Factors Associated with Infection Following Anterior Cruciate Ligament Reconstruction

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Background: Although rare, infection can be devastating after anterior cruciate ligament (ACL) reconstruction. The purpose of this study was to test the association between infection after ACL reconstruction and potential risk factors such as age, body mass index (BMI), smoking, diabetes, and graft choice.

Methods: We reviewed the Multicenter Orthopaedic Outcomes Network (MOON) cohort from 2002 to 2005 to identify patients with a postoperative infection. The age, BMI, smoking status, history of diabetes, and graft choice were recorded for each patient. A multivariable regression analysis was constructed to examine which baseline risk factors were independently associated with postoperative infection after ACL reconstruction requiring surgical intervention.

Results: There were 2198 eligible patients in the cohort, with seventeen (0.8%) reporting a postoperative infection. Diabetes was found to be a significant risk factor for infection (odds ratio [OR] = 18.8; 95% confidence interval [CI] = 3.8 to 94.0; $p < 0.001$). Compared with bone-tendon-bone autograft, both hamstring autograft and other grafts (e.g., the majority of allografts, with some that were both autograft and allograft) also increased the risk of infection (OR = 4.6 [95% CI = 1.2 to 17.9; $p = 0.026$] for hamstrings and 4.3 [95% CI = 1.0 to 18.1; $p = 0.047$] for other grafts). Although the OR for infection in smokers was 2.5, this finding did not reach significance.

Conclusions: Patients with diabetes undergoing ACL reconstruction have a significantly elevated risk of postoperative infection (18.8-times higher odds) compared with that for patients without diabetes. Use of bone-tendon-bone autograft is associated with a lower risk of infection after ACL reconstruction.

Level of Evidence: Prognostic Level II. See Instructions for Authors for a complete description of levels of evidence.

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Infection is a relatively rare but potentially serious complication after anterior cruciate ligament (ACL) reconstruction[1-4]. Because of the low prevalence of infection after ACL reconstruction, a study of such infections requires a large cohort in order to control for heterogeneous factors and to facilitate meaningful analysis of associated risk factors. Recent studies on infection after ACL reconstruction have demonstrated that graft choice may be a risk factor[1,4]. Smoking has been shown to be a risk factor for infection after orthopaedic surgery[5,6], and obesity increases the risk of infection after spinal surgery[7,8] and arthroplasty[9,10]. Diabetes is well known to be associated with an elevated risk of surgical site infections in a variety of surgical specialties[11-13], including orthopaedics[8,14-19].

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TABLE I Patient Characteristics by Infection Status

	No. of Patients with Data	Infection Status			Test Statistic
		No (N = 2181)	Yes (N = 17)	Combined (N = 2198)	
Age* *(yr)*	2198	26.8 ± 11.0 (17/24/35)	24.5 ± 9.6 (18/20/30)	26.8 ± 11.0 (17/24/35)	$F_{1,2196} = 0.25$, p = 0.62†
BMI* *(kg/m²)*	2161	25.7 ± 4.8 (22.4/25.0/28.1)	25.2 ± 6.1 (23.0/24.4/25.8)	25.7 ± 4.8 (22.4/25.0/28.1)	$F_{1,2159} = 1$, p = 0.31†
Diabetes	2198				$\chi(2/1) = 19$, p < 0.001†
No		99% (2160/2181)	88% (15)	99% (2175/2198)	
Yes		1% (21/2181)	12% (2)	1% (23/2198)	
Smoker	2160				$\chi(2/1) = 1.2$, p = 0.28†
No		90% (1933/2143)	82% (14)	90% (1947/2160)	
Yes		10% (210/2143)	18% (3)	10% (213/2160)	
Graft type§	2198				$\chi(2/2) = 4.7$, p = 0.098†
BTB autograft		43% (928/2181)	18% (3)	42% (931/2198)	
Hamstring autograft		29% (631/2181)	47% (8)	29% (639/2198)	
Other		29% (622/2181)	35% (6)	29% (628/2198)	

*The values are given as the mean and standard deviation, with percentiles (25th, 50th, and 75th) for continuous variables in parentheses. †Wilcoxon test. ‡Pearson test. §BTB = bone-tendon-bone.

One study of infections after ACL reconstruction noted that <1% of 801 patients undergoing this surgery had diabetes[20]. Therefore, in order to study the potential impact of diabetes on patients undergoing ACL reconstruction, a very large cohort would be necessary. The prospective cohort followed by the Multicenter Orthopaedic Outcomes Network (MOON) Group[21] provides an excellent opportunity to look at risk factors for infection after ACL reconstruction. The purpose of the present study was to test the hypothesis that patient age, body mass index (BMI), smoking status, diabetes, and graft choice are associated with the risk of infection in patients undergoing ACL reconstruction.

Materials and Methods

For the present study, we reviewed the cases of patients who had been initially enrolled between 2002 and 2005 in the prospectively followed MOON ACL reconstruction cohort[21]. All patients undergoing unilateral ACL reconstruction during this time period were eligible. Following documentation of informed consent, patients completed a questionnaire regarding self-reported demographic information, injury characteristics, sports participation history, and health status prior to their surgery[21,22]. Patients who self-reported diabetes on the basis of comorbidity questions within the questionnaire prior to surgery were identified from the database. Six-year follow-up data on subsequent surgical procedures were obtained, and all procedures were categorized.

For the purposes of this study, an infection was defined as an ACL reconstruction that required a postoperative surgical irrigation and debridement. Clinical data such as the absence or presence of an effusion, fever, or culture were not available. Infections that were managed with antibiotics alone were not included in this study.

Only twenty-three (1%) of 2198 patients who had an ACL reconstruction had diabetes. In order to confirm the accuracy of the diagnosis, the medical records from ten patients with accessible information were reviewed as a convenience sample. All ten of these patients identified in the MOON database as having a diagnosis of diabetes were confirmed through a review of their medical charts to have the disease at the time of ACL reconstruction.

Patient age, BMI, smoking status, a diagnosis of diabetes at the time of surgery, and graft choice were the independent variables evaluated. These variables were summarized to assess their individual distribution; continuous variables were expressed as percentiles (i.e., 25th, 50th, and 75th) with their mean and standard deviation, and categorical variables were given as frequencies and percentages. Multivariable regression analysis was performed to examine which baseline risk factors were independently associated with the dependent outcome variable of surgical irrigation and debridement for infection after ACL reconstruction. A multivariable logistic regression model was fit to the data, and parameter estimates were exponentiated to obtain odds ratios (ORs) and 95% confidence intervals (CIs). To avoid casewise deletion of records with missing covariates, we employed multiple imputations via predictive mean matching. Statistical analysis was performed using the R statistical software.

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Results

A total of 2198 patients were available for analysis. The average age (and standard deviation) of the cohort was 27 ± 11 years, with a BMI of 25.7 ± 4.8 kg/m². Ten percent were smokers, and 1% of the cohort had diabetes at the time of ACL reconstruction. Bone-tendon-bone (BTB) autograft was the most common graft choice, making up 43% of the overall cohort, with hamstring autograft used in 29% of the reconstructions and other grafts

TABLE II Model Estimates

Characteristic	Odds Ratio	95% CI	P Value
Age	0.956	0.91-1.01	0.106
BMI	0.977	0.87-1.09	0.680
Diabetes mellitus	18.807	3.76-93.97	<0.001
Smoker	2.541	0.68-9.55	0.167
Graft type, relative to BTB autograft			
Hamstring autograft	4.631	1.20-17.91	0.026
Other	4.295	1.02-18.11	0.047

(defined in the present study as any allograft or both allograft and autograft) used in 29%.

The overall rate of infection in the cohort was 0.77% (seventeen of 2198 patients). The distribution of risk factors between those with and those without infection was noted (Table I). In a comparison of the distribution of risk factors between patients who developed a postoperative infection after ACL reconstruction and those who did not, the only significant factor was diabetes, as the rate of infection was 8.7% in patients with diabetes and 0.7% in patients without diabetes ($p < 0.001$).

In the model estimates of the odds for infection (Table II), diabetes and graft choice were found to be significant risk factors for infection. Diabetes increased the odds of infection by 18.8 times (95% CI = 3.8 to 94.0; $p < 0.001$). Hamstring autograft and other graft choices were associated with an increased odds of infection (OR = 4.6 [95% CI = 1.2 to 17.9; $p = 0.026$] and 4.3 [95% CI = 1.02 to 18.1; $p = 0.047$], respectively) compared with BTB autograft. Patient age and BMI were not associated with the risk of infection in this cohort. Although the OR for infection in smokers was 2.5, the finding did not reach significance in this cohort.

Discussion

Postoperative infection is a rare event after ACL reconstruction, but diabetes and graft choice affect the relative risk of this complication. The present study is the first, to our knowledge, to establish diabetes as a risk factor for infection after ACL reconstruction, while the influence of graft choice is consistent with findings in previous studies[1,4]. Patient age and BMI did not influence the risk of postoperative infection after ACL reconstruction in this cohort, and there was insufficient evidence to establish an association between smoking and infection.

The rate of infection after ACL reconstruction in the present study is similar to rates previously reported in the literature. Maletis et al.[4] reported an overall rate of infection of 0.48% after 10,626 ACL reconstructions, while Barker et al.[1] reported a rate of 0.58% in 3126 patients. Judd et al.[3] reported a rate of 0.68% in 1615 ACL reconstructions compared with an overall rate of 0.75% in 801 ACL reconstructions reported by Katz et al.[20].

The increased risk of infection associated with diabetes is not surprising, considering similar evidence for other types of orthopaedic surgery. In a study of orthopaedic procedures in an ambulatory surgery center, diabetes was a significant risk factor (OR = 3.05) for surgical site infection[23]. Multiple studies have demonstrated that diabetes is associated with an elevated risk of infection after spine surgery[8,14,16,19]. In studies on joint arthroplasty involving patients with diabetes, most have found that such patients have a greater risk of infection[15,17,18], although a few have not found diabetes to be a significant risk factor[10]. Patients with diabetes should be counseled about their increased risk of infection at the time of ACL reconstruction. What we could not measure in the present study was the influence of glycemic control, which has been shown to be an important variable affecting infection risk after other knee operations[24], on the relative risk of infection after ACL reconstruction.

While there has been some evidence that hamstring autograft is associated with a higher risk of infection than BTB autograft[1,4], this is the first study, as far as we know, to demonstrate an increased risk of infection associated with allograft compared with BTB autograft. The prevalence of infection was 0.3% in patients receiving BTB autograft compared with 1.3% in patients receiving hamstring autograft and 1.0% in patients receiving other grafts. This suggests that BTB autograft may be preferable in patients with diabetes to mitigate their increased risk of infection. Two of the seventeen patients with diabetes developed infections; one had a hamstring graft and the other had an allograft. More research is needed to assess why infection rates vary by graft type and whether the use of BTB autograft could partially offset the increased risk of infection in patients with diabetes.

While the difference in the risk of infection between BTB autograft and hamstring autograft is significant, the clinical relevance may be debated, particularly since the underlying mechanisms contributing to graft-based differences in infection risks are not immediately obvious. Perhaps the timing of the graft harvest during the procedure influences this risk as surgeons often harvest the hamstring tendon early in the operation and may harvest a BTB autograft later in the procedure, although this is not always the case. The elevated risk of infection with hamstring autograft may be due to the more extensive deep dissection required, with the potential for hematoma formation in the area of the graft harvest. Alternatively, there may be an intrinsic aspect of the BTB autograft that provides innate protection against infection.

Age and BMI did not have any association with the risk of infection after ACL reconstruction in this model. The present cohort was relatively young (mean, 27 ± 11 years old) and lean (mean BMI, 25.7 ± 4.8 kg/m^2), which may have limited the sensitivity of the analysis for these variables, particularly for older and heavier patients. However, the cohort is representative of patients typically undergoing ACL reconstruction, which supports the generalizability of this finding. In the recent study by Maletis et al.[4], BMI was not associated with the overall rate of infection but was associated with an increased risk of superficial surgical site infections.

Smoking has been associated with an increased risk of infection in other types of orthopaedic surgery[5,6]. With a 10% prevalence of smoking in this cohort, it is possible that the study was not adequately powered to assess the impact of smoking on

infection risk in this patient group. There are relatively few data on the effect of smoking on outcomes after ACL reconstruction[25], and we are not aware of any previous study on the relationship of smoking status to infection risk in patients having ACL reconstruction. The elevated odds ratio for infection among smokers, which did not reach significance in our cohort, suggests further research is needed.

The present study has numerous strengths and several weaknesses. The MOON cohort is prospective and relatively large and has data collected at several centers, which improves generalizability. The diabetes diagnosis is self-reported within a comorbidity section of the questionnaire. Although we confirmed that those who reported diabetes did in fact have the disease, it is possible that we are underreporting if some patients were not aware that they had diabetes at the time of their ACL reconstruction. Screening for diabetes prior to ACL reconstruction is not currently the standard of care. The study may have been underpowered, particularly to measure the effect of smoking and possibly patient age and BMI as well. With an effective sample size of seventeen, small changes in the data can have a substantial influence on the analysis. Furthermore, only five variables were included in the regression model to avoid "overfitting" the data. As a result, other variables that could conceivably relate to the risk of infection, such as use of a tourniquet, tourniquet time, or surgical center, were not included in the multivariable analysis. Data on whether preoperative antibiotics were used and, if so, which antibiotics were used were not available. The type and location of fixation were other potential variables of interest that were not available in the data set for analysis. Finally, data on the type and antibiotic sensitivity of the infecting microorganisms were not available for the infections.

Despite these limitations, this is the first study, to our knowledge, to demonstrate that diabetes is a risk factor for infection after ACL reconstruction. Patients with diabetes were over eighteen times more likely to have a postoperative infection than were nondiabetic patients. BTB autograft is associated with a lower risk of infection after ACL reconstruction than other graft choices. Further research could more precisely define the association of BMI and smoking with the risk of infection after ACL reconstruction. These findings will help surgeons and patients to have an informed discussion of the risk of infection after ACL reconstruction and, hopefully, lead to further research efforts into ways to mitigate these risk factors. ■

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