RISK OF PERI-OPERATIVE MORBIDITY ASSOCIATED WITH TISSUE GRAFT TYPE FOLLOWING ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION SURGERY

By

Sara E. Hallvik

A THESIS

Presented to the Department of Public Health & Preventive Medicine
and the Oregon Health & Science University
School of Medicine
in partial fulfillment of
the requirements for the degree of

Master of Public Health

May 2010

Department of Public Health and Preventive Medicine

School of Medicine

Oregon Health & Science University

CERTIFICATE OF APPROVAL

This is to certify that the Master's thesis of

Sara E. Hallvik

has been approved

Lynn M. Marshall, ScD

Dennis C. Crawford, MD PhD

Jodi A. Lapidus, PhD

TABLE OF CONTENTS

LIST OF FIGURES & TABLES

LIST OF ABBREVIATIONS

ACL	Anterior Cruciate Ligament
BMI	Body Mass Index
CI	Confidence Interval
CMH	Cochran Mantel Hanszel
RD	Risk Difference
RR	Relative Risk

ACKNOWLEDGEMENTS

I am truly appreciative of my committee – Lynn Marshall, ScD, Dennis Crawford, MD PhD, and Jodi Lapidus, PhD – for their inspiration, guidance, and support throughout this thesis process. I also want to thank Ryan Petering, MD, and Sam Quilici, PA, for their work abstracting medical records, and Stephanie Lavigne for her assistance and advice. I am grateful for the support I received from the Department of Public Health & Preventive Medicine and the Department of Orthopedics & Rehabilitation. Finally, I am thankful for the unwavering support of my husband, family, and friends.

ABSTRACT

Anterior cruciate ligament (ACL) tears are a common knee injury. Surgical reconstruction of the ligament requires graft tissue. Autograft tissue, the standard of care, is obtained from the patient's own leg during surgery. Allograft tissue is procured from deceased human donors. Risk of peri-operative complication events associated with graft type is poorly characterized.

We used a retrospective cohort design to quantify risk of morbidity, defined as complication events in six months following primary arthroscopic ACL reconstruction. The patient cohort was identified through billing record queries for specific diagnostic and procedure codes. Patient demographics, graft type, and surgical information were abstracted from medical records. Complication events were identified through queries for specific diagnostic and treatment codes occurring in the six months following surgery. Risk of morbidity among patients receiving allograft tissue was compared to risk among patients receiving autograft tissue with Cochran Mantel Haenszel adjusted estimates of relative risk (RR) and 95% confidence intervals (CI).

The cohort included 413 patients. Average age was 33 (±12) years, 65% were male, and 66% received allograft tissue for ACL reconstruction. The six month risk of morbidity was 5% in the cohort: 7% among patients receiving allograft and 2% among patients receiving autograft tissue. After adjustment for patient sex, the RR for any complication was 3.0 (95% CI: 0.9-9.7) comparing allograft use with autograft use.

These results will help patients and surgeons weigh the short term risks and benefits of choosing allograft or autograft tissue for use in ACL reconstruction.

INTRODUCTION

Anterior cruciate ligament (ACL) tears are the most common ligamentous knee injury in the United States [1]. Over 100,000 people undergo ACL reconstruction surgery every year [2]. ACL tears lead to knee instability and associated dysfunction. Anatomic reconstruction is necessary to reliably regain full utility of the knee [3]. Reconstruction requires the use of tissue grafts to replace the damaged ligament. Historically, autograft tissue has been used to reconstruct the ACL. Autograft tissue is obtained at the time of surgery from the patient's hamstring or patellar tendon. In 2001, the United States Food and Drug Administration (FDA) approved tissue procurement and processing guidelines for tissue obtained from deceased human donors. Since then, allograft tissue has been increasingly used as an alternative to autograft tissue for ACL reconstruction [4].

Reconstruction of the ACL with allograft tissue has several advantages over the reconstructions performed with autograft tissue. These include reduced surgical and anesthesia time [1, 5, 7], lower pain scores in the 3 month period after surgery [5, 6], and more rapid achievement of rehabilitation goals [6]. One study suggested that reconstruction surgery with allograft tissue is less costly than surgeries using autograft tissue and that patients receiving allografts take less time off from work [7].

Physical functioning of the knee, allowing the patient to participate in running, jumping, or other physical activities following ACL reconstruction surgery, is comparable between patients with allograft tissue and patients with autograft tissue with two to five years of follow up [1, 8-12]. Physical functioning is commonly measured by

instrumented laxity measurements. A systematic review of seven studies reported laxity measurements of ≤5mm, signifying satisfactory physical functioning, among 91% to 100% of patients with autograft tissue and among patients with allograft tissue [9]. A meta-analysis of three studies comprised of 349 patients ages 18-43 years indicated that patients with allograft tissue were just as likely to not return to sport as patients with autograft tissue (odds ratio: 1.2, 95% CI: 0.72 – 2.0) [13]. Not returning to sport was used as a measure of unsatisfactory knee function. Similarly, the risk of graft re-rupture is comparable between allograft and autograft. With respect to graft re-rupture, one meta-analysis found that bone-patellar tendon-bone autografts were not significantly favored over allografts (p=.37) [13]. Another study found no occurrences of re-rupture in patients with either allograft or autograft tissue [10].

Complications are often measured by risk of graft failure or graft infection. A meta-analysis of twenty studies comparing patients with allograft and autograft tissue with a minimum of two years follow-up showed that the prevalence of graft abnormal stability, usually representing graft failure, was nearly three times greater in allografts than autografts [16]. Supporting this, a retrospective review documented a 23% prevalence of revision ACL reconstruction for graft failure among allograft tissue recipients with 42 to 74 months of follow-up, although no autograft patients were reviewed for comparison [17]. In contrast, one study demonstrated that the risk of infection of autograft tissue was nearly double the risk of infection of allograft tissue [18]. Finally, several other studies suggested that there was no difference in the risk of complications between patients with allograft and patients with autograft [8, 9, 18-21].

However, these studies were too small to exclude the possibility of differences in the risk of outcomes according to graft type used. Additionally, previous studies only examined the risk of deep infection of the knee joint (e.g. septic arthritis), or restricted study patients to those with a specific type of graft (e.g. bone-patellar tendon-bone allograft vs. bone-patellar tendon-bone autograft).

Allograft tissue is incorporated more slowly into the body than autograft tissue through a process called ligamentization [14, 15]. Slower ligamentization could increase the risk of infection or device removal in the peri-operative period following ACL reconstruction, but this issue has not been studied. The potential for infection among allograft tissue recipients has received lay press attention, suggesting that this is an important issue and of concern to patients [22, 23]. As the incidence of ACL tears increases with increasing population participation in sports, good outcomes from ACL reconstruction surgery are important to a large and growing number of people [24].

To date, risks of complication, including infection and device removal, occurring during the standard clinical course following primary ACL reconstruction with allograft tissue have not been directly compared to the risk of these complications using autograft tissue. To address this gap, we conducted a retrospective cohort study with 6 months of follow-up after ACL reconstruction to compare the risk of complications according to allograft and autograft tissue use.

METHODS

Data Sources

We performed a retrospective cohort study using medical records from a board certified orthopedic surgeon at Oregon Health and Science University (OHSU). The study procedures described here were approved by the OHSU Institutional Review Board. The study cohort was comprised of patients age 12 to 60 years undergoing ACL reconstruction between January 1, 2003 and June 30, 2009 from the surgical practice of one of the authors. We used queries of billing databases and electronic medical records to assemble the patient cohort. Follow-up for six months from the date of surgery was also accomplished with queries of the billing system for records regarding complications. A schematic representation of the cohort development and follow-up is shown in Figure 1. The details of our approach are now described.

OHSU used the LCR Signature© (Malvern, PA) system before implementing the Epic© (Verona, WI) medical record system in October 2005. Because both systems were used during the study period, an identical query was performed on records stored in each system to identify eligible patients. Records in the LCR Signature© system were queried for dates of service from 1/1/2003 through 9/30/2005 and records in the Epic© system were queried from 10/1/2005 through 6/30/2009. The remaining query parameters were: 1) consultation and ACL reconstruction performed by one of the authors, 2) International Classification of Disease, 9th Revision (ICD9) code for ACL tear (844.2), and 3) any of three specified Current Procedural Terminology (CPT) codes for ACL reconstruction

(29888, 27428, or 20924). Electronic query reports from both systems yielded the following information: patient medical record number, date of birth, sex, date of service, attending physician, ICD9 code, and CPT code.

Of the 487 patients identified by the queries, we excluded 65 (13.3%) due to previous ACL reconstruction on the same knee, 2 (0.4%) because of missing information on graft type used in ACL reconstruction, and 7 (1.4%) who were older than age 60. The remaining 413 patients comprised the study cohort.

Ascertainment of Patient and Surgical Characteristics

Two authors (including the MPH candidate) manually abstracted data from electronic medical records on patient characteristics at the time of surgery. Patient characteristics and surgical notes are stored on different screens in the medical record that cannot be viewed at the same time. Abstractors recorded the demographic information on all patients in the cohort before proceeding to the screen that displayed the surgical information. In this way, abstraction of the patient characteristics was blinded to graft type. All records were abstracted with numeric codes on to a standardized paper form (Appendix A). Data were then entered manually to an electronic database.

Patient characteristics included sex, ethnicity (Hispanic or non-Hispanic), marital status (married or not married), smoking status at the time of surgery (any smoking reported in the last month), diabetes status at the time of surgery, age at the time of surgery (calculated as the difference in years between the date of birth and date of

surgery) and body mass index (calculated from weight and height measurements on the day of surgery).

The variables regarding surgical characteristics included graft type (allograft or autograft), the main exposure variable, in addition to graft harvest site (hamstring, patellar tendon, anterior tibialis tendon, or Achilles tendon), concomitant procedures (none, cartilage, ligaments, transplants or alignment), sciatic nerve block use, spinal nerve block use, femoral nerve block use (none, single nerve block, or home pump catheter), general anesthesia (monitored anesthesia care or general anesthesia), tibial fixation device (washer lock, interference screw, or bio-intra-fix), femoral fixation device (endobutton or interference screw), prior non-ACL knee surgery on the same knee, length of anesthesia care (in minutes), length of surgery (measured in minutes from incision to wound closure), and tourniquet use (in minutes).

A research manual with abstraction guidelines including specific locations of information within the medical record was used to maintain consistency between abstractors (Appendix B). To verify consistency, an inter- and intra- rater reliability assessment was conducted on a 10% random sample of records. Inter-rater and intra-rater agreement was calculated for each record abstracted in the random sample, then averaged across all records and assessed for agreement. Only variables manually abstracted from medical records were assessed. On average, inter-rater agreement was 98% and intra-rater agreement was 97%. The few discrepant values were reviewed and resolved by the abstractors.

Follow-up and Ascertainment of Outcomes

Complications of ACL reconstruction that occurred during follow-up were identified by specific CPT and ICD9 codes (Table 1), obtained with a second query of the OHSU billing systems. The following search parameters were used: 1) date of diagnosis and service between January 1, 2003 and December 31, 2009, 2) consultation and treatment provided by one of the authors, and 3) at least one ICD-9 or CPT code listed in Table 1 indicative of infection, complication of the fixation device, surgical incision and drainage, debridement, or implant removal.

Each patient was followed from his or her date of surgery for 6 months. Six months is the standard length of clinical follow-up for ACL reconstruction patients. To determine the complications experienced only for patients in the study cohort, we eliminated records returned by the query for patients that were not in the cohort. We accomplished this by merging the medical record numbers for the cohort with the medical record numbers retrieved from the query and deleting any that did not match. Records for events that did not occur within the 6 month follow-up period for each patient were also excluded. Finally, we merged patient cohort records with complication records, creating the analysis dataset (Figure 1).

Complication outcome events were defined as follows. The first complication occurring within 6 months of ACL reconstruction was noted from the billing record query. We separated complications into categories for infectious and non-infectious primary complication events. Infections included deep infections of the knee joint and

superficial wound infections. Non-infectious complications included painful orthopedic fixation device and subsequent removal, arthrofibrosis, and neuropathy. Some patients experienced multiple complications. Therefore, for additional analyses we also classified complications occurring anytime during the follow-up period.

Strategy to Minimize Loss to Follow-up

Complications treated outside of the OHSU system may have been missed by our review of billing records. Therefore, to document external hospital admissions, emergency department visits, or outpatient visits we reviewed written records of phone calls made by the OHSU orthopedic clinic staff to patients. The orthopedic clinic staff routinely contact patients within one week of ACL reconstruction surgery. A phone conversation was recorded for 185 (44.8%) patients, 90 (48.6%) of whom reported no concerns. Only 7 (3.8%) patients expressed concern about symptoms indicative of a potential complication, all of which were documented in the billing system query. The remaining 88 (47.6%) patients had concerns about pain and medication, which were not examined as outcomes of this study.

Evaluation of Outcome Misclassification

To evaluate the possibility that complications were missed because of our use of billing record queries, we reviewed the clinic notes for 70 patients without a previously identified complication. We sampled 10 patients from each study year such that distribution of graft type was in proportion to that for the clinical practice in the particular year. We abstracted details regarding any mention of complication events within 6

months of ACL reconstruction surgery and the date of every follow-up visit within 6 months.

Statistical Analysis

In separate descriptive analyses, distributions of patient and surgical characteristics were examined according to graft type used in ACL reconstruction and then according to complication status. Differences in proportion of categorical variables were compared with chi-square of Fisher's exact tests, and differences in mean of continuous variables were compared with independent two sample t-tests. Variables that were associated both with graft type and with risk of complication were considered as potentially confounding variables and evaluated in stratified analyses.

Outcome frequency was measured with an incidence proportion. The crude and adjusted association between graft type and risk of any complication was evaluated, and then separated into infectious and non-infectious complications based on the index event. First we estimated difference in proportions using Fisher's exact tests. Then we used Cochran Mantel Hanszel (CMH) statistics to estimate crude risk ratios (relative risk [RR]) and 95% confidence intervals (CI). CMH provides a weighted average of stratum-specific estimates, effectively controlling for confounding in the relatively small sample size available in this study. Then we estimated the risk difference (RD) to determine the percentage of risk among patients with allograft tissue that was over and above the background risk, established as the risk among patients with autograft tissue. A variable

was considered to be a confounder if control for it in the stratified analysis resulted in an adjusted RR estimate that differed from the crude RR estimate by 10%.

To quantify the effect of missed outcome complications, we re-calculated the association between graft type and the risk of any complication under the assumption that the proportion of complications missed in the random patient sample accurately estimate the proportion of complications events missed in the entire cohort. First we calculated the number and proportion of patients for whom a complication event was potentially missed. Then we added the number of patients for whom a complication was observed, and evaluated the crude association between graft type and risk of any complication with estimates of risk ratios (relative risk) and risk difference.

Last, we performed a descriptive analysis among the patients who had undergone ACL reconstruction revision. These patients were excluded from the primary cohort, because they were not at risk for an index complication resulting from a primary ACL reconstruction surgery. However, there is little information on outcomes of ACL reconstruction revision according to graft type and the data could provide useful observations to guide further investigations.

All analyses performed using SAS ® software, Version 9.2 of the SAS System for OHSU (Cary, NC).

RESULTS

The study cohort included 413 patients with a mean age of 33 (±12) years (Table 2). Two thirds (66%) of the patients received allograft tissue for surgical reconstruction of their ACL. Patients who received allograft tissue were on average older and with higher body mass index (BMI) compared to those who received autograft tissue, and were more likely to be female or married.

Information on cigarette smoking and diabetes status were often not recorded in the medical records. Although the proportion of missing smoking information was comparable among patients who had received allograft and autograft tissue, missing information on diabetes status was more frequent among patients who had received autograft tissue. We compared patients with missing values to patients without missing values to assess the impact of these missing data. Nonetheless, proportions of patients recorded as having diabetes were similar among the graft types.

All allograft tissue was procured from one tissue bank accredited by the American Association of Tissue Banks (AATB). Allografts included 198 (72.8%) anterior tibialis tendons, 36 (13.2%) hamstring tendons, 14 (5.2%) Achilles tendons, 2 (0.7%) patellar tendons, and 22 (8.1%) allograft patients for whom the graft source was not recorded. All allograft tissue was irradiated at a low dose. The surgeon followed a standard single-incision arthroscopic technique in all primary ACL reconstruction surgeries. Of 413 procedures, a tourniquet was only used on one patient. We examined annual trends of patient and surgical characteristics to evaluate the role of potential changes over time.

The proportion of patients with allograft tissue increased across the study years (Figure 4). No other annual trends were observed.

The risk of any complication varied according to sex and cigarette smoking (Table 3). While 3.0% of men experienced any complication, 9.7% of women experienced any complication (p=.01). Among smokers, 8.3% developed any complication, while 5.7% of non-smokers developed any complication (p=.27). The risk of any complication did not differ by any other patient or surgical characteristic. The length of anesthesia care was examined as an indicator of surgery length. Anesthesia care was, on average, 48 minutes longer in autograft surgeries than allograft surgeries ($p<0.01$). The length of anesthesia care was, on average, 11 minutes longer for patients with any concomitant procedure. Changes to the anesthesia record system prevented analysis of surgery time (incision to wound closure) for the entire cohort. The length of surgery was only collected in 2008 and 2009. In these years, the average length of anesthesia care was 2.3 times longer than the length of surgery (Figure 3).

Peri-operative antibiotic administration is standardized by OHSU hospital protocols and was applied to all patients, regardless of graft type. All patients were given Ancef 1 gram IV or Clindamycin if an allergy to Penicillin based antibiotics was known.

Distributions of sex, marital status, diabetes, age, and BMI differed according to graft type, and were therefore considered potentially confounding factors (Table 4). Distributions of sex and cigarette smoking were associated with the presence of any complication event, and therefore added to the list of potentially confounding factors.

However, only sex was independently associated with both graft type and complication risk, so was considered a potentially confounding variable.

Within six months of ACL reconstruction, 22 (5.3%) patients experienced at least one complication (Table 5). Of 272 patients who received allograft tissue, 19 (7.0%) experienced at least one complication. Of 141 patients who received autograft tissue, 3 (2.1%) experienced at least one complication (p=0.04). The relative risk of any complication was 3.3 (95% CI: 1.0 – 10.9) times greater among patients who received allograft tissue than the risk among patients who received autograft tissue. When the association of graft type and complication was adjusted for sex, the risk of a complication occurring in the six months following reconstruction surgery remained 3-fold greater among those who received allograft tissue compared to those who received autograft tissue (RR=3.0, 95% CI: 0.9 – 9.7). This translates into a risk difference of 5% (95% CI: 1% - 9%), which means that the risk of any complication among patients with allograft tissue was 5% greater than the background risk of complication within 6 months following ACL reconstruction surgery. To address the concern that the billing system change in October 2005 could have resulted in differential misclassification of complications, we restricted analysis of ACL reconstructions recorded in a single billing system, between 2006 and 2009. Our findings corroborated the results of the full analysis cohort.

Non-infectious complications, such as painful orthopedic fixation device and subsequent removal, were observed as a primary complication event in 14 (3.4%) patients (Table 6). We observed 12 (4.4%) primary non-infectious events among patients

receiving allograft tissue compared to 2 (1.4%) patients who received autograft tissue. The adjusted RR is consistent with a 2.7-fold greater risk of non-infectious complication among patients receiving allograft tissue compared to those who received autograft tissue, although the 95% CI for this estimate is wide due to the small number of events. The risk difference was 3% (95% CI: 0% - 6%), which means that the risk of a non-infectious complication among patients with allograft tissue was estimated to be 3% greater than the background risk of non-infectious complication within 6 months following ACL reconstruction surgery. Over the entire course of follow-up, we observed 7 (2.6%) primary non-infectious events among patients receiving allograft tissue compared to 2 (1.4%) patients who received autograft tissue. The adjusted RR was 1.5 (95% CI: 0.3-7.6) which translated into a risk difference of 1% (95% CI: 0% - 4%).

Deep infection of the knee joint requiring graft removal was observed in 5 (1.2%) patients. We observed infections leading to graft removal in 4 (1.5%) patients receiving allograft tissue compared to 1 (0.7%) patient who received autograft tissue.

Infectious complications, including infections at the surgical incision site and deep infections of the knee joint, were observed as a primary complication event in 8 (2.6%) patients (Table 7). We observed infections in 7 (2.6%) patients who received allograft tissue compared to infection in 1 (0.7%) patient who received autograft tissue. Although the adjusted RR is consistent with a 3.5 fold greater risk of infection among patients receiving allograft tissue compared to those who received autograft tissue, this estimate lacks precision due to the small number of events. The risk of infection among patients who received allograft tissue was 2% (95% CI: 0% - 4%) greater than the

background risk of infection within 6 months following ACL reconstruction surgery. Over the entire course of follow-up, 13 (3.1%) patients experienced an infectious complication, inclusive of the 8 (2.6%) patients with an index infection. The risk of any infection during the course of follow-up was 5.7 (95% CI: 0.8 – 39.8) times greater among patients receiving allograft tissue than the risk among patients receiving autograft tissue, which translated into a risk difference of 4% (95% CI: 1% - 7%).

The risk of any complication differed according to sex. Therefore, in further descriptive analyses, we evaluated the association between graft type and complications stratified by sex (Table 8, Figure 2). Among men, the proportion of patients with an infection who received allograft tissue was 3.6% compared to 0 who received autograft tissue. Non-infectious complications were observed in 1 (0.6%) patient with allograft tissue and 1 (1.0%) patient with autograft tissue. Among women, the proportion with an infection among those who received allograft tissue was 1% compared to 2.4% who received autograft tissue. The proportion of patients with a non-infectious complication who received allograft tissue was 10.7% compared to 2.4% who received autograft tissue.

To further examine the potential for outcome misclassification, we reviewed the clinic notes from the follow-up visits of 70 patients (Table 9). All 70 (100%) patients were seen for at least one follow-up appointment which occurred, on average, 10 (±8) days following ACL reconstruction surgery. Morover, most patients (n=52 (74.3%)) were seen for a third appointment, which occurred on average 76 (± 35) days following surgery, the time at which the patient may be released to linear physical activities such as running or cycling if they are healing as expected. Slightly more than half (57%) the

patients returned for a fourth follow-up visit occurring, on average, 116 (±79) days after surgery.

Within this random sample, a complication event was observed within the follow-up period in the clinic note of 5 (7.1%) patients, 4 (10%) with allograft and 1 (3%) with autograft, for whom a complication was not identified through the billing record query. The distribution of missed complications according to graft type is similar to the distribution of observed complications in the analysis cohort. Complication events included one potentially infected surgical incision, one graft rupture following a fall, and three instances of painful orthopedic fixation devices.

We evaluated the impact of missed outcome complications in Table 10. Applying the proportion of missed outcome complications from the sample population to the entire study cohort, there would be 8 (5.7%) patients with autograft tissue and 47 (17.3%) patients with allograft tissue who experienced any complication within six months of ACL reconstruction. The RR would be relatively unchanged at 3.0 (95% CI: 1.5 – 6.3), although the smaller confidence interval indicates a more precise estimate, due to the increased number of observations. The magnitude of the risk difference would increase substantially from 5% to 12%.

All analyses were based on the first complication event for patients with any complication, but some patients experienced more than one complication. We reviewed the clinical course of those with any complication to examine the risk of all complications during the follow-up period according to graft type (Table 11).

Ultimately, most patients had satisfactory clinical outcomes following ACL reconstruction. A satisfactory clinical outcome is defined as full functionality of the knee, even if the patient experienced a painful orthopedic fixation device, superficial wound infection, or other inconsequential complication. Poor clinical outcomes are defined as infection of the knee joint and subsequent graft removal. Poor clinical outcomes were observed in 4 (1.5%) patients who received allograft tissue compared to 1 (0.7%) patient who received autograft tissue. All 5 (1.2%) patients had their grafted ACL removed within six months of surgery due to deep infection of the knee joint. The remaining 17 (4.1%) patients who experienced any complication ultimately achieved positive clinical outcomes, returning to sport and activities of daily living without limitation.

Seven patients, all with an allograft, experienced a superficial wound infection any time following ACL reconstruction surgery. Among patients who presented with any complication within 6 months of ACL reconstruction, the tibial fixation device of 14 (3.4%) patients was ultimately removed. Of 331 patients in whom a WasherLoc (Biomet) was used, the fixation device was removed in 12 (3.6%) cases. Of 65 patients in whom a Bio-Intra Fix (Mitek, a J&J Company) was used, the fixation device was removed in 2 (3.1%) cases. Metal interference screws (Arthrex) were used in 17 patients, but none were removed. Complications among the remaining four patients were appropriately treated and resolved.

Revision Cohort Results

Patients having undergone ACL reconstruction revision surgery were entered into a separate cohort and analyzed (Table 12). Within this cohort, 60 patients (92.3%) received allograft tissue. Patients who received allograft tissue were more likely than patients who received autograft tissue to be female, not married, or a smoker at the time of surgery. Within six months of ACL reconstruction revision, 7 (10.8%) patients experienced at least one complication (Table 13). Among patients who received allograft tissue, 7 (11.7%) experienced a complication. No patients who received autograft tissue experienced a complication.

DISCUSSION

In this retrospective cohort study we observed that the risk of complication, including infection or device removal, in the six months following the first ACL reconstruction surgery was 5%. This risk fits within the reported range of risk in literature, from 0 to 9% risk by laxity measurements, and 0 to 12% by graft failure [9]. A 5% risk of any complication event is quite low, especially given that the most common complication events in this study, painful orthopedic fixation devices and superficial wound infections, were treated and patients ultimately achieved positive clinical outcomes.

Risk of complications varied according to type of graft tissue used. Among patients who received allograft tissue, the risk of complication was 7% compared to 2% among patients who received autograft tissue. This means that the risk of complication among patients who received allograft tissue was 5% greater than the risk of complication among patients who received autograft tissue. This is notable, given that the physical functioning of the knee is comparable between patients with allograft tissue and patients with autograft tissue after two to five years of follow up [1, 8-12].

The risk of infection within six months appeared to be greater among patients who received allograft tissue than patients who received autograft tissue, although the small number of patients experiencing infection reduced the precision of the relative risk estimate. It is unlikely the observed infections in this study were caused by infected graft tissue. In cases in which infected graft tissue was used, symptom onset occurred within 1 to 3 days [22]. In this study, infection symptoms presented, on average, 25 days

following reconstruction surgery, suggesting that infection was caused by bacterial exposure following surgery, not the graft itself.

The present results enhance our understanding of the short term risk of complication following ACL reconstruction. While previous studies have examined differences in graft-associated risk of complications, the studies were too small to exclude the possibility of differences in risk of outcomes according to graft type used [9]. This study was powered to detect a relative risk difference of 2.8. By expanding the definition of complications, including all graft harvest sites, and extending the study period over 7 years, we achieved sufficient power to detect a difference in risk of outcomes according to graft type used.

We have no explanation for the apparent sex difference in type of complication experienced among those who received allograft tissue. We reason that men who receive allograft tissue may resume physical activity more quickly than men who receive autograft tissue, which could increase the likelihood of infection. Thus, it is possible that the surgical wound is not completely healed, and therefore remains vulnerable to bacterial exposure. Although few men in the study cohort experienced an infection following their surgery, our results indicate that it may be prudent to include information on hygienic practices in the discharge instructions. For women, we posit that the size of the graft could explain the increased frequency of device removal among those receiving allograft tissue compared to those receiving autograft tissue. Autograft tissue tends to be proportionally sized to the patient's knee, while allograft tissue is generally larger [1]. Larger grafts require larger tunnels, which may increase discomfort. We were unable to

evaluate this possibility because graft size was not recorded. This topic should be examined in future research.

The retrospective cohort design used in this study presented some possible limitations that we addressed systematically. Loss to follow-up is a common concern in cohort studies. The institution of the present study serves patients from the geographic region, without a clear catchment area. Additionally, this patient population was relatively young (average age of 33 years) and mobile (56% not married). Complications experienced by patients who sought care from an external provider could be misclassified non-differentially, potentially underestimating the overall risk of any complication. We attempted to minimize this potential loss to follow-up by recording the topic of telephone conversations within the week following ACL reconstruction, and noting any hospital admittances and emergency department visits at the study institution. The short follow-up period also reduces the risk of patients moving out of the area. Additionally, every patient included in our random 70-patient sample was seen at least once following surgery. Within 10 weeks of surgery, 74% had been seen at least three times, suggesting loss to follow-up is unlikely to be a substantial threat to internal validity.

It is clinically recommended that patients continue follow-up visits through 6 months following surgery, when they are released to full activity. However, if a patient is healing without complication, they may be less likely to adhere to this recommendation. Additionally, rehabilitation protocols progress stepwise, allowing patients to begin running, cycling, and other linear activities around 3 months. For many patients, these activities are more strenuous than their desired activities. While patient attendance at

follow-up visits past 3 months dropped off, this may be due to patient satisfaction with rehabilitation.

Our data suggest that complications may have been missed by using billing records. The potentially missed complications identified in the random sample were somewhat more likely to have occurred among those with autograft tissue. The effect of missed complications therefore was to slightly overestimate the RR estimate in the cohort studied. Nonetheless, inference regarding the association of allograft tissue with a risk of complications did not change: accounting for potentially missed complications still resulted in a 3-fold greater risk of complications associated with allograft tissue use compared to autograft tissue use in the 6 months following ACL reconstruction.

The precision of the relative risk estimate, however, increased with additional complication events, evidenced by the smaller confidence interval. The magnitude of the risk difference increased substantially. This experience illustrates that effects of outcome misclassification are likely to differ depending on whether the measure of association is a risk ratio or a difference. In this setting, a combination of billing record queries and medical record abstraction may be necessary to accurately ascertain complications.

From an administrative perspective, the observed discrepancy between complication events noted in patient medical records and complication events that lead to a billed charge may highlight a need for collaboration between physicians and administrative staff to ensure the department is reimbursed for all services rendered. Alternatively, this observed discrepancy could be attributed to working diagnoses, or

provider suspicions, compared to billed diagnoses, which require a therapeutic intervention.

Pain following surgery is an important aspect of patient satisfaction with ACL reconstruction. This study did not examine pain following surgery. However, existing literature suggests that patients in whom allograft tissue is used in ACL reconstruction report less subjective pain than patients in whom autograft tissue is used [1, 6].

Identification of septic arthritis complications were confirmed with positive culture results. Superficial wound infections were often indolent, but were not confirmed by positive culture results. That is, superficial wound infections were subjectively determined based on surgeon assessment. Cultures are not routinely taken for superficial wound infections because of the high risk of false positives. As such, each was treated as a typical wound infection with routine antibiotics. Surgeon caution regarding infection of the surgical incision may have lead to an over-estimate of risk for superficial wound infection.

The results of this study may be applicable to the regional population. The study population is shares a demographic distribution similar to the population in the study center's geographic region [26]. Additionally, patient characteristics of our cohort were similar to the study population in a large Danish ACL registry according to sex, duration of surgery, and peri-operative complications, suggesting our results may applicable to a larger population [27].

Limiting our cohort to patients from a single surgeon's practice may have introduced surgeon bias. The attending physician may have noted more, or less, concern

over potential complications for patients with allograft tissue relative to patients with autograft. Limiting our cohort may also have limited the sample size of this study. However, by including only patients from a single surgeon's practice in our cohort, we controlled for differences such as surgeon preference and experience, which are common potential confounders [9, 13, 16]. Additionally, the risk of any complication did not change materially across the study years, suggesting that surgeon experience was not a factor in the risk of complication within six months of primary ACL reconstruction.

Treatment decisions regarding graft type used for ACL reconstruction are informed by discussion with patients about the risks and benefits of the graft type. Our study indicates that clinical decision making about graft choice should recognize the possibility that risk of infection or device removal within six-months following ACL reconstruction with allograft tissue is somewhat greater than risk of these outcomes when autograft tissue is used. Further, patients and surgeons may find reassurance that the majority of these complications resolve quickly and without need for revision surgery. Additional work is needed to determine the most effective ways to minimize risk of infection and to elucidate the reasons device removal primarily occurs among women.

REFERENCES

1. Baer, G.S. and C.D. Harner, *Clinical outcomes of allograft versus autograft in anterior cruciate ligament reconstruction.* Clin Sports Med, 2007. **26**(4): p. 661-81.
2. Fu, F., et al., *Graft selection for anterior cruciate ligament reconstruction.* Instr Course Lect, 2009. **58**: p. 337-54.
3. Clayton, R.A. and C.M. Court-Brown, *The epidemiology of musculoskeletal tendinous and ligamentous injuries.* Injury, 2008. **39**(12): p. 1338-44.
4. Vangsness, C.T., Jr., et al., *Allograft transplantation in the knee: tissue regulation, procurement, processing, and sterilization.* Am J Sports Med, 2003. **31**(3): p. 474-81.
5. Kuhn, M.A. and G. Ross, *Allografts in the treatment of anterior cruciate ligament injuries.* Sports Med Arthrosc, 2007. **15**(3): p. 133-8.
6. Poehling, G.G., et al., *Analysis of outcomes of anterior cruciate ligament repair with 5-year follow-up: allograft versus autograft.* Arthroscopy, 2005. **21**(7): p. 774-85.
7. Bach, B.R., Jr., et al., *Primary anterior cruciate ligament reconstruction using fresh-frozen, nonirradiated patellar tendon allograft: minimum 2-year follow-up.* Am J Sports Med, 2005. **33**(2): p. 284-92.
8. Indelli, P.F., et al., *Septic arthritis in postoperative anterior cruciate ligament reconstruction.* Clin Orthop Relat Res, 2002(398): p. 182-8.

9. Carey, J.L., et al., *A systematic review of anterior cruciate ligament reconstruction with autograft compared with allograft.* J Bone Joint Surg Am, 2009. **91**(9): p. 2242-50.

10. Zhang, L., et al., *[Comparison of the clinical outcome of anterior cruciate ligament reconstruction using allograft anterior tibialis and autologous hamstring tendon]*. Zhongguo Gu Shang, 2009. **22**(3): p. 166-9.

11. Ozenci, A.M., et al., *Proprioceptive comparison of allograft and autograft anterior cruciate ligament reconstructions.* Knee Surg Sports Traumatol Arthrosc, 2007. **15**(12): p. 1432-7.

12. Sun, K., et al., *[A prospective study of the anterior cruciate ligament reconstruction: allograft versus autograft]*. Zhonghua Wai Ke Za Zhi, 2004. **42**(16): p. 989-92.

13. Krych, A.J., et al., *A meta-analysis of patellar tendon autograft versus patellar tendon allograft in anterior cruciate ligament reconstruction.* Arthroscopy, 2008. **24**(3): p. 292-8.

14. Lomasney, L.M., P.M. Tonino, and M.R. Coan, *Evaluation of bone incorporation of patellar tendon autografts and allografts for ACL reconstruction using CT.* Orthopedics, 2007. **30**(2): p. 152-7.

15. Menetrey, J., et al., *"Biological failure" of the anterior cruciate ligament graft.* Knee Surg Sports Traumatol Arthrosc, 2008. **16**(3): p. 224-31.

16. Prodromos, C., B. Joyce, and K. Shi, *A meta-analysis of stability of autografts compared to allografts after anterior cruciate ligament reconstruction.* Knee Surg Sports Traumatol Arthrosc, 2007. **15**(7): p. 851-6.

17. Singhal, M.C., J.R. Gardiner, and D.L. Johnson, *Failure of primary anterior cruciate ligament surgery using anterior tibialis allograft.* Arthroscopy, 2007. **23**(5): p. 469-75.

18. Katz, L.M., et al., *A retrospective comparison of the incidence of bacterial infection following anterior cruciate ligament reconstruction with autograft versus allograft.* Arthroscopy, 2008. **24**(12): p. 1330-5.

19. Matava, M.J., et al., *Septic arthritis of the knee following anterior cruciate ligament reconstruction: results of a survey of sports medicine fellowship directors.* Arthroscopy, 1998. **14**(7): p. 717-25.

20. Sun, K., et al., *Anterior cruciate ligament reconstruction with bone-patellar tendon-bone autograft versus allograft.* Arthroscopy, 2009. **25**(7): p. 750-9.

21. Barrett, G., D. Stokes, and M. White, *Anterior cruciate ligament reconstruction in patients older than 40 years: allograft versus autograft patellar tendon.* Am J Sports Med, 2005. **33**(10): p. 1505-12.

22. Labi, N., *Deadly transplants.* Time, 2002. **160**(9): p. 50-1.

23. Blakeslee, S., *Lack of oversight in tissue donation raising concerns.* NY Times (Print), 2002: p. A1, A22.

24. Arendt, E.A., J. Agel, and R. Dick, *Anterior Cruciate Ligament Injury Patterns Among Collegiate Men and Women.* J Athl Train, 1999. **34**(2): p. 86-92.

25. Ahn, J.H., Y.S. Lee, and H.C. Ha, *Comparison of revision surgery with primary anterior cruciate ligament reconstruction and outcome of revision surgery between different graft materials.* Am J Sports Med, 2008. **36**(10): p. 1889-95.

26. *2006-2008 American Community Survey Fact Sheet: Multnomah County, Oregon.* 2006-2008 [cited 2010 3/13]; Available from: http://factfinder.census.gov/servlet/ACSSAFFFacts?_event=&geo_id=05000US41051&_geoContext=01000US|04000US41|05000US41051&_street=&_county=Multnomah+County&_cityTown=Multnomah+County&_state=04000US41&_zip=&_lang=en&_sse=on&ActiveGeoDiv=&_useEV=&pctxt=fph&pgsl=050&_submenuId=factsheet_1&ds_name=null&_ci_nbr=null&qr_name=null&reg=null%3Anull&_keyword=&_industry=.

27. Lind, M., F. Menhert, and A.B. Pedersen, *The first results from the Danish ACL reconstruction registry: epidemiologic and 2 year follow-up results from 5,818 knee ligament reconstructions.* Knee Surg Sports Traumatol Arthrosc, 2009. **17**(2): p. 117-24.

Figure Titles

Figure 1 Cohort Development and Ascertainment of Outcomes for Primary ACL Reconstruction Patients: Portland, OR 2003-2009

Figure 2 Risk of any Complication According to Infection Status, Sex, and Graft Type used in ACL Reconstruction: Portland, OR 2003-2009

Figure 3 Correlation of Length of Anesthesia Care to Length of Surgery among Primary ACL Reconstruction Patients: Portland, OR 2008-2009

Figure 4 Frequency of Allograft vs. Autograft Use in ACL Reconstruction Surgery According to Year: Portland, OR 2003-2009

Figure 1

Figure 2

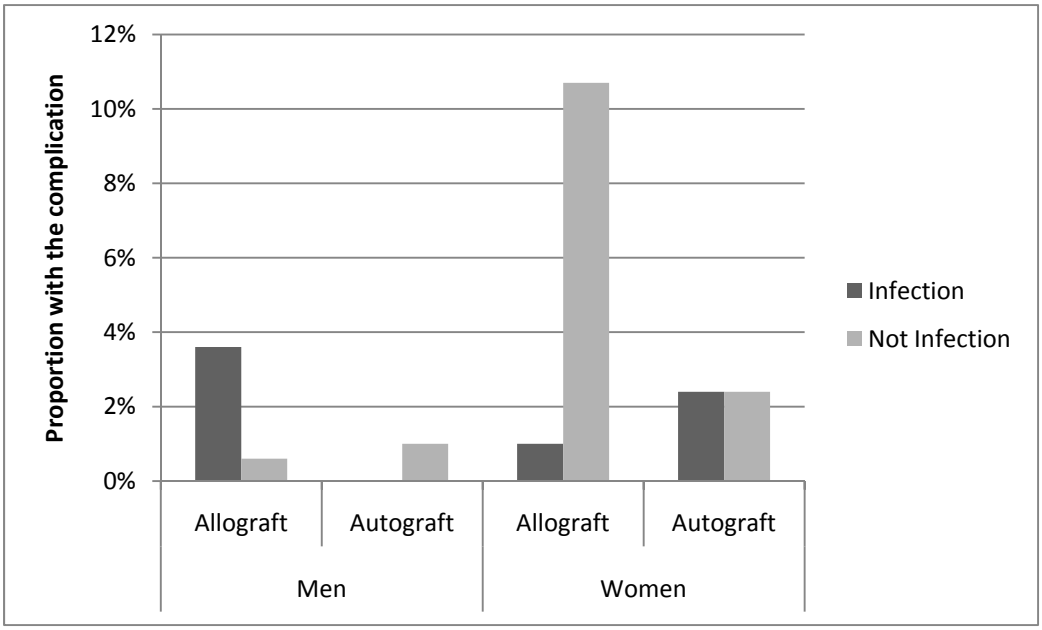
12%
10%
8%
6%
4%
2%
0%
Proportion with the complication
Allograft
Autograft
Allograft
Autograft
Men
Women
Infection
Not Infection

Figure 3

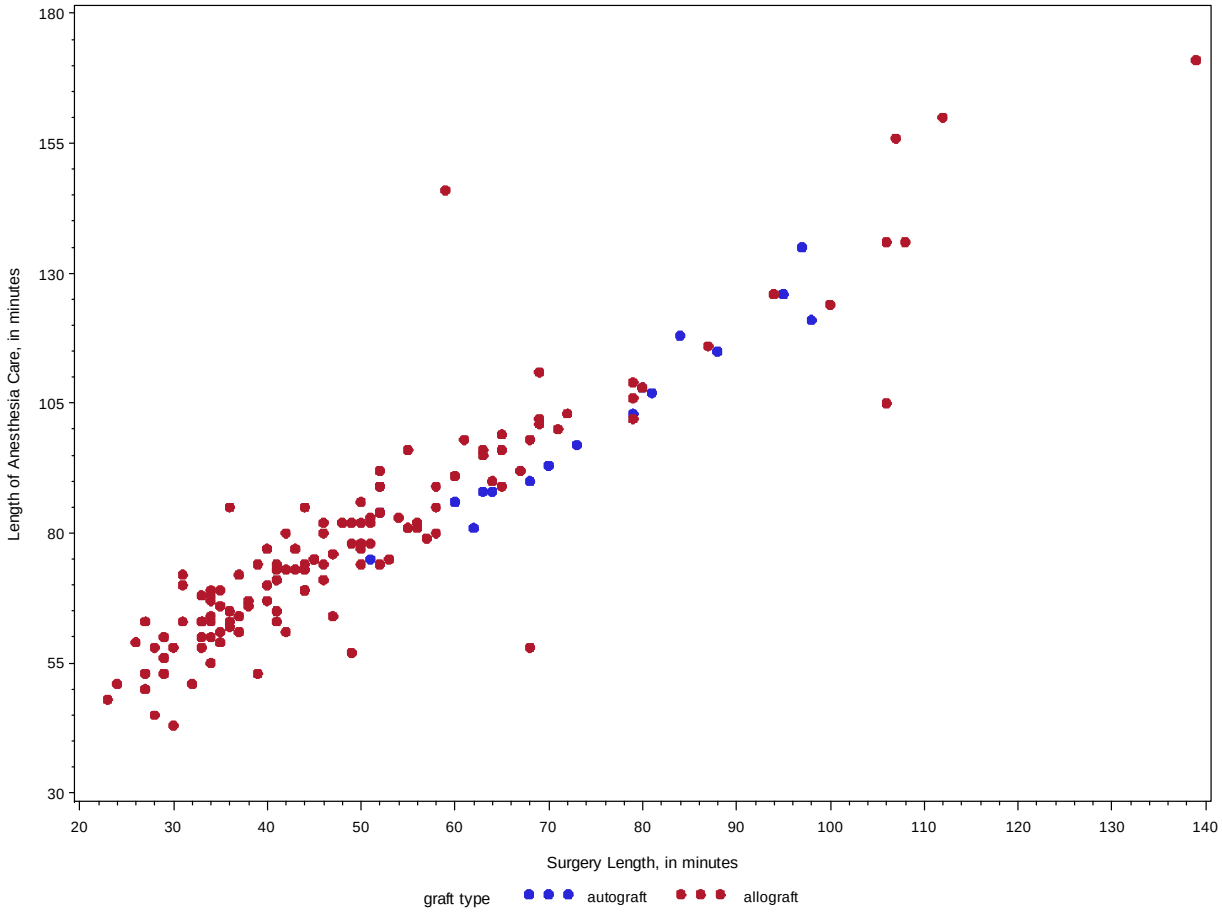
Length of Anesthesia Care, in minutes
180
155
130
105
80
55
30
20
30
40
50
60
70
80
90
100
110
120
130
140
Surgery Length, in minutes
graft type
autograft
allograft

Figure 4

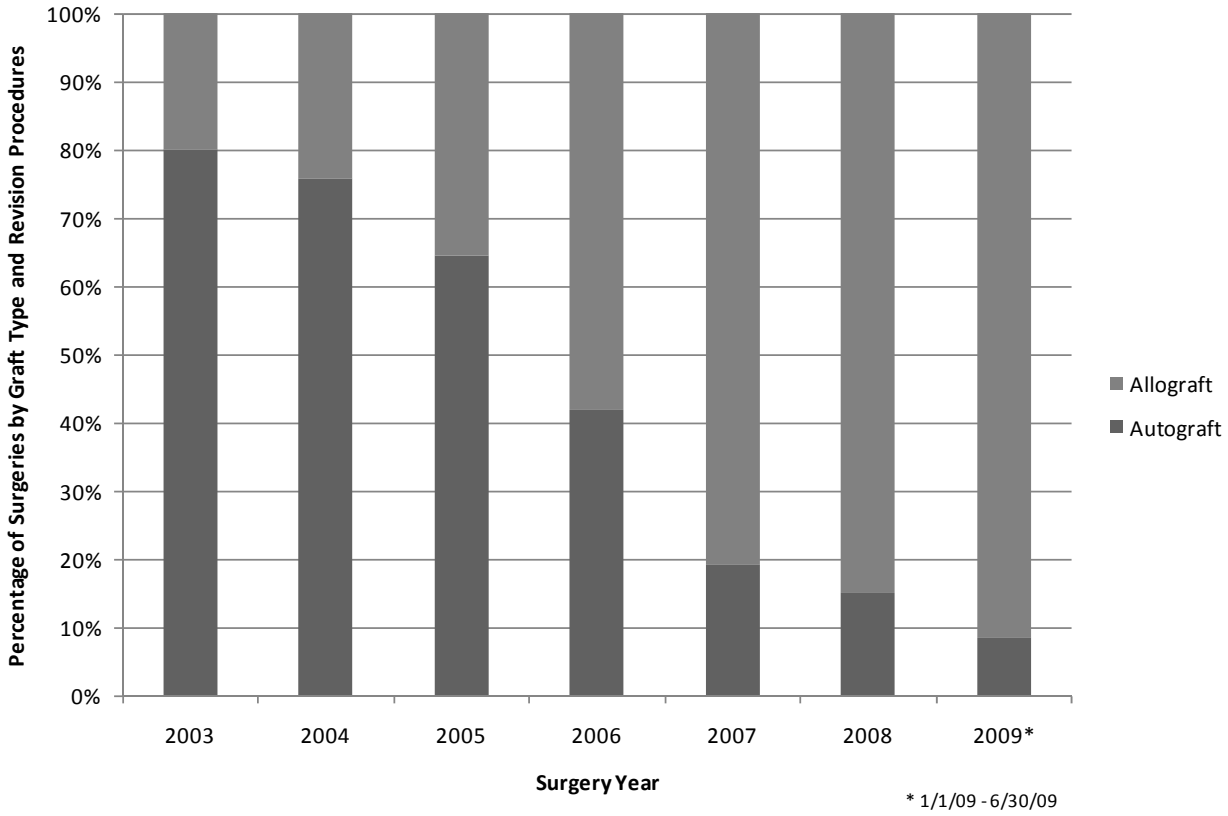
Percentage of Surgeries by Graft Type and Revision Procedures
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
2003
2004
2005
2006
2007
2008
2009*
Surgery Year
Allograft
Autograft
* 1/1/09 - 6/30/09

Table 1: Diagnosis (ICD-9) and procedure (CPT) codes used to identify complications occurring within 6 months of ACL reconstruction: Portland, OR 2003-2009

ICD-9 codes for complication diagnosis		CPT codes for treatment of complications	
711.06	Pyogenic arthritis of knee	10180	Incision and drainage; complex, postoperative wound infection.
730.06	Acute osteomyelitis of lower leg		
730.16	Chronic osteomyelitis of lower leg	11010	Debridement including - removal of foreign material; skin and subcutaneous tissue.
730.26	Unspecified osteomyelitis of lower leg		
998.59	Other post-operative infection (e.g. wound infection)	11011	- removal of muscle fascia,
716.96	Arthropathy, unspecified, knee	11012	- removal of muscle fascia, muscle, and bone
718.56	Ankylosis (arthrofibrosis) of joint, knee	11044	- removal of muscle and bone
996.78	Other complication of prosthetic device, implant and graft; due to other internal orthopedic device, implant and graft (e.g. loose hardware).	20670	Removal of implant, superficial (e.g. buried wire, pin or rod)
		20680	Removal of implant, deep (e.g. buried wire, pin, screw, metal band, nail, rod or plate)
451.11	Deep Vein Thrombosis, femoral		
451.19	Deep Vein Thrombosis, other leg veins	27301	Incision and drainage; deep abscess, bursa, or hematoma, thigh or knee region
453.40	Deep Vein Thrombosis, unspecified deep vessels of lower extremity		
453.41	Deep Vein Thrombosis, proximal lower extremity	27310	Arthrotomy, knee, with exploration, drainage, or removal of foreign body (e.g. infection)
453.42	Deep Vein Thrombosis, distal lower extremity		
956.0	Injury to sciatic nerve	27570	Manipulation of knee joint under anesthesia
956.1	Injury to femoral nerve		
956.2	Injury to posterior tibial nerve	29870	Arthroscopy, knee – diagnostic, with or without synovial biopsy
956.3	Injury to peroneal nerve		
956.4	Injury to cutaneous sensory nerve lower limb	29871	-for infection, lavage and drainage
956.5	Injury to other specified nerve(s) of pelvic girdle / lower limb	29875	-synovectomy, limited (e.g. plica or shelf resection)
956.8	Injury to multiple nerves of pelvic girdle / lower limb	29877	-debridement/shaving or articular cartilage
956.9	Injury to unspecified nerve of		

	pelvic girdle / lower limb	29884	-with lysis of adhesions, with or without manipulation
729.92	Non-traumatic hematoma, soft tissue	47407	Repair of cruciate ligament

Table 2: Distribution of patient characteristics according to graft type used in ACL reconstruction: Portland, OR 2003-2009[‡]

	Total	Autograft	Allograft	
Number (%)	413	141 (34.1)	272 (65.9)	
	Mean (SD)	Mean (SD)	Mean (SD)	P-value
Age (in years)				
Mean (SD)	32.9 (11.8)	27.9 (10.2)	35.4 (11.7)	<.01*
Median	32	27	34	
Body Mass Index				
Mean (SD)	27.4 (5.9)	25.9 (4.9)	28.2 (6.2)	.02*

	Total	Autograft	Allograft	
Number (%)	413	141 (34.1)	272 (65.9)	
	N (%)	N (%)	N (%)	P-value
Age (years)				
13 – 24	120 (29.1)	60 (42.6)	60 (22.1)	<0.01*
25 – 34	119 (28.8)	41 (29.1)	78 (28.7)	
35 – 44	98 (23.7)	32 (22.7)	66 (24.3)	
45+	76 (18.4)	8 (5.7)	68 (25.0)	
Gender				
Male	268 (64.9)	99 (70.2)	169 (62.1)	0.10*
Female	145 (35.1)	42 (29.8)	103 (37.9)	
Ethnicity				
Hispanic	19 (4.7)	7 (5.2)	12 (4.5)	0.77
Non-Hispanic	384 (95.3)	129 (94.8)	255 (95.5)	
Marital Status				
Married	184 (44.5)	54 (38.3)	130 (47.8)	0.07*
Not Married	229 (55.5)	87 (61.7)	142 (52.2)	
Body Mass Index (kg/m^2)				
Normal (18.5 – 24.9)[+]	151 (37.1)	68 (48.4)	83 (30.6)	<0.01*
Overweight (25.0 – 29.9)	153 (37.6)	48 (34.0)	105 (38.6)	
Obese (>30.0)	103 (25.3)	22 (15.6)	81 (29.8)	
Smoking				
Current Smoker	60 (14.5)	17 (12.1)	43 (15.8)	0.56 (0.55)[++]
Non-Smoker	246 (59.6)	85 (60.3)	161 (59.2)	
Missing	107 (25.9)	39 (27.6)	68 (25.0)	
Diabetes				
Diabetic	9 (2.2)	3 (2.1)	6 (2.2)	0.02* (<0.01)[++]
Not Diabetic	346 (83.8)	109 (77.3)	237 (87.1)	
Missing**	58 (14.0)	29 (20.6)	29 (10.7)	

* *These variables will be considered potential confounders if also associated with complication outcomes*

** *75.9% of missing observed in 2005*

[+] *Underweight and Normal categories were combined to conduct the chi-square test*

[++] *Significance of difference between 'missing' and 'not missing'*

[‡] Patient cohort includes 413 people age 12 to 60 with arthroscopic ACL reconstruction performed between 2003 and 2009 at Oregon Health & Science University in Portland, Oregon.

Table 3: Risk of any complication within 6 months of ACL reconstruction according to patient and surgical characteristics: Portland, OR 2003-2009‡

Number (%)	Any Complication 20 (4.8) N (%)	No Complications 393 (95.2) N (%)	Fisher's Exact p-value
Age			
13 – 24 years	5 (4.2)	115 (95.8)	
25 – 34 years	10 (8.4)	109 (91.6)	.44
35 - 44 years	4 (4.1)	94 (95.9)	
45+	3 (4.0)	73 (96.0)	
Sex			
Male	8 (3.0)	260 (97.0)	.01
Female	14 (9.7)	131 (90.3)	
Marital Status			
Single	12 (5.2)	217 (94.8)	1.0
Married	10 (5.4)	174 (94.6)	
Body Mass Index			
Mean (SD)	28.0 (6.5)	27.4 (5.8)	
Normal	9 (5.7)	148 (94.3)	
Overweight	7 (4.6)	146 (95.4)	.88
Obese	6 (5.8)	97 (94.2)	
Smoking			
Smoker	5 (8.3)	55 (91.7)	.27 (.22)*
Non-Smoker	14 (5.7)	232 (94.3)	
Missing	3 (2.8)	104 (97.2)	
Diabetes			
Diabetic	0	9 (100.0)	.72 (.53)*
Not Diabetic	18 (5.2)	328 (94.8)	
Missing	4 (6.9)	54 (93.1)	
Year			
2003	0	25 (100.0)	
2004	2 (6.9)	27 (93.1)	
2005	4 (6.8)	55 (93.2)	
2006	3 (4.8)	59 (95.2)	.91
2007	6 (6.8)	82 (93.2)	
2008	4 (5.1)	75 (94.9)	
2009	3 (4.2)	68 (95.8)	
Harvest Site			
Hamstring	6 (3.8)	162 (96.2)	
Patellar Tendon	0	11 (100.0)	.39
Anterior Tibialis	12 (6.1)	186 (93.9)	
Achilles	2 (14.3)	12 (85.7)	

Missing	2 (9.1)	20 (90.9)	
Any Concurrent Procedure			
Yes	11 (5.1)	205 (94.9)	.83
No	11 (5.6)	186 (94.4)	
Previous Surgery, non-ACL			
Yes	2 (5.6)	34 (94.4)	1.0 (1.0)*
No	9 (5.4)	159 (94.6)	
Missing	11 (5.3)	198 (94.7)	
Any Nerve Block**			
Sciatic	3 (2.7)	109 (97.3)	.22
Spinal	1 (2.4)	40 (97.6)	.71
Femoral – Single	6 (6.4)	88 (93.6)	
Femoral – Home	14 (5.1)	260 (94.9)	.89
Pump[+]			

	Any Complication N=22 Mean (SD)	No Complication N=391 Mean (SD)	P-value
Anesthesia Care Mean (SD)	135.1 (53.1)	120.5 (53.6)	.21
Surgery Length[++] Mean (SD)	61.7 (28.1)	52.5 (21.0)	.26
Age Mean (SD)	31.9 (9.2)	32.9 (11.9)	.16

	Any Complication N=22 Median (IQR)	No Complication N=391 Median (IQR)	P-value
Anesthesia Care Median (IQR)	205.5 (176 – 282)	190.0 (127-259)	.21
Surgery Length[++] Median (IQR)	57.0 (43.0 – 80.0)	48.5 (36.0 – 64.0)	.26

[*] *Significance of difference between 'missing' and 'not missing'*
** *Column proportions may not total 100% due to overlap in nerve block application.*
[+] *Restricted to 2006 – 2009*
[++] *Restricted to 2008 - 2009*
[‡] Patient cohort includes 413 people age 12 to 60 with arthroscopic anterior cruciate ligament reconstruction performed between 2003 and 2009 at Oregon Health & Science University in Portland, Oregon.

Table 4: Potential confounders according to association with exposure (graft type) and outcome (any complication) variables: Portland, OR 2003-2009[‡]

Independent variables associated with exposure: graft type (p-val)	Independent variables associated with outcome: any complication (p-val)
Sex (.10)	Sex (.02)
Marital Status (.07)	Smoking (.27)
Diabetes (.02)	
Age (<.0001)	
Body Mass Index (.0002)	

[‡]Patient cohort includes 413 people age 13 to 60 with arthroscopic anterior cruciate ligament reconstruction performed between 2003 and 2009 at Oregon Health & Science University in Portland, Oregon.

Table 5: Risk of any complication according to graft type used in ACL reconstruction: Portland, OR 2003-2009*

	Analysis Cohort (2003-2009)		Restricted Cohort (2006-2009)	
	Cohort	Any Complication	Cohort	Any Complication
Number (%)	413	22 (5.3)	300	16 (5.3)
	N	N(%)	N(%)	N(%)
Allograft	272	19 (7.0)	239	15 (6.3)
Autograft	141	3 (2.1)	61	1 (1.6)
Crude p-val[1]		.04		.21
Crude RR (95% CI)[2]		3.3 (1.0 – 10.9)		3.8 (0.5 – 28.4)
Adjusted p-val[3]		.06		.16
Adjusted RR (95% CI)[4]		3.0 (0.9 – 9.7)		3.7 (0.5-28.7)
RD (95% CI)[5]		0.05 (0.01 – 0.09)		0.05 (0.00 – 0.09)

[1] Crude p-value using Fisher's exact test
[2] Crude risk ratio (relative risk) estimate
[3] Adjusted p-value controlling for sex, using exact Cochran Mantel Haenszel statistics
[4] Adjusted risk ratio (relative risk) estimate controlling for sex, using Cochran Mantel Haenszel statistics
[5] Risk Difference
* Patient cohort includes 413 people age 12 to 60 with arthroscopic anterior cruciate ligament reconstruction performed between 2003 and 2009 at Oregon Health & Science University in Portland, Oregon. The restricted cohort includes only patients with reconstruction performed between 2006 and 2009.

Table 6: Risk of non-infectious complication according to graft type used in ACL reconstruction: Portland, OR 2003-2009*

	Cohort	Primary Non-Infectious Complication	Any Non-Infectious Complication
Number (%)	N=413	14 (3.4)	9 (2.2)
	N	N(%)	N(%)
Allograft	272	12 (4.4)	7 (2.6)
Autograft	141	2 (1.4)	2 (1.4)
Crude p-val[1]		0.15	0.70
Crude RR (95% CI)[2]		3.1 (0.7 – 13.7)	1.8 (0.4 – 8.6)
Adjusted p-val[3]		0.18	0.60
Adjusted RR (95% CI)[4]		2.7 (0.6 – 12.1)	1.5 (0.3 – 7.6)
RD (95% CI)		0.03 (0.0 – 0.06)	0.01 (0.0 – 0.4)

[1] Crude p-value using Fisher's exact test
[2] Crude relative risk estimate
[3] Adjusted p-value controlling for sex, using exact Cochran Mantel Haenszel statistics
[4] Adjusted relative risk estimate controlling for sex, using Cochran Mantel Haenszel statistics
* Patient cohort includes 413 people age 12 to 60 with arthroscopic anterior cruciate ligament reconstruction performed between 2003 and 2009 at Oregon Health & Science University in Portland, Oregon.

Table 7: Risk of infection according to graft type used in ACL reconstruction: Portland, OR 2003-2009*

	Cohort	Primary Infection	Any Infection
Number (%)	N=413	8 (1.9)	13 (3.1)
	N	N(%)	N(%)
Allograft	272	7 (2.6)	12 (4.4)
Autograft	141	1 (0.7)	1 (0.7)
Crude p-val[1]		0.27	0.04
Crude RR (95% CI)[2]		3.6 (0.5 – 29.2)	6.2 (0.8 – 47.4)
Adjusted p-val[3]		0.18	0.05
Adjusted RR (95% CI)[4]		3.5 (0.5 – 25.4)	5.7 (0.8 – 39.8)
RD (95% CI)		0.02 (0.0 – 0.04)	0.04 (0.01 – 0.07)

[1] Crude p-value using Fisher's exact test
[2] Crude relative risk estimate
[3] Adjusted p-value controlling for sex, using exact Cochran Mantel Haenszel statistics
[4] Adjusted relative risk estimate controlling for sex, using Cochran Mantel Haenszel statistics
* Patient cohort includes 413 people age 12 to 60 with arthroscopic anterior cruciate ligament reconstruction performed between 2003 and 2009 at Oregon Health & Science University in Portland, Oregon.

Table 8: Risk of any complication according to infection status, sex, and graft type used in ACL reconstruction: Portland, OR 2003-2009*

	Men			Women		
	N	Infection N (%)	Not Infection N (%)	N	Infection N (%)	Not Infection N (%)
Allograft	169	6 (3.6)	1 (0.6)	103	1 (1.0)	11 (10.7)
Autograft	99	0	1 (1.0)	42	1 (2.4)	1 (2.4)

* Patient cohort includes 413 people age 12 to 60 with arthroscopic anterior cruciate ligament reconstruction performed between 2003 and 2009 at Oregon Health & Science University in Portland, Oregon.

Table 9: Potentially missed complication events according to frequency and distribution of clinic visits following ACL reconstruction surgery in a random sample, Portland, OR 2003-2009*

Visit	Graft	Patients completing visit N (%)	Total patients completing visit N (%)	Days between surgery and follow-up visit Mean (SD)	Total days between surgery and follow-up Mean (SD)	Possible Complications Noted N
1	Allograft	39 (100.0)	70 (100.0)	11.0 (9.5)	10.0 (8.4)	0
	Autograft	31 (100.0)		8.7 (6.7)		0
2	Allograft	32 (82.1)	62 (88.6)	37.5 (21.7)	35.1 (28.8)	1
	Autograft	30 (96.8)		32.7 (35.1)		0
3	Allograft	28 (71.8)	52 (74.3)	79.9 (35.2)	75.5 (35.0)	0
	Autograft	24 (77.4)		70.4 (34.8)		1
4	Allograft	20 (51.3)	40 (57.1)	139.1 (63.6)	115.8 (79.4)	3
	Autograft	20 (64.5)		92.5 (88.0)		0
5	Allograft	8 (20.5)	18 (25.7)	186.5 (79.6)	163.7 (64.1)	0
	Autograft	10 (32.3)		145.4 (44.8)		0

* Random sample of the patient cohort includes 70 people age 13 to 60 with arthroscopic anterior cruciate ligament reconstruction performed between 2003 and 2009 at Oregon Health & Science University in Portland, Oregon. Random sampling included 10 patients from each study year without previously identified complication events, and mirrored graft proportions by year.

Table 10: Risk of any complication observed and potentially missed according to graft type: Portland, OR 2003-2009*

	Cohort	Observed	Potentially Missed	Total
Number (%)		22 (5.3)	33 (8.0)	55 (13.3)
		N(%)	N(%)	N(%)
Autograft	141	3 (2.1)	5 (3.5)	8 (5.7)
Allograft	272	19 (7.0)	28 (10.3)	47 (17.3)
RR (95% CI)[1]		3.3 (1.0 – 10.9)	2.9 (1.1 – 7.4)	3.0 (1.5 – 6.3)
RD (95% CI)[2]		0.05 (0.01 – 0.09)	0.07 (0.02 - 0.12)	0.12 (0.06 – 0.18)

[1] Crude relative risk estimate

[2] Crude risk difference estimate

* Patient cohort includes 413 people age 12 to 60 with arthroscopic anterior cruciate ligament reconstruction performed between 2003 and 2009 at Oregon Health & Science University in Portland, Oregon. Patients with an observed complication were identified through a billing record query. Patients with a potentially missed complication represent the proportion of patients whom we estimate to have a complication not identified in the billing record. This estimation is based on results of a medical record review on a random sample of patients without previously identified complications. Total is the addition of patients with an observed, and patients with a potentially missed, complication.

Table 11: Case Review of Individuals with Any Complication within 6 Months of ACL Reconstruction: Portland, OR 2003-2009

	Case	Time Post- Op	Symptoms/Diagnosis	Action
Removal of ACL graft	1	7 weeks	Septic arthritis, ACL tear	ACL graft removal, hardware removal, irrigation & debridement, antibiotics
		28 weeks	Knee instability	Autograft ACL reconstruction
	2	4 weeks	Tibial incision dehiscence	Surgical wound closure
		5 weeks	Tibial wound infection extending to joint	Irrigation and debridement, ACL allograft removal, hardware removal, antibiotics; plan to reconstruct ACL with allograft, however patient lost to follow up
	3	10 weeks	Painful hardware	
		16 weeks	Painful hardware, erythema at tibial incision	Irrigation & debridement, arthroscentisis, antibiotic
		17 weeks	Septic arthritis confirmed with synovial fluid cultures	Irrigation & debridement, ACL graft removal
		24 weeks	Knee instability	ACL reconstruction with allograft
	4	1 week	Peri-incisional erythema and edema	Oral antibiotic
		2 weeks	Deep vein thrombosis, continued erythema with drainage from incision	Seen by external provider who started coumain, and antibiotics, irrigated and debrided incision
		8 weeks	Infected hardware	Admitted to OHSU hospital for hardware removal, ACL graft removal, irrigation and debridement
		14 weeks	Continued pain, loss of function	Total knee arthroplasty, follow-up with external provider
	5	1 week	Peri-incisional erythema and edema	Oral antibiotics
		2 weeks	Worsening cellulitis	Irrigation & debridement, hematoma evacuation
		4 weeks	Infected ACL graft, infected	Hardware removal, ACL

			hardware	graft removal, antibiotics
		104 weeks	Knee instability	ACL reconstruction with allograft
Neuropathy	6	7 weeks	Anterior-medial lower extremity numbness	Referral for EMG study
		23 weeks	EMG reveals superficial nerve injury, possible due to proximity of tibial screw	
		30 weeks		Hardware removal; follow-up with external provider
Arthrofibrosis	7	8 weeks	Limited range of motion	
		16 weeks	Limited range of motion, Cyclops lesion, arthrofibrosis	Hardware removal, debridement, manipulation under anesthesia
Superficial Wound Infection	8	4 weeks	Superficial infection at tibial incision,hematoma, wound dehiscence	Patient presented to urgent care, then emergency department before admittance to OHSU hospital for irrigation & debridement, and antibiotics
		19 weeks	Painful hardware, question of chronic infection	Hardware removal
		24 weeks	No pain, no infection, off antibiotics	
	9	2 weeks	Wound dehiscence with possible superficial infection	Surgical closure, antibiotics
		3 weeks	Culture positive for S. aureas and Pseudomonas	Antibiotics
		10 weeks	Resolved infection, now with painful hardware	Hardware removal
	10	3 weeks	Wound dehiscence, possible infection	Irrigation & Debridement
		20 weeks	Infection diagnosed at outside hospital	Course of antibiotics prescribed by an external provider
		22 weeks	Concern for possible continuance of infection	Irrigation & Debridement
	11	2 weeks	Wound dehiscence, hematoma	Irrigation & Debridement, Antibiotic
		3 weeks	Symptom resolution	No further treatment

	12	2 weeks	Wound dehiscence, hematoma	Irrigation & Debridement
		3 weeks	Continued drainage from wound	Arthroscopic, irrigation & debridement
	13	1 week	Wound dehiscence, hematoma	Irrigation & debridement, no evidence of infection
		6 weeks	Clinical evidence of surgical wound infection	Irrigation & debridement, antibiotics
		7 weeks	Clinical evidence of surgical wound infection, one positive culture	Irrigation & debridement, hardware removal
		9 weeks	Continued drainage of wound	Wound-vac placed; aneurysm of middle cerebral artery 1 year post-op
	14	2 weeks	Peri-incisional erythema	No intervention, patient to return for wound check
		3 weeks	Patient sustained new trauma with complaint of infection at shoulder and hand, no evidence of infection at tibial incision site	Patient admitted to OHSU hospital. Joint aspiration, no organisms grown on culture, antibiotics (for other co-morbidities)
Painful Hardware	15	4 weeks	Painful hardware	
		24 weeks	Painful hardware	Hardware removal, meniscectomy
		28 weeks	Drainage from incision, possible mild cellulitis	Oral antibiotic, no surgical intervention
		164 weeks	Failed ACL reconstruction	ACL reconstruction – revision
	16	23 weeks	Painful hardware, bursitis, tibial screw prominent	Hardware removal, bursectomy
	17	12 weeks	Painful hardware	Issue resolved without treatment
	18	5 weeks	Painful hardware	
		12 weeks	Painful hardware, bursitis	
		20 weeks	Painful hardware, bursitis	Hardware removal; follow-up with external provider
	19	10 weeks	Painful hardware	
		21 weeks	Painful hardware	Hardware removal
	20	6 weeks	Painful hardware	
		22 weeks	Painful hardware	Hardware removal
Other	21	3 weeks	Patient fell multiple times, pain, swelling	Exam negative for ligament or cartilage injury
		12 weeks	Pain and stiffness	

		18 weeks	Possible torn meniscus on MRI (re-tear from repair concurrent to ACL reconstruction)	Removal of loose body, hardware removal. Meniscus intact
		32 weeks	Continued pain and swelling, possible meniscus tear	Cortisone shot. Patient declines surgical intervention
	22	12 weeks	Knee instability after trauma to surgical knee	ACL tear confirmed by MRI
		16 weeks	ACL tear	ACL reconstruction – revision, hardware removal
		8 weeks (from revision)	Patient notes exudates from proximal femoral guide pin site	Incisions are clean and dry on exam
		32 weeks (from revision)	Patient continues to complain of exudates from proximal femoral guide pin site	Debridement of abscess (thigh), tibial hardware removal, antibiotics

Table 12: Distribution of patient characteristics according to graft type used in ACL reconstruction REVISION: Portland, OR 2003-2009*

	Total	Autograft	Allograft
Number (%)	65	5 (7.7)	60 (92.3)
	N (%)	N (%)	N (%)
Age (years)			
13 – 24	17 (26.2)	2 (40.0)	15 (25.0)
25 – 34	27 (41.5)	1 (20.0)	26 (43.3)
35 – 44	12 (18.5)	0	12 (20.0)
45+	9 (13.9)	2 (40.0)	7 (11.7)
Gender			
Male	29 (44.6)	3 (60.0)	26 (43.3)
Female	36 (55.4)	2 (40.0)	34 (56.7)
Ethnicity			
Hispanic	3 (4.7)	0	3 (5.1)
Non-Hispanic	61 (95.3)	5 (100.0)	56 (94.9)
Marital Status			
Married	20 (30.8)	3 (60.0)	17 (28.3)
Not Married	45 (69.2)	2 (40.0)	43 (71.7)
Body Mass Index (kg/m^2)			
Normal (18.5 – 24.9)	29 (44.6)	3 (60.0)	26 (43.3)
Overweight (25.0 – 29.9)	21 (32.3)	2 (40.0)	19 (31.7)
Obese (>30.0)	15 (23.1)	0	15 (25.0)
Smoking			
Current Smoker	14 (21.5)	0	14 (23.3)
Non-Smoker	38 (58.5)	5 (100.0)	33 (55.0)
Missing	13 (20.0)	0	13 (21.7)
Diabetes			
Diabetic	1 (1.5)	0	1 (1.7)
Not Diabetic	56 (86.2)	3 (60.0)	53 (88.3)
Missing	8 (12.3)	2 (40.0)	6 (10.0)

* Patient cohort includes 413 people age 13 to 60 with arthroscopic anterior cruciate ligament reconstruction revision performed between 2003 and 2009 at Oregon Health & Science University in Portland, Oregon.

Table 13: Risk of complication according to graft type used in ACL reconstruction - revision: Portland, OR 2003-2009*

Number (%)	Cohort 65 N	Any Complication 7 (10.8) N(%)	Infection 5 (7.7) N(%)	Non-Infection 2 (3.1) N(%)
Allograft	60	7 (11.7)	5 (8.3)	2 (3.3)
Autograft	5	0	0	0
Crude p-val[1]		1.0	1.0	1.0
Adjusted p-val[2]		.40	.45	.72

[1] p-value (crude), using Fisher's exact test

[2] p-value adjusted for sex, using Cochran Mantel Haenszel statistics

* Patient cohort includes 413 people age 13 to 60 with arthroscopic anterior cruciate ligament reconstruction performed between 2003 and 2009 at Oregon Health & Science University in Portland, Oregon.

APPENDIX A

Record Abstraction Code Key

Age Inclusion Criteria		
Surgery Year: Minimum Birth Year / Maximum Birth Year		
2003: 1943/1991		**2006**: 1946/1994
2004: 1944/1992		**2007:** 1947/1995
2005: 1945/1993		**2008:** 1948/1996
Patient Information		
DOB		(record date in mm/dd/yy format)
Gender	1	Male
	2	Female
BMI at surgery		(record BMI)
Ethnicity	1	Hispanic
	2	Non-Hispanic
Marital Status	1	Married
	2	Single
Height (if BMI not available)		(record in feet and inches)
Weight (if BMI not available)		(record in killograms or pounds)
Diabetes	0	No
	1	Yes
Current smoking status	1	Current smoker
	2	Not a current smoker
Surgical Characteristics		
Surgery date		(record date in mm/dd/yy format)
Concurrent procedures	0	None
	1	Cartilage (meniscal, removal of loose bodies, chondroplasty, microfracture)
	2	Ligaments (PCL, LCL, MCL, MPFL)
	3	Transplants (OCA/OCTS/OCT/OATS, meniscus)
	4	Alignment (HTO/osteotomy, correction)
Revision	0	No
	1	Yes
Graft type	1	Autograft
	2	Allograft
Harvest Site	1	Hamstring
	2	Patellar tendon
Sciatic Regional Anesthesia	0	None
	1	Single
Spinal Regional Anesthesia	0	None
	1	Single
Femoral Regional Anesthesia	0	None
	1	Single
	2	Home pump/home catheter
Anesthesia	0	No GA or MAC
	1	Yes - General
	2	Yes - MAC
Length of tourniquet use		(record in minutes)
Femoral Hardware - Type	1	Endo Button
	2	Interference Screw
Tibial Hardware - Type	1	Washerlock
	2	Interference Screw
	3	Bio Intra Fix
Surgery Start Time - Incision		(record in 24-hour time)
Surgery End Time - Wound closure		(record in 24-hour time)
Follow-up surgery	0	No
	1	Yes

APPENDIX B

Complications Following Anterior Cruciate Ligament Reconstruction

Abstraction Details

Abstraction Packet

- This instruction sheet
- Code Key (paper)
- Data Entry Worksheet (paper)
- Study List (electronic)
- Data Entry Worksheet (electronic)

Abstraction Process

1. From "Study List," enter patient's MRN in Epic
2. Open patient chart
3. Verify study eligibility with CPT code (study list), surgery date (study list), surgery and consultation with Dr. Crawford (study list), patient age at surgery between 12 and 60 years (table below), and no mention of prior complications associated with ipsilateral knee reconstructive surgery (medical record: encounter list, procedures, proc notes, etc.)
    a. Valid DOB years by year of surgery:

Surgery Year	Minimum Birth Year	Maximum Birth Year
2003	1943	1991
2004	1944	1992
2005	1945	1993
2006	1946	1994
2007	1947	1995
2008	1948	1996

    b. If patient is not eligible, note this and list exclusion criteria in "Study List." Close medical record and move on.
4. Use this document as a guide on where to find various pieces of personal information in Epic
5. A study ID will be assigned to each patient in the study list before the abstraction process begins. Record Study ID from Study List to paper Data Entry Worksheet.
6. Enter data (numerically) on paper copy of Data Entry Worksheet and enter into electronic database later. Use "Code Key" to determine numeric codes.
7. While collecting personal information, review PROC NOTES, PROC, and ENCOUNTERS for ER visits or hospital admissions within 6 months of date of surgery. If any, record in "For Review" worksheet.
8. Save, repeat with all patients
9. Repeat the same process, this time abstracting surgical information.

10. Refer to billing extract for list of patients with specified complication codes. Per instructions below, cross-reference with study list and enter appropriate data in Data Entry worksheet.
11. Save, repeat with all patients

With two people completing data abstraction, surgery years will be divided between abstractors. For example, Sara will collect information from 2003, 2005, and 2007 and Ryan will collect information from 2004, 2006, and 2008. This will increase consistency within abstractions, and reduce confusion in the tracking process.

At regular intervals, each abstractor will enter data from paper records into the electronic database. For every 20 records collected, we will re-abstract one record (5%), and re-enter a different record. This will ensure abstractors are pulling data from medical records in a consistent manner and that there are no errors in data entry. Data validation controls are already in place in the electronic database.

As questionable cases arise, or complications need review, abstractors will enter the study ID number, surgery date, and question into a tracking sheet. Sara will match the study ID numbers with patient names and MRNs. Every Friday, Sara will meet with Dr. Crawford in the OR to review questionable cases. Decisions will be recorded in the same spreadsheet, and entries completed in Data Entry Worksheet.

Details

Patient Information Data Extraction

1. From "Study List – Key," enter patient's MRN in Epic
2. Open patient chart
3. Record SEX and DOB from top info bar
4. Snapshot: Profile to record BMI
    a. If not recorded here, it may be on "anesthesia pre-op evaluation"
5. Demographics: to record Ethnicity
6. Chart Review: Proc Notes to confirm surgery date from "study list – key" (don't open any documents)
7. Chart Review: Proc tab and open Anesthesia/Sedation rows from surgery date
    a. Open "Anesthesia PreOp Evaluation" to record BMI, SMOKING, and DIABETES [smoking under Social History in top History section or under "Substance Use"]
    b. [if needed] Open "Anesthesia Questionnaire PreOP" to record BMI, SMOKING, and DIABETES.
8. Anesthesia PreOp Evaluation and Anesthesia Questionnaire PreOP may also be in Chart Review: Encounters tab under "Scanned Documents" from surgery date
    a. Open "Anesthesia PreOp Evaluation" to record BMI, SMOKING, and DIABETES [smoking under Social History in top History section or under "Substance Use"]
    b. [if needed] Open "Anesthesia Questionnaire PreOP" to record BMI, SMOKING, and DIABETES.

Surgery Characteristics Data Extraction

1. From "Study List – Key," enter patient's MRN in Epic
2. Open patient chart
3. Chart Review: Proc Notes to confirm surgery date
4. Chart Review: Proc and open "Operation Record" row from surgery date
    a. Record Surgery Date at top of record
    b. Record Procedures Performed from numbered list as concurrent procedures
    c. Record Anesthesia, Nerve Block, Complications, and Tourniquet Time
        i. Anesthesia and nerve block information may also be in the text body or "Anesthesia Record," one of the "Anesthesia/Sedation" rows
    d. Scan Operation Record for type of surgery (ALLOgraft vs. AUTOgraft), harvest site if autograft procedure, and graft fixation method.
5. Note previous surgeries if mentioned in Operation Record, or if listed in another row of Proc Notes.

Complications Data Extraction

1. Get list of patients within date parameters from Gentry who are identified by specified CPT and/or ICD9 complication codes. [these could be people who may or may not have had an ACL surgery]
2. Make sure study list has study ID numbers assigned already.
3. Using AbleBits.com, download Duplicate Finder application. In excel, select spreadsheet with CPT complication patients as Table 1; study list should be Table 2.
4. Find duplicates by searching MRN column in both tables, and COPY (don't cut!) duplicates to a new worksheet.
5. Use duplicate finder application again, this time select spreadsheet with ICD9 complication patients as Table 1; study list should be Table 2.
6. Find duplicates by searching MRN column in both tables, and COPY (don't cut!) duplicates to a new worksheet.
7. Combine study list, CPT complication patients, and ICD9 patients into one table with each group to the right of the previous. Patient names will not match up.
8. Highlight one group at a time (i.e. start with study list) and search within this table alone for duplicates, with instructions to HIGHLIGHT duplicates. These will be people with more than one ACL procedure. KEEP the first ACL procedure and delete future episodes (noting this in the "Ineligible spreadsheet").
9. Highlight duplicates within ICD9 complication and CPT complication tables, keeping all duplicates.
10. Manually move rows between all three tables so that each row represents one study patient and prior and/or subsequent complications.
11. Delete patients with complication code who were not on study list – they do not meet inclusion criteria.
12. Classify complications by major and minor. All CPT complications are major.
13. Remember: for complications not identifiable by CPT or ICD9 code (ER visits and hospitalizations), review the PROC NOTES, PROC, and ENCOUNTER tabs

in the “Chart Review” section while recording demographics. Search for ER visits or hospital admissions only within 6 months following surgery. If found, record in “for review” spreadsheet for Dr. Crawford’s review on Fridays.