Published in final edited form as:

Med Sci Sports Exerc. 2016 June ; 48(6): 969–973. doi:10.1249/MSS.0000000000000876.

Outcomes of ACL Reconstruction in Patients with Diabetes

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Abstract

Purpose—Diabetes has been associated with adverse outcomes following various types of surgery. There is no previously published data regarding the impact of diabetes on outcomes from anterior cruciate ligament (ACL) reconstruction (ACLR). The purpose of this study was to test the hypotheses that diabetes is associated with worse clinical outcomes and a higher prevalence of subsequent surgeries following ACLR.

Methods—ACL deficient patients (n=2198) undergoing unilateral ACLR from a multicenter prospective study were included. Patients who self-reported diabetes based on comorbidity

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Author Contributions. RHB developed the study concept and design. RHB, RWW, CCK, RDP, JTA, RGM, ECM, AA, BRW, WRD, MLW, and KPS acquired data. RHB, LJH, and SKN analyzed and interpreted data. RHB and LJH drafted the manuscript. RHB, LJH, RWW, SKN, CCK, RDP, JTA, RGM, ECM, AA, BRW, WRD, MLW, and KPS critically revised the manuscript for important intellectual content. SKN performed the statistical analysis. KPS obtained funding. RHB and LJH are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Conflicts of Interest. No potential conflicts of interest relevant to this article were reported. The results of this study do not constitute an endorsement by the American College of Sports Medicine.

questions prior to surgery were identified from the database. They were compared with the remainder of the cohort who did not self-report diabetes. All patients were followed up for a minimum of 2 years following their index surgery. Minimum 2 year follow-up was attained on 1905/2198 (87%) via completed outcome questionnaires and 2096/2198 (95%) regarding subsequent surgery. The primary outcome measures were three validated outcome instruments. Secondary outcome measure was the incidence of additional surgery on the ipsilateral and contralateral knees.

Results—Patients with diabetes had significantly higher activity level at 2 years (OR=2.96; 95% CI=1.30–6.77; $p=0.01$), but otherwise slightly worse clinical outcomes, compared to patients without diabetes (OR range = 0.42–0.59). The prevalence of subsequent surgeries in patients with diabetes was not significantly different from the prevalence in patients without diabetes.

Conclusions—Patients with diabetes maintain a higher activity level after ACLR despite slightly lower patient reported outcomes scores compared to patients without diabetes and do not have a higher rate of subsequent surgery.

Keywords

anterior cruciate ligament; patient reported outcomes; activity level; knee instability

INTRODUCTION

Diabetes mellitus is a significant and growing concern in the United States and around the world. A prevalence of 7.3% among adults in the United States noted in the early 2000s (20) had increased to 11.3% by 2011 (2). In adults, over 90% have type 2 diabetes (6), characterized by resistance to insulin and defects in insulin secretion, caused by a combination of genetic and environmental factors. However, most pediatric and adolescent patients have type 1 diabetes (9) which is caused by loss of insulin production, usually due to an autoimmune process, which can occur at any age but usually occurs before the age of 30. Between 2001 and 2009, the prevalence of type I diabetes in children and adolescents increased 21.1% while the prevalence of type II diabetes in the same population increased 30.5% (9).

Physical activity is important for disease management in patients with type 1 diabetes (23) and a recent study demonstrated that physical activity modifies the risk of first acute myocardial infarction in these patients (19). Furthermore, physical activity is protective against the development of type 2 diabetes (15). Active individuals are at risk for injury of the anterior cruciate ligament (ACL) in the knee, which is often treated with surgical reconstruction in order to facilitate maintenance of physical activity. However, studies have demonstrated that activity level decreases significantly at 2 years after ACL reconstruction (ACLR) (11), with even further decline at 6-year follow-up (28).

While diabetes and hyperglycemia is estimated to occur in 5–30% of all types of patients admitted to the hospital (29), there is limited data on the prevalence of diabetes in outpatient orthopedic surgery (24). Based on two recent studies, the prevalence of diabetes in patients undergoing ACLR appears to be approximately 1% (4, 21). Patients with diabetes

undergoing ACLR are likely to have type 1 diabetes, particularly among adolescent and young adult patients, although some young, and more likely mature, patients may have type 2 diabetes. While a recent study demonstrated that diabetes is associated with a higher risk of infection after ACLR (4), there is no data on whether diabetes influences other outcomes in patients undergoing ACLR. In addition to influencing the risk of infection, diabetes could also affect the risk of additional surgery in a number of other ways, such as risk for manipulation due to stiffness, or revision due to compromised healing rates, as well as clinical outcomes. The purpose of this study was to test the hypotheses that diabetes is associated with, (a) patient-reported outcome, and specifically activity level, at 2 years following ACLR; and (b) the risk of subsequent surgery 2 years following ACLR.

METHODS

With Institutional Review Board approval, we reviewed patients who had been initially enrolled in our prospective longitudinal cohort between 2002 and 2005. After obtaining written informed consent, patients completed a questionnaire including but not limited to a series of validated patient-reported outcome measures (Knee Injury and Osteoarthritis Outcome Score [KOOS] (26), International Knee Documentation Committee [IKDC] Subjective Knee form (13), and the Marx activity rating scale (17)) and general health information prior to their surgery. Patients who self-reported diabetes based on comorbidity questions within the questionnaire prior to surgery were identified from the database.

Twenty-three of 2,198 ACLR patients (1.0%) self-reported diabetes at the time of their ACLR. In order to confirm the accuracy of the diagnosis, the medical records from these patients with accessible information were reviewed. Twenty-two of our twenty-three patients identified in the database as having a diagnosis of diabetes were confirmed to have the disease at the time of ACLR, while one patient had no information available within their medical record that could either confirm or deny this self-reported diagnosis.

The main outcome measures of interest were 2 year IKDC, KOOS subscales (symptoms, pain, activity of daily living, sports/recreation, knee-related quality of life), and Marx activity level outcome scores, subsequent surgery on the ipsilateral knee, and subsequent surgery on the contralateral knee. In this study, we defined “subsequent surgery” to include any revision ACLR (on the ipsilateral knee); primary ACLR (on the contralateral knee); arthroscopic procedure involving meniscal, articular cartilage, hardware removal, arthrofibrosis, or infection; or total knee arthroplasty procedure. Given a previous study demonstrating a higher risk of infection after ACLR in patients with diabetes (4), we also reported the rate of subsequent surgery excluding infection on the ipsilateral knee.

Patient-specific covariates that were evaluated in our model included age, sex, body mass index (BMI), smoking status, diagnosis of diabetes, reconstruction type (primary or revision ACLR), graft type (bone-tendon-bone autograft, hamstring autograft, or ‘other’, which included all allografts, as well as any autograft+allograft combination), and baseline IKDC, KOOS, and Marx activity scores.

To describe our patient sample, we summarized categorical variables with frequencies and percentages and continuous variables with their median and interquartile range. To examine evidence for unadjusted associations with diabetes status, we used the Pearson Chi-Square test for categorical variables and the Wilcoxon test for continuous variables.

We used multivariable regression analyses to characterize the independent (adjusted) associations between the baseline risk factors and the dependent outcome variables of subsequent surgery (both ipsilateral and contralateral) and the clinical outcome scores after ACLR (IKDC, KOOS, Marx scores). For the binary outcome measures (subsequent surgery of ipsilateral and contralateral knees; yes/no) multivariable logistic regression models were fit, and for the ordinal continuous outcome measures (IKDC, KOOS, Marx scores), proportional odds regression models were fit. When fitting the multivariable models, the estimates for the continuous variable effects were reported on a linear scale, we thus interpret the odds of the outcome per one unit change in each of the patients' continuous characteristics. For each model the associated regression parameter estimates were exponentiated to obtain odds ratios (OR) along with their 95% confidence intervals (CI). To avoid case-wise deletion of records with missing covariates, we employed multiple imputation via predictive mean matching. Statistical analysis was performed using open source R statistical software (www.cran.r-project.org).

RESULTS

The only significant difference in baseline demographics between patients with diabetes and those without was the KOOS pain subscale (Table 1). There were trends toward more males, higher BMI and lower baseline activity among patients with diabetes. The overall follow-up rate for the entire cohort was 1905/2198 (87%) for patient-reported outcomes and 2096/2198 (95%) for subsequent surgery information. Among patients with diabetes ($n=23$), there was 100% follow-up for patient-reported outcomes and subsequent surgeries. Among the patients without diabetes, there was 87% (1882/2175) follow-up for patient-reported outcomes and 96% (2073/2175) follow-up for subsequent surgeries.

Patient-Reported Outcome Measures

At 2 years after ACLR, univariate results indicate that patients with diabetes have a higher Marx activity level but lower (poorer) IKDC and KOOS pain, activities of daily living (ADL) and sports/recreation outcomes scores (Table 2). Utilizing our multivariable modeling to control for our independent variables of interest, we found that diabetes was a significant positive influence on 2 year Marx activity scores, but was a negative influence on 2 year IKDC, KOOS pain, ADL, and sports/recreation subscores (Table 3).

For example, based on our adjusted regression analysis, patients with diabetes in our study were approximately 3 times more likely (OR=2.96, 95% CI 1.30 to 6.77) to have a higher Marx activity level score than a non-diabetic patient at 2 years post ACL surgery. Patients with diabetes were more likely to have significantly worse IKDC and KOOS pain, ADL, and sports/recreation subscale scores compared with a non-diabetic patients. For instance, at 2 years post ACL surgery, patients with diabetes were associated with a 53% decrease (OR=0.47, 95% CI 0.23 to 0.98) in the odds of a higher IKDC score; a 56% decrease

(OR=0.44, 95% CI 0.21 to 0.90) in the odds of a higher KOOS pain score; a 58% decrease (OR=0.42, 95% CI 0.19 to 0.93) in the odds of a higher KOOS ADL score; and a 56% decrease (OR=0.44, 95% CI 0.22 to 0.88) in the odds of a higher KOOS sports/recreation score.

Incidence of Subsequent Surgery

Among the patients with diabetes, 21.7% (5/23) underwent additional surgery on the ipsilateral knee (13% excluding surgical treatment of infection) and 8.7% (2/23) underwent surgery on the contralateral knee (Table 4). The rate of additional surgery in patients without diabetes was 15.4% (319/2073) on the ipsilateral knee (14.7% excluding surgical treatment of infection) and 6.2% (129/2069) on the contralateral knee. The multivariable model indicated no significant differences between the two groups in terms of additional surgery on the ipsilateral or contralateral knee.

DISCUSSION

Patients with diabetes maintain a higher level of activity after ACLR than patients without diabetes, despite having slightly worse patient reported outcomes. A history of diabetes does not increase the risk of overall additional surgery on the ipsilateral or contralateral limb following ACLR, despite an increased risk of surgical treatment for post-operative infection (4).

It is clinically relevant that these patients maintain a higher activity level after ACLR, considering the importance of physical activity for glycemic control and overall health in patients with diabetes. While it is not clear what would happen to activity level in patients with diabetes if they did not undergo ACLR, the conventional wisdom is that activity level decreases in patients with ACL tears who do not undergo ACLR. This suggests that ACLR has a tangible health benefit for patients with diabetes, i.e. keeping them active. Why patients with diabetes have a higher activity level following ACLR than patients without diabetes is not clear. Most likely, it reflects the motivation of patients with diabetes to stay active as part of their disease management. In studies studying return to play after ACLR in football (18) and soccer (3) players, athletes were more likely to cite life changes, such as graduation, employment or starting a family, as the main reason for not returning to sport rather than the injury itself. Patients with diabetes may be more motivated to maintain their activity in the face of these life changes.

Another notable finding is that patients with diabetes do not have an overall higher risk of subsequent surgery after ACLR compared to patients without diabetes, even though patients with diabetes do have a higher risk for infection after ACLR (4). In a previous study, the likelihood of infection following ACLR increased 18.8 fold in patients with diabetes compared to patients without diabetes (4). While patients with diabetes undergoing ACLR should be made aware of their increased risk for infection, they can also be reassured that they do not face an elevated risk of overall subsequent surgery, such as revision ACLR or debridement/manipulation for loss of motion.

Short-term patient-reported outcomes following ACLR are slightly worse in patients with diabetes. It is important to note that the decrement in KOOS pain (-3) and ADL (-6) scores for patients with diabetes does not exceed the minimal clinically important difference (MCID) for the KOOS instrument of 8–10 points (12, 17, 25, 26). In contrast to the decreased KOOS and IKDC scores, patients with diabetes have a higher level of activity following ACLR. However, the MCID for the Marx activity scale has not been established to date (27).

Other studies have shown worse outcomes after other types of orthopedic surgery in patients with diabetes. Diabetes has been associated with a higher rate of complications following lumbar fusion (5, 12), total knee arthroplasty (14, 30) and total shoulder replacement (22). Uncontrolled diabetes has been shown to be particularly devastating after total joint arthroplasty (16), although a recent study did not find an association between diabetes, both controlled and uncontrolled, and complications after total knee replacement (1). Diabetes has been shown to be associated with less range of motion and worse clinical outcomes after arthroscopic rotator cuff repair (8, 10), as well as a lower health related quality of life (7), similar to our findings in ACLR patients.

While this cohort is prospective, relatively large, and is collected at several centers which improves generalizability, our study is limited by the self-reporting of diabetes within the comorbidity section of questionnaire. Although we confirmed that those who reported diabetes do in fact have the disease, it is possible that we are under reporting if some patients did not know they have diabetes. Screening for diabetes is not currently the standard of care prior to ACLR. Furthermore, we do not have data on glycemic control, which has been shown to be an important variable affecting infection risk after other knee surgeries (16). The study also lacks direct physical exam measures of outcome such as stability and knee range of motion. Range of motion could be particularly important as diabetes is associated with tendon stiffness. However, the lack of physical examination should not influence the incidence of subsequent surgery, nor the 2 year clinical outcome measurements. Finally, the relatively small sample of patients with diabetes may be underpowered to pick up relevant differences in baseline demographics or patient reported outcomes. The wide confidence intervals in the reported odds ratios reflect the limitations of the small sample size. There is the risk of Type II error, particularly for events such as subsequent surgery. Nevertheless, this study did find statistically significant differences between patients with and without diabetes that are likely to be clinically relevant. Other differences may exist as well and further study of this area with larger datasets is likely warranted.

Despite these limitations, this is the first study to look at the effect of diabetes on outcomes following ACLR. These patients maintain a higher activity level after ACLR than patients without diabetes despite lower patient reported outcomes, although the decrement in outcomes may not be clinically significant. Diabetes is not associated with a higher risk for subsequent surgery overall even with an increased risk of surgical washout for infection (4). While patients with diabetes should be counseled about their increased risk of infection and slightly worse clinical outcomes, ACLR can be an appropriate treatment for symptomatic ACL tears in this population, particularly given the potential to maintain a higher level of

physical activity which is an integral component of disease management and health optimization for these patients.

Acknowledgments

The authors thank the research coordinators, analysts and support staff from the Multicenter Orthopaedic Outcomes Network (MOON) knee sites (Cleveland Clinic, Cleveland, OH; Vanderbilt University Medical Center, Nashville, TN; The Ohio State University, Columbus, OH; University of Iowa, Iowa City, IA; Washington University in St. Louis, St. Louis, MO; Hospital for Special Surgery, New York, NY; University of Colorado, Denver, CO), whose efforts related to regulatory, data collection, subject follow-up, data quality control, analyses, and manuscript preparation make this consortium possible. We also thank all the subjects who generously enrolled and participated in this study.

Funding. Research reported in this publication was partially supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health under Award Number R01AR053684 (K.P.S.). The content is solely the responsibility of the authors and do not necessarily represent official views of the National Institutes of Health.

The project was also partially supported by the Orthopaedic Research and Education Foundation and the Vanderbilt Sports Medicine Research Fund, which received unrestricted educational gifts from Smith & Nephew Endoscopy and DonJoy Orthopaedics.

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Table 1

Baseline Patient Characteristics between Groups

	Diabetes Cohort (n=23)	Rest of Cohort (n=2175)	Combined (n=2198)	p value
Male sex	74% (17)	56% (1209)	56% (1226)	0.08
Age (years)	32 (18,41)	24 (17,35)	24 (17,35)	0.11
BMI (kg/m ²)	26 (24,30)	25 (22,28)	25 (22,28)	0.07
Current Smoker	13% (3)	10% (210)	10% (213)	0.61
Reconstruction Type				0.06
• Primary	78% (18)	90% (1963)	90% (1981)	
• Revision	22% (5)	10% (212)	10% (217)	
Graft Type				0.83
• Autograft – bone-tendon-bone	39% (9)	42% (922)	42% (931)	
• Autograft – hamstrings	35% (8)	29% (631)	29% (639)	
• Other (allografts, auto+allo)	26% (6)	29% (622)	29% (628)	
Marx Activity Level (score 0–16)	9 (3,16)	12 (8,16)	12 (8,16)	0.07
IKDC (score 0–100)	47 (33,59)	52 (40,64)	52 (40,63)	0.17
KOOS (score 0–100)				
• Symptoms	64 (48,79)	68 (54,82)	68 (54,82)	0.32
• Pain	67 (53,79)	75 (61,89)	75 (61,89)	0.03 *
• Activities of daily living	82 (68,96)	88 (72,97)	88 (72,97)	0.30
• Sports/recreation	50 (22,78)	50 (30,75)	50 (30,75)	0.52
• Knee-related quality of life	31 (19,47)	38 (25,50)	38 (22,50)	0.40

Key:

Data are % (n) unless otherwise indicated.

a (b,c) represent the median *a*, lower quartile *b*, and the upper quartile *c* for continuous variables.

* significant at p 0.05 level

Table 2

Median (25%, 75% Quartile) Outcome Scores between Groups at 2 Years

	Diabetes Cohort (n=23)	Rest of Cohort (n=2175)	Combined (n=2198)	p value
Marx Activity Level	12 (4,16)	8 (4,13)	8 (5,13)	0.15
IKDC	83 (61,89)	85 (72,92)	85 (72,92)	0.13
KOOS				
• Symptoms	82 (64,93)	86 (75,93)	86 (75,93)	0.09
• Pain	89 (78,94)	92 (83,97)	92 (83,97)	0.04 *
• Activities of daily living	93 (90,99)	99 (93,100)	99 (93,100)	0.04 *
• Sports/recreation	80 (59,90)	85 (70,95)	85 (70,95)	0.13
• Knee-related quality of life	69 (42,81)	75 (56,88)	75 (56,88)	0.20

Key:

a (b,c) represent the median *a*, lower quartile *b*, and the upper quartile *c* for continuous variables.

* significant at p 0.05 level

Table 3

Modeling Estimates at 2 Years (Diabetic Cohort only)

	Odds Ratio	95% C.I.	p value
Marx Activity Level	2.96	1.30 – 6.77	0.010 *
IKDC	0.47	0.23 – 0.98	0.044 *
KOOS			
• Symptoms	0.55	0.26 – 1.19	0.130
• Pain	0.44	0.21 – 0.90	0.025 *
• Activities of daily living	0.42	0.19 – 0.93	0.032 *
• Sports/recreation	0.44	0.22 – 0.88	0.021 *
• Knee-related quality of life	0.59	0.27 – 1.29	0.183
Subsequent Surgery			
• Ipsilateral knee	2.22	0.79 – 6.25	0.130
• Contralateral knee	1.91	0.43 – 8.46	0.394

Key:

Reference value = non-diabetic cohort

* significant at p 0.05 level

Table 4

Number (%) of Subsequent Ipsilateral and Contralateral Surgeries between Groups

	Diabetes Cohort (n=23)	Rest of Cohort (n=2073)	Combined (n=2096)	p value
Ipsilateral knee	5 (22%)	319 (15%)	324 (15%)	0.40
• Excluding infection	3 (13%)	304 (15%)	307 (15%)	
Contralateral knee	2 (9%)	129 (6%)	131 (6%)	0.58