

Project Title: Contributing factors to short and long-term reoperation after surgical treatment of ankle fracture.

I. Specific Aims (250 words maximum):

In this section please define the clinical or basic science problem that exists that deserves investigation. Provide a null hypothesis and specific aims. It should be brief and concise.

Ankle fracture is a common orthopaedic injury, behind only hip and wrist fractures in the elderly (Sporer et al., 2006). Ankle fractures have been implicated in the development of post-traumatic arthritis which is the leading cause of secondary ankle arthritis. Therefore the goal of surgical intervention is to attain an anatomic reduction, and thereby reduce abnormal joint reactive forces across that may predispose to the development of post-traumatic arthritis. The time-frame to end-stage arthritis is not well understood. There are numerous complications that may result in reoperation, including failed hardware, failed fixation, and infection. In the longer-term, surgical treatment for post traumatic arthritis may include ankle debridement, arthroplasty, or fusion. Neither the rates of re-operation, nor the factors that predict re-operation are clear in the current literature.

Research Questions:

In patients who suffer an ankle fracture:

1. What is the burden of re-operation of the ankle?
 - a. Which patient, provider, and/or surgical factors modify the risk?
2. What proportion of treated ankle fracture patients proceed to develop post traumatic osteoarthritis requiring ankle debridement, arthroplasty or fusion?
 - a. Which patient, provider, and/or surgical factors modify the risk?
 - b. What is the risk of these procedures compared to matched, uninjured population controls?

Hypothesis:

HO1: There is no association between patient, provider, and surgical factors, and the rate of complications or the rate of re-operation of the involved ankle.

HO2: There will be no increase in the rate of ankle debridement, arthroplasty or fusion after ankle fracture compared to a matched cohort of uninjured controls.

II. Background & Significance (350 words maximum; if preliminary data is available, include here):

Briefly present the impact you think your research might have on orthopaedic trauma clinical practice or for future research effects.

Ankle fracture is a common orthopaedic injury, behind only hip and wrist fractures in the elderly (Sporer et al., 2006). Ankle fractures have been implicated in the development of post traumatic arthritis (Beris et al. 1997; Burwell & Charnley 1965; Lindsjo 1985) and therefore the goal of surgical intervention is to attain an anatomic reduction with a congruent mortise, and thereby reduce abnormal joint reactive forces across the tibio-talar joint that may predispose to the development of post-traumatic arthritis. The most current estimates for the burden of degenerative joint disease of the ankle is >50,000 cases reported each year in the United States (Buckwalter et al. 2004), up to 90% of which have been attributed to trauma (Saltzman et al. 2005).

Following initial ankle fracture treatment there are numerous complications that may result in reoperation. Reoperation itself can pose a large burden on the health-care system and overall patient morbidity. Additionally, treatment for post traumatic arthritis may include ankle debridement, arthroplasty or fusion. What is not clear is how these are impacted by patient demographics and provider factors (surgeon experience, volume, timing of surgery).

Previous work by our group which looked at the risks of complications, re-operation, and conversion to total knee replacements following surgically repaired tibia plateau fractures showed high level of success with our methodology (Leroux et al., 2014, Wasserstein et al., 2013, Wasserstein et al., 2014).

Aims of the proposed study:

We will:

1. Characterize the medical and surgical complication rates associated with ORIF of ankle fractures in a population-based cohort.
2. Characterize the risk of re-operation following ORIF of the ankle.
3. Identify independent patient, provider, and surgical factors associated with re-operation or medical complication after ORIF ankle.
4. Identify independent patient, provider, and surgical factors associated with surgical treatment for post traumatic osteoarthritis (ankle debridement, arthroplasty or fusion).

Therefore, treating physicians (orthopaedic surgeons including traumatologists and non-traumatologists) will be provided with prognostic information for use in counselling patients. Modifiable factors (e.g., surgeon volume, after-hours surgery) that are identified will be relevant data for healthcare planning. Finally, baseline rates of operative intervention serve as valuable pilot data for our group (and others once published) in the generation of hypotheses and design of focussed prospective comparative studies in ankle trauma.

III. Research Design and Method (1,000 words maximum):

Give a brief review of your study design and research method (as one would in an abstract for a meeting presentation).

All patients in Ontario, Canada, who suffered an ankle fracture will be identified in administrative healthcare databases held at the Institute for Clinical Evaluative Sciences (ICES). Patients aged less than 16 years old and non-Ontario residents will be excluded. Outcomes will include re-operation (irrigation and debridement, repeat ORIF, debridement, fusion, or arthroplasty) which will be identified in a similar manner.

A matched cohort design to compare the risk of ankle debridement, arthroplasty or fusion after ankle fracture is a technique we will employ to account for factors (age, sex, socioeconomic status) that independently predict treatment for post traumatic osteoarthritis and may not be related to the index event (Borkhoff et al., 2008; Hawker et al., 2000; Hawker et al., 2002).

Methods for taking measurements:

The primary databases include the Ontario Health Insurance Plan (OHIP) physician billing database and the Ontario Registered Persons Database. The OHIP database identifies paid claims for inpatient and outpatient services provided by physicians and surgeons. The Ontario Registered Persons database provides demographic information on patients. This information can be used to extrapolate other patient factors. For instance, socioeconomic status can be estimated by linking each patient's residential postal code to the corresponding Statistics Canada neighbourhood median household income.

Additional information is available through the Discharge Abstract Database (DAD) of hospital admissions, administered by the Canadian Institute for Health Information. The DAD database contains detailed diagnostic and procedural information for all acute care hospital admissions in the province of Ontario, Canada. Within the DAD are ICD-9 and ICD-10 diagnostic codes, and Canadian Classification of Intervention (CCI) procedural codes. ICD, CCI and OHIP fee codes will be used to define the cohort, identify covariates and define outcomes.

Metrics to evaluate outcomes of the project:

Index (Cohort Entry) Event: We will study all ankle fractures occurring between January 1994 and December 2011 (which will be identified using Ontario Health Insurance Plan (OHIP) physician fee codes, Discharge Abstracts and Same Day Surgery Databases (for ICD, CCI/P coding), and the Registered Persons Database). The maximum follow-up date will be December 2013, permitting a minimum 2-year follow-up.

Outcome Variables:

Outcomes will include known short-term complications of the index procedure and potential long-term sequelae of the injury (ankle fracture). These will be defined by subsequent OHIP fee code, and include:

Non-operative cohort

- Repeat closed reduction (<6weeks from index event)

Operative cohorts

- Repeat of index event (< 1 year following index event)
- Removal of Hardware (< 2 years from index event) in absence of other outcome
- Infection (< 1 year following index event)
- Amputation (from 6 weeks to 1 year following the index event)
- Ankle debridement (survival analysis – examine until end of study date or censor event)
- Ankle fusion (survival analysis – examine until end of study date or censor event)
- Ankle arthroplasty (survival analysis – examine until end of study date or censor event)

Subset analysis

- Revision ankle fixation for mal-union (from 6 weeks to 1 year following the index event)
- Revision ankle fixation for non-union (from 6 weeks to 1 year following the index event)

A 2-year outcome window will be sought for re-operation, except those in the spectrum of post-traumatic arthritis treatment (debridement, fusions or arthroplasty) which will be sought until study end date using a time-to-event analysis.

Covariates:

Patient factors:

- Age (continuous/categorical)
- Sex
- Charlson-Deyo Comorbidity Index
- Johns Hopkins' Collapsed Aggregate Diagnosis Groups (CADG) score
- Frailty score (Weiner and Abrams, 2011)
- Income quintile (using an established method based on Statistics Canada estimations of average income per single-person equivalents in geographic enumeration areas by postal code)
- Length of hospital stay

Provider factors:

- Academic or non-academic hospital status where the index event was performed (based on membership in the Council of Academic Hospitals of Ontario)
- Surgeon volume by quartile distribution of patients (volume calculated as number of index procedures in the calendar year prior)
- Surgeon experience by year of index event minus year of licensure in Ontario.

Surgical factors:

- Open fracture

- Medial malleolus
- Lateral malleolus
- Lateral malleolus + syndesmosis

Methods for data management and analysis:

Descriptive statistics will be used to characterize the cohort and covariates. Outcomes will also be described in a similar manner. The influence of covariates (patient, provider and surgical factors) on risk of re-operation and medical complications will be assessed using multivariate logistic regression analysis, with the type 1 error rate (alpha) set at 0.05.

Patients from the general population of Ontario who have not had a previous ankle fracture in Ontario will be matched to case patients (non-operative and operative cohorts) on a 2:1 basis. Matching will be according to age, sex, neighbourhood median household income quintile and rurality of the patient's home address. Survival analysis will be performed using the Kaplan-Meier approach. Censoring events will include death, emigration from Ontario (loss of OHIP), having the outcome, and the end of the study follow-up. A modified log-rank test will be used to compare the survival among cohorts at 1-year, 2-years, 3-years, 5-years, 10-years for each of those outcomes. A multivariate Cox Proportional Hazards model will be used to generate Hazards Ratios (with 95 CI) for each outcome with the covariates listed.

All analyses will be performed at the Institute for Clinical Evaluative Sciences (ICES) using SAS version 9.1 for UNIX (SAS Institute, Cary, NC), with the Type I error probability (alpha) set at 0.05.

IV. Role of the Resident (200 words maximum):

Thoroughly describe the role the resident will play in the research project, including development of the proposal, data collection and analysis and formulation of the manuscript.

The responsibilities of Dr. Thomas Zochowski for this proposed study will include assisting with study and statistical design, assisting to guide the analysis, interpretation of the study results, submission of grant applications, and finally manuscript preparation. Additionally, this research project is part of the core curriculum for residency as well as an area of interest. Dr. Andrea Veljkovic will supervise/mentor Dr. Zochowski in the process.

The expected duration will be approximately 12 months, starting from November 2014 and ending October 2015.

The completion of the project will follow a strict timeline involving study approval (1 month), data collection (first 5 months), data analysis and refinement (3 months), and manuscript preparation (3 months). Regular meetings with programming and statistical experts at the Institute for Clinical Evaluative Sciences (ICES) will take place in the first few months. Bi-weekly

meetings between the resident and supervising AO mentor will also occur to ensure the project's progress and guidance.

V. References (1 page maximum)

Beris AE, Kabbani KT, Xenakis TA, Mitsionis G, Soucacos PK, Soucacos PN. 1997. Surgical treatment of malleolar fractures. A review of 144 patients. *Clin Orthop Relat Res*; 341:90-98.

Borkhoff C, Hawker G, Kreder H, Glazier R, Mahomed N, Wright J. The effect of patients' sex on physician's recommendations for total knee arthroplasty. *CMAJ*. 2008;178(6):681-687.

Buckwalter JA, Saltzman C, Brown T. The impact of osteoarthritis: implications for research. *Clin Orthop Relat Res*. 2004; Oct;(427 Suppl):S6-15.

Burwell HN, Charnley AD. 1965. The treatment of displaced fractures of the ankle by rigid internal fixation and early joint movement. *J Bone Joint Surg Br*; 47:634-660.

Hawker G, Wright J, Coyte P, et al. Differences between men and women in the rate of use of hip and knee arthroplasty. *N Engl J Med*. 2000;342(14):1016-1022.

Hawker G, Wright J, Glazier R, et al. The effect of education and income on need and willingness to undergo total joint arthroplasty. *Arthritis Rheum*. 2002;46(12):3331-3339.

Leroux T, Ogilvie-Harris D, Dwyer T, Chahal J, Gandhi R, Mahomed N, Wasserstein D. The risk of knee arthroplasty following cruciate ligament reconstruction: a population-based matched cohort study. *J Bone Joint Surg Am*. 2014;96(1):2-10.

Lindsjo U. 1985. Operative treatment of ankle fracture-dislocations. A follow-up study of 306/321 consecutive cases. *Clin Orthop Relat Res*; 199:28-38.

Sporer M, Weinstein JN, Koval KJ. 2006. The geographic incidence and treatment variation of common fracture of elderly patients. *J Am Acad Orthop Surg*; 14:246-255.

Saltzman CL, Salamon ML, Blanchard GM, Huff T, Hayes A, Buckwalter JA, Amendola A. Epidemiology of ankle arthritis: report of a consecutive series of 639 patients from a tertiary orthopaedic center. *Iowa Orthop J*. 2005; 25:44-6.

Wasserstein D, Henry P, Paterson JM, Kreder HJ, Jenkinson R. Risk of total knee arthroplasty after operatively treated tibial plateau fracture: a matched-population-based cohort study. *J Bone Joint Surg Am*. 2014; 96(2):144-50.

Wasserstein D, Khoshbin A, Dwyer T, Chahal J, Gandhi R, Mahomed N, Ogilvie-Harris D. Risk factors for recurrent anterior cruciate ligament reconstruction: a population study in Ontario, Canada, with 5-year follow-up. *Am J Sports Med*. 2013; 41(9):2099-107.

OTA Resident Research Grant Budget Sheet

Budget cannot exceed \$20,000

Submitting a budget over this amount disqualifies your application for consideration

- Salaries and Wages: Enter name, percentage of time on project and salary requested as well as fringe benefits charged to the grant. Please also state what each person will be doing.
- Permanent Equipment: Justification to be appended.
- Consumable Supplies: Excludes animals and animal care.
- Animals and Animal Care: Justify all requests where need is not apparent.
- All Other Expenses: Charges for overhead are not covered by OTA Grants. No indirect costs will be funded.

SALARIES AND WAGES (List all personnel for whom money is requested)	% Of Time on this project	Requested from OTA Funds (Omit Cents)
Data Analyst/procurement	100%	\$2,000.00
Statistical Analysis	100%	\$2,000.00
	%	
	%	
Fringe Benefits - 0% of Salaries and Wages		
Salaries and Wages plus Fringe Benefits	TOTAL	

PERMANENT EQUIPMENT (Justification to be appended)	
Subtotal	

CONSUMABLE SUPPLIES (Exclude animals and animal care)	
Subtotal	

ANIMALS AND ANIMAL CARE	
Subtotal	

ALL OTHER EXPENSES	
Secure Integrated Data Platform Technical Costs	8,500.00
Unix Fees	3,500.00
Study set-up and approval	2,500.00
Subtotal	18,500.00

TOTAL DIRECT COSTS \$20,000

Justification of Budget

“Data Analyst/procurement” are fees incurred by accessing and compiling data from multiple databases based on search criteria defined by the research team. During the course of data compiling this individual will spend 100% of their time on the project. The cost has been estimated based on similar previous data procurement by our group.

“Statistical Analysis” are fees incurred by analyzing the data compiled from various health care databases as outline by the research team. During the time course of data analysis this individual will spend 100% of their time on the project. The cost has been estimated based on similar previous data procurement by our group.

"Secure Integrated Data Platform Technical Costs" are fees incurred by accessing and linking multiple databases held within collaborating government institutions. This is a requirement in order to complete this study which depends on information from multiple databases (physician billing, hospital admission, etc.). In addition to fixed costs for accessing the database we estimate costs related to crosslinking and validating database entries to ensure the same patient is being followed. Information on cost is obtained directly from ICES and relates to the size of the project(s) and dataset (expected >50,000 patients).

"UNIX fees" relate to secure data processing and storage that will be required to obtain the stated information. Data contains personal identifying information, and is required (as per the Ministry of Health for Ontario) to be handled in this manner. After study completion, the Ministry requires data be held securely for a period of 7 years before being destroyed. Costs incurred by data storage have been estimated based on ICES budget guidelines for a project in 2014/5.

"Study set-up and approval" costs include those related to privacy impact assessments and project activation which are fixed costs for doing this research at the Institute for Clinical Evaluative Sciences.

All costs are estimates based on the research teams extensive experience using these databases and with known fixed costs associated with budget forms at the Institute for Clinical Evaluative Sciences (our partner in this project).