Prevalence and Risk Factors for Total Knee Arthroplasty after Cruciate Ligament Surgery: A Study of the UK BioBank

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INTRODUCTION:

The purpose of this study is to determine an individual's age-specific prevalence of total knee arthroplasty (TKA) and revision TKA after ACL reconstruction (ACLr) and to identify clinical and genetic risk factors associated with undergoing TKA.

METHODS: The UK Biobank – a prospective cohort of 500,000 adults (age 40-69 at time of enrollment) containing health, physical measures, genotyping data, and linked data on hospitalizations – was utilized to identify individuals with a history of ACL surgery (i.e., "cruciate ligament surgery") during initial health interviews. Individuals were considered to have progressed to end-stage knee osteoarthritis requiring arthroplasty (i.e., "osteoarthritis") if they endorsed a procedural history of TKA at time of enrollment or underwent hospitalization with a procedural code for TKA after enrollment in the Biobank cohort. To define an individual's relative risk of TKA following ACLr, age-specific cumulative incidence of TKA was compared between patients with and without a history of ACLr. To determine clinical risk factors associated with undergoing TKA after ACLr, age-adjusted logistic regression modeling was utilized to calculate odds ratios (OR) for undergoing TKA. SNP associated were tested for association with TKA using allele counts for typed and imputed SNPs in a logistic regression model.

RESULTS: A total of 2,576 individuals with a history of ACLr were identified, with 290 (11.3%) undergoing TKA. In patients with prior ACLr, prevalence of TKA was 0.75% at 45 years of age, 9.1% at 65 years of age, and 20.43% at 80 years of age (Figure 1). Patients with prior ACLr were 4.6x more likely to have undergone TKA by age 55. In the ACLr cohort, BMI >30 kg/m2 (odds ratio = 4.01, 95% confidence interval = 2.74–5.87) (Table 1), a job that always involved heavy manual or physical labor (odds ratio=2.72, 95% confidence interval=1.57-4.71), or walking and standing (odds ratio=2.58, 95% confidence interval=1.58–4.20) were associated with greater TKA prevalence. After adjusting for age, no difference was noted in revision rates between individuals with TKA after ACLr and individuals undergoing TKA without a history of ACLr (Figure 2). No single nucleotide polymorphisms (SNPs) were associated with requiring TKA in patients with prior ACLr (Figure 3).

DISCUSSION AND CONCLUSION: Patients with prior ACLr are 4.6x more likely to undergo TKA by age 55 than the general population. Patients with BMI >30 and jobs that involve heavy manual labor or walking/standing are at greatest risk for undergoing TKA. These data can be used to counsel patients at time of index ACLr on both their life-time risk of TKA and lifestyle modifications that may limit the need for future TKA. After adjusting for age, ACLr was not independently associated with revision TKA. No genetic risk factors for TKA after ACLR were identified.
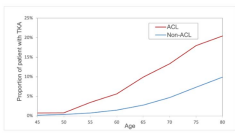

Figure 1: Proportion of individuals requiring TKA with (red) and without (blue) history of prior ACL reconstruction.
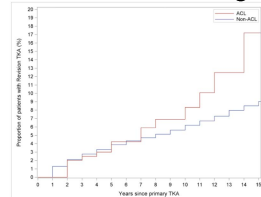

Figure 2: Proportion of individuals requiring revision TKA with (red) and without (blue) history of prior ACL reconstruction.
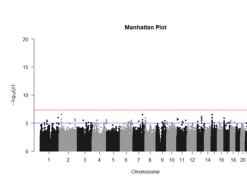

Figure 3: Manhattan plot displaying association of SNPs with history of TKA. Red line indicates the threshold for genome-wide significance (p-value <= 5 x 10-8)'

Table 1: Age-adjusted logistic regression for TKA in individuals with prior history of ACL reconstruction.

Variable	Age-adjusted Logistic Regression[a] (n = 2576)	
	OR (95%CI)	p-value
Age at enrollment, median (IQR)	1.08 (1.07 - 1.1)	<.0001
Race, N (%)		
White	Ref	Ref
Asian	1.70 (0.77 - 3.76)	0.1902
Black	1.15 (0.40 - 3.32)	0.8009
Mixed	1.63 (0.61 - 4.38)	0.3341
Unknown	0.27 (0.04 - 2.69)	0.2682
BMI, N (%)		
Underweight (BMI <18.5 kg/m2)		
Healthy (18.5< BMI <25.0 kg/m2)	Ref	Ref
Overweight (25.0< BMI <30.0 kg/m2)	1.80 (1.24 - 2.62)	0.0021
Obese (30.0 kg/m2< BMI)	4.01 (2.74 - 5.87)	<.0001
Job involves heavy manual or physical work, N (%)		
Never/rarely	Ref	Ref
Sometimes	1.42 (0.96 - 2.09)	0.0756
Usually	1.46 (0.77 - 2.78)	0.2497
Always	2.72 (1.57 - 4.71)	0.0004
Job involves mainly walking or standing, N (%)		
Never/rarely	Ref	Ref
Sometimes	2.31 (1.36 - 2.22)	0.0006
Usually	1.86 (0.96 - 2.87)	0.0725
Always	2.58 (1.58 - 4.20)	0.0001

a. Exclude 1 patient who withdrew from UK biobank. Logistic regression model for each risk factor adjusting for age. b. Exclude patients with the "Unknown" category of "BMI". "Job involves heavy manual or physical work" and "Job involves mainly walking or standing". Combine the "underweight" & "healthy" categories of BMI due to collinearity issues.