patient has a iOS or Android smartphone capable of running FitBit and FocusMotion applications

Exclusion criteria:

1. Revision TKA
2. Bilateral TKA
3. Pregnancy
4. Prisoners
5. Pre-existing functionally-limiting neurologic disorder
6. Narcotic dependence, defined as oxycodone/hydrocodone use >5days/week
7. History of unprovoked VTE/PE
8. Inability to complete baseline functional testing

Recruitment: We will be recruiting patients from the clinical practices of Dr. Ryan Nunley, Dr. Robert Barrack and Dr. Charles Lawrie.

Design: The proposed study is a prospective, single blinded, randomized clinical trial with 2 study groups

For purposes of randomization, patients will be randomized into one of two groups tourniquet or no tourniquet, stratified by surgeon,using randomization sequences generated a priori using a computerized formal probability model with a block design and 1:1:1:1 allocation ratio. Patients will

be blinded to study group membership. As a result of the blocking, the desired allocation ratio will be maintained at periodic intervals throughout the recruitment process. The randomization sequences will be uploaded to REDCap so that allocations will be elicited using the REDCap randomization module in the immediate pre-operative period to minimize loss to follow-up.

Number of participants:

A pre-hoc power analysis for the primary outcome measure of VAS pain score was performed. A medium effect size of 0.5, power of 0.8, and alpha error of 0.05 were used for the analysis. With these assumptions, 128 patients were required to be enrolled in the study. With the dropout rate assumed to be 10%, 144 patients will be enrolled in the study.

Data collection:
Data collection will be done preoperatively, intraoperatively, 4 weeks post operatively, and at 12 weeks post operatively and at 1 year postoperatively. The data will be analyzed by site staff. All data to be collected can be found in tables 1-8.

All procedures will be performed by three surgeons (R.B., R.N., C.L) within a single institution at one site (Barnes Jewish West County and Progress West Hospital).

All participants will undergo standard admission and pre-operative procedure for primary total knee arthroplasty per institution protocol. Participants will be admitted to hospital on day of surgery for elective procedure. Spinal anaesthesia will be placed in pre-op holding area per regional anaesthesia team. Participants will be positioned in standard supine position. Per operative protocol each patient will undergo standard prep and drape. There will be no application of tourniquet for those randomized to no-tourniquet arm. If tourniquet is to be used, it will be applied after induction and will be deflated after incision closure. Maximum tourniquet time will be 120 mintues, TKA implant choice will be made based on surgeon preference. Transexamic acid will be given 1g IV prior to incision and 1g IV at end of case. The procedure for all participants will be via midvastus approach to the knee. At the end of the procedure, all patients will receive standard ipericapsular injection of 30mL 0.25% Marcaine with epinephrine and 30mL toradol prior to closure.

PT treatment and evaluation will take place on day of surgery post-operative day one prior to discharge. All patients will be placed on Aspirin EC 325mg BID for VTE prophylaxis. Pain medications will be standardized during admission, and an uncontrolled pain protocol will be available for implementation at physician discretion; see Tables 1 and 2) The final set of standard blood labs will be drawn at midnight. Discharge medications will be standard(Table 3)., Patients will be contacted at 1 week post-operatively to evaluate clinical progress, general concerns and compliance with study protocols, including use of the Fitbit HR platform and FocusMotion platforms.

Participants will be scheduled for a standard clinical visit at 4 weeks.

Participants will undergo final clinical evaluation at 3 months post-operatively with a PT visit and phone call from the research team as well as a final questionnaire about their experience with the app and Fitbit and knee brace which will be completed by paper, phone, or electronically.

Fitbit Activity Tracker and Focus Motion knee brace apps

During the pre-operative arthroplasty class, participants in the study will be set-up with a FitBit wrist-based activity tracker and FocusMotion knee brace and the appropriate software. Participants will be instructed to use the device in the 2 weeks prior to undergoing surgery, to gather baseline data on narcotic use, pain, use of assistive device and sleep quality. They will continue to use the devices for 3 months postoperatively(Table 7).

Subject Payment

Honorarium of $100 provided at 3 months following completion of 3 month evaluation. Participants will be gifted the Fitbit Inspire HR and the FocusMotion smart-brace and platform and given an honorarium of $50 for completion of the 1 year app based survey.

Participants Lost to follow-up: Some participants will not return for follow-up at the required intervals. A member of the research team shall contact non-respondent participants using phone calls, regular mail, e-mail, certified letters, or other means to urge participants to return for clinic follow-up or ascertain if a participant has moved, died, or otherwise become lost to follow-up. The following flow chart identifies the steps for attempts to locate lost participants. These actions, along with any other options available to the site, should be followed to exhaust all reasonable means in locating lost participants. These actions should be documented in the participant's records and may be performed concurrently or in parallel.

Phone call to last known number → Contact → Follow-up with participant
↓
No Contact
↓
Phone call to other numbers (spouse, relative, etc.) → Contact → Follow-up with participant
↓
No Contact
Note: There will be a minimum of 3 calls to different numbers
↓
Mail letter to last known patient address → Contact → Follow-up with participant
↓
No Contact
↓

Mail letter to secondary addresses → Contact → Follow-up with participant
↓
No Contact
↓
Mail “certified” type of letter to last address and any secondary address → Contact → Follow-up with participant
↓
No Contact
↓
Social Security Death Index to determine if participant has died → Confirm death
↓
Not Confirmed
↓
End attempts.

INFORMED CONSENT

Enrollment and consent will begin in the clinics of Dr. Ryan Nunley, Dr. Robert Barrack and Dr. Charles Lawrie, and will be the same for both study groups. The consent process will occur by one of the following means:

1) The study coordinator will meet with each potentially eligible participant to review the study requirements (including additional screening for eligibility) and answer any questions the patient may have.

If the patient has any clinical questions that cannot be answered by the study coordinator they will be answered by the physician or the physician's nurse. The patient will have the opportunity to review the consent form, discuss with family/friends, and do his/her own research on the subject if desired. Qualified patients who agree to participate in the study will be required to sign an Informed Consent Document. Valid enrollment is not granted until after surgery, once it has been verified that the participant qualifies for total knee replacement.

2) The consent discussion and review of the Informed Consent Document may occur over the phone. In this case, the study coordinator will call the patient to present the study to the participant and gauge interest in participation. If the patient expresses interest in participation, the study coordinator will e-mail, mail or fax the Informed Consent Document to the participant. The patient will be given the opportunity to ask questions. If the patient has any research questions beyond the scope of the study coordinator, arrangements will be made for the participant to speak with the applicable member of the research team, including the PI. After review of the Informed Consent Document, the participant will sign the applicable sections of the Informed Consent Document and email, mail or fax the consent for back to the study coordinator. The Informed Consent Document will be signed by the consenting study coordinator upon receipt. Valid enrollment is not granted until

after surgery.

PROCEDURES FOR MAINTAINING CONFIDENTIALITY

Data Security: Hard copies of patient questionnaires and CRFs will be stored in individual patient binders. The binders will be kept in a locked filing cabinet in an office that has password protected access and is locked when not in use.

Data collected on questionnaires and CRFs will be entered into electronic databases for analysis and tracking. These databases are on a secure server and can only be accessed by authorized research team members. There is no intention that the electronic records will be transported. We will not use laptops/jump drives/CD/DVDs to store, analyze, or input this data.

For data collected by the Fitbit platform including health monitoring and app-generated data, pre-assigned study ID numbers and anonymous email addresses will be used for all patient-reported and patient-generated data collection and transmission. No ePHI is seen or handled by the smartphone application or its data collection platform. The electronic key will be available only to the study team, not the mobile health platform or app developers.

De-identification of Data: All information will be collected by the research team in a confidential manner. PHI will be de-identified. All data will be entered into a master database that is password and security protected. Only members of the research team will be able to access information on study participants. Electronic key linking participant to data will be kept on a secured, password-protected network. All electronic information will be encrypted and stored in a password-protected database. All research files will be kept in a secure, locked location which can only be accessed by the study team. Once all manuscript submission is complete, all study documents, including the master list, will be retained for seven years after close of the study.

ASSESSMENT OF RISKS AND BENEFITS

There is a slight risk that patients may feel a small amount of psychological discomfort answering the questionnaires.

In addition there is the risk of breach of confidentiality.

Benefits: Participants will receive no direct medical benefit from study participation. However, this prospective study is the first to investigate tourniquet use as a factor affecting sleep quality and pain by collecting both subjective and objective data on the subject that is not be appreciable during admission. Furthermore, the study device design of adjusting tourniquet pressure in real-time based on intra-operative patient data measurements may allow for the tourniquet to be inflated at a lower mean pressure while still maintaining efficacy.

G1. Tables

Table 1: Post-operative pain protocol

Medication	Dose and Route	Timing	PRN
Percocet 5mg/325mg	1-2 tablets PO	Q6 hours	Yes
Toradol	30mg IV	Q6 hours	No
Morphine	2-4 mg IV	Q4 hours	Yes

*Toradol withheld in patients with sulfa allergy

Table 2: Discharge medication protocol

Medication	Dose and Route	Timing	Duration/PRN
Aspirin	325mg PO	BID	6 weeks
Percocet 5mg/325mg	1-2 tablets PO	Q6 hours	PRN
Celebrex*	200mg PO	BID	5 days
Senna-docusate	8.6mg/50mg PO	BID	PRN

*Celebrex withheld in patients with sulfa allergy

Table 3: Pre-operative data within 4 weeks of procedure

Test	Unit	Collected by
Knee circumference	cm	PT measurement
Passive Knee ROM	degrees	PT measurement
Active Knee ROM	degrees	FocusMotion Brace
Balance: tandem stance	scale	PT measurement
Balance:Standing on one leg	Scale	PT measurement
10m walk test for speed	Seconds	PT measurement
6 minute walk test	Meters	PT measurement
Timed up and go test	seconds	PT measurement
5 times sit to stand	Seconds	PT measurement
30 sec chair stand test	count	PT measurement
Timed Stair climb	seconds	PTmeasurement
Quadriceps strength	N	PT measurement
Hamstrings strength	N	PT measurement
Pittsburgh Sleep Quality Index	scale	FocusMotion App Survey
Oxford knee score	scale	FocusMotion App Survey
FJS	scale	FocusMotion App Survey
Visual Analog Scale pain score thigh	scale	FocusMotion App Survey
Visual Analog Scale pain score knee	scale	FocusMotion App Survey

Visual Analog Scale pain score leg/calf	scale	FocusMotion App Survey
% normal knee	Scale	FocusMotion App Survey
Use of assistive device	incidence	FocusMotion App Survey
Narcotic requirement, daily	Daily MME/hr	FocusMotion App survey
Sleep duration	min	Fitbit
Sleep quality (REM sleep/non-REM sleep)	percentage	Fitbit
Sleep disturbances	count	Fitbit
Sleep efficiency(time asleep/time in bed)	percentage	Fitbit
Charleston Comorbidity Index	Score	EPIC CPAP documentation
PROMIS	Score	WUPRO

Table 4: Intra-operative data during procedure

Test	Unit	Collected by
Tourniquet time		Surgeon
Tourniquet pressure		Surgeon
Length of surgery		Surgeon

Table 5: Post-operative data during hospital stay

Test	Unit	Collected by
Length of stay	Hours	Chart review
Day of discharge	number	Chart review
Total calculated blood loss	mL	Chart review
Occurrence of transfusion	incidence	Chart review
VAS pain score (q8hr)	scale	Nursing
Narcotic requirements, PACU to discharge	MME/hr	Chart review
Perioperative complications	incidence	Chart review

Table 6: Daily data points, from postop day 0 to 12 weeks postop

Data	Unit	Collected by
VAS pain score	Scale	FocusMotion App Survey
Total prescribed morphine equivalents	Pills/day	EPIC
Narcotic requirement, daily	MME/hr	FocusMotion App Survey
Sleep duration	Min	Fitbit
Sleep disturbances	Count	FItbit

Sleep efficiency (time asleep/time in bed)	percentage	Fitbit
Sleep quality (REM sleep/non-REM sleep)	Percentage	Fitbit
Step count	Count	Fitbit
Use of assistive device	Incidence	FocusMotion App Survey
Active Knee ROM	degrees	FocusMotion Brace
Passive Knee ROM	degrees	FocusMotion Brace
Compliance with home PT protocol	incidence	FocusMotion App

Table 7: Post-operative data at 3 months following procedure

Knee circumference	cm	PT measurement
Passive Knee ROM	degrees	PT measurement
Active Knee ROM	degrees	FocusMotion Brace
Balance: tandem stance	scale	PT measurement
Balance: Standing on One Leg	scale	PT measurement
10m walk test for speed	seconds	PT measurement
6 minute walk test	meters	PT measurement
Timed up and go test	seconds	PT measurement
5 times sit to stand	seconds	PT measurement
30 sec chair stand	count	PT measurement
Timed stair climb	seconds	PT measurement
Quadriceps strength	N	PT measurement
Hamstrings strength	N	PT measurement
PSQI	scale	FocusMotion App Survey
Oxford Knee Score	scale	FocusMotion App Survey
% normal knee	scale	FocusMotion App Survey
FJS	scale	FocusMotion App Survey
VAS pain score	scale	FocusMotion App Survey
Use of assistive device	incidence	FocusMotion App Survey

Narcotic requirement	daily MME/hr	FocusMotion App Survey
Sleep duration	min	Fitbit
Sleep disturbances	count	Fitbit
Sleep efficiency (time asleep/time in bed)	percentage	Fitbit
Sleep quality (REM sleep/non-REM sleep)	percentage	Fitbit
PROMIS	score	WUPRO
Wound complications	incidence	EPIC documentation
DVT/PE	incidence	incidence
Infection	incidence	EPIC documentation
Return to OR	incidence	EPIC documentation
Patient questionnaire about app and Fitbit/brace usage	questionnaire	Paper questionnaire or through app

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