Video Abstract

Factors Associated With an Intra-articular Infection After Anterior Cruciate Ligament Reconstruction

A Large Single-Institution Cohort Study

Niv Marom,* MD, Milan Kapadia, BS, Joseph T. Nguyen, MPH, Brittany Ammerman, MBS, Isabel Wolfe, BS, Kristin C. Halvorsen, BS, Andy O. Miller, MD, Michael W. Henry, MD, Barry D. Brause, MD, Jo A. Hannafin, MD, Robert G. Marx, MD, and Anil S. Ranawat, MD
Investigation performed at the Hospital for Special Surgery, New York, New York, USA

Background: An intra-articular infection after anterior cruciate ligament (ACL) reconstruction (ACLR) is a rare complication but one with potentially devastating consequences. The rare nature of this complication raises difficulties in detecting risk factors associated with it and with worse outcomes after one has occurred.

Purpose: To (1) evaluate the association between an infection after ACLR and potential risk factors in a large single-center cohort of patients who had undergone ACLR and (2) assess the factors associated with ACL graft retention versus removal.

Study Design: Case-control study; Level of evidence, 3.

Methods: All ACLR procedures performed at our institution between January 2010 and December 2018 were reviewed; a total of 11,451 procedures were identified. A retrospective medical record review was performed to determine the incidence of infections, patient and procedure characteristics associated with an infection, infection characteristics, incidence of ACL graft retention, and factors associated with the retention versus removal of an ACL graft. Multivariable logistic regression analysis was used to identify potential risk factors for an infection after ACLR.

Results: Of the 11,451 ACLR procedures, 48 infections were identified (0.42%). Multivariable logistic regression analysis revealed revision ACLR (odds ratio [OR], 3.13 [95% CI, 1.55-6.32]; $P = .001$) and younger age (OR, 1.06 [95% CI, 1.02-1.10]; $P = .001$) as risk factors for an infection. Compared with bone–patellar tendon–bone autografts, both hamstring tendon autografts (OR, 4.39 [95% CI, 2.15-8.96]; $P < .001$) and allografts (OR, 5.27 [95% CI, 1.81-15.35]; $P = .002$) were independently associated with an increased risk of infections. Overall, 15 ACL grafts were removed (31.3%). No statistically significant differences besides the number of irrigation and debridement procedures were found for retained versus removed grafts, although some trends were identified ($P = .054$).

Conclusion: In a large single-center cohort of patients who had undergone ACLR and those with an infection after ACLR, patients with revision cases and younger patients were found to have a higher incidence of infection. The use of bone–patellar tendon–bone autografts was found to be associated with the lowest risk of infection after ACLR compared with both hamstring tendon autografts and allografts. Larger cohorts with a larger number of infection cases are needed to determine the factors associated with graft retention versus removal.

Keywords: ACL reconstruction; infection; septic arthritis; autografts; allografts; risk factors

Septic arthritis is a relatively rare complication after anterior cruciate ligament (ACL) reconstruction (ACLR), with a reported incidence of 0.12% to 1%.[2-6,11,20,21,23] Multiple studies have investigated and reported on factors associated with this major complication; however, the low incidence of knee joint infections after ACLR has limited the ability of the existing literature to do so.

In the past decade, multiple studies assessing the infection risk with different types of grafts noted an increased risk of infections for hamstring tendon autografts compared with bone–patellar tendon–bone (BPTB) autografts.[2,3,6,17,23] Evidence regarding the infection risk associated with the use of allograft tissue revealed conflicting data, with some suggesting a higher risk of infections[6,9]

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and others reporting no difference compared with BPTB autografts.[3,16,18,23] Other factors, such as patient characteristics and/or comorbidities,[6,23] treatment protocols,[1,3,5,11,29] and isolated pathogens,[1] were also investigated in small- to medium-sized cohorts.

Based on the rationale that a larger cohort may provide important information, the purposes of this study were (1) to evaluate the association between an infection after ACLR and potential risk factors in a large single-center cohort of patients who had undergone ACLR and (2) to assess the factors associated with ACL graft salvage versus removal. We hypothesized that graft type, revision surgery, age, body mass index (BMI), and bacterial profile would be associated with both the risk of infection in patients undergoing ACLR and the risk of graft removal after one has occurred.

METHODS

Institutional review board approval was attained before study initiation. We retrospectively identified all patients who had ACLR performed at a single tertiary care orthopaedic institution between January 2010 and December 2018. A clinical data repository, with information extracted from electronic medical records, was queried to identify ACLR cases. Patient characteristics, comorbidities, and operative data including graft type and previous ACL surgery were collected. To identify infection cases, we chose patients who had undergone ACLR with at least 1 of the following International Classification of Diseases diagnosis codes indicating an infection (M00, M01, T81.4, T84.5, T84.6, T84.7, M86, 711, or 996.6) for a complete manual chart review to confirm postoperative septic arthritis secondary to ACLR and to collect additional data. All patients in this cohort had deep tissue infections as defined by National Healthcare Safety Network/Centers for Disease Control and Prevention guidelines for deep tissue infections.[15] These included signs and symptoms of an infection with evidence of a septic knee joint with at least 1 of the following: purulent drainage from a deep incision, knee joint aspiration suggestive of a bacterial infection, culture-positive aspiration, and physical examination findings consistent with an intra-articular infection. For infection cases, the following patient data were collected: age, sex, comorbidities, previous ACL surgery, graft type, tourniquet time, and concomitant procedures. Infection data including symptoms, laboratory values, microorganism, graft retention, and postoperative antibiotic treatment were collected. Charlson and Elixhauser comorbidity indices were calculated based on International Classification of Diseases diagnosis codes.[25]

Before ACLR, all patients at our institution were instructed to prepare the surgical site (using an antiseptic, antimicrobial wash) at home before presentation at the hospital. At the hospital, in the presurgical holding area, hair at the incision site was removed using clippers (as needed), and an alcohol-based solution was used for preliminary preparation. In the operating room, surgical preparation was initially performed using either a povidone-iodine scrub or alcohol-based scrub by the circulating nurse. The leg was then kept sterile while the surgeon performed a second povidone-iodine scrub or alcohol-based scrub using paint sticks. All patients received weight-appropriate antibiotics within 30 minutes of the skin incision consisting of cefazolin or vancomycin (if there was a significant penicillin or cephalosporin allergy). Sterilization of instruments was performed per the standard hospital protocol.

All primary and revision ACLR procedures were performed by fellowship-trained sports medicine surgeons at a single tertiary care institution. Methods of graft harvest, preparation including antibiotic soaking of the ACL graft before its insertion, and fixation were at the individual discretion of the attending surgeon. Postoperative rehabilitation protocols also varied according to graft fixation method, graft type, surgeon preference, and concomitant procedures. The type of ACL graft was chosen based on the attending surgeon's and patient's preference. There were multiple surgeons in each graft type group. All allograft tissue was obtained from the Musculoskeletal Transplant Foundation, American Red Cross Tissue Services, or Community Tissue Services. Antibacterial detergents, antiviral detergents, and gamma irradiation were utilized at each of these organizations per their individual standard protocols. All allograft tissue was fresh-frozen and stored at –80°C at our institution before use in surgery.

All infection cases at our institution involved a consultation with infectious disease specialists. Treatment of infections consisted of arthroscopic irrigation and debridement (I&D) of the knee including consideration for graft removal, exploration of the surgical wound around donor sites and bone tunnels, and antibiotic therapy. The number of I&D procedures and the need for subsequent graft removal in specific cases were decided according to patient

*Address correspondence to Niv Marom, MD, Department of Orthopaedic Surgery, Meir Medical Center, 59 Tchernichovsky Street, Kfar Saba, 4428164 Israel (email: niv.marom@gmail.com) (Twitter: @NivMaromMD).

All authors are listed in the Authors section at the end of this article.

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factors, the pathogen, ongoing clinical symptoms, and laboratory results. Antibiotic therapy prescribed by the infectious disease specialist was guided by microbiological culture results. Intravenous, oral, or combination therapy was prescribed based on clinical and microbiological profiles for 4 to 6 weeks. Oral antibiotic suppression was typically continued for a duration of ≥12 weeks from the I&D procedure. Serial blood tests were performed to assess for signs of antibiotic toxicity including nephrotoxicity, hepatotoxicity, and myelotoxicity.

Statistical Analysis

The assumption of the normal distribution of continuous data was assessed using the Shapiro-Wilk test. Descriptive statistics are summarized as the mean and SD for continuous variables that met the assumption of normal distribution. Continuous variables that did not meet this assumption are reported as the median and interquartile range (IQR). Discrete variables are reported as the frequency and percentage. Continuous variables were analyzed using an independent-samples *t* test (or nonparametric Mann-Whitney *U* test if the normality assumption was violated). Discrete variables were analyzed using the chi-square test or Fisher exact test depending on the sample size.

Multivariable logistic regression analysis was used to identify potential risk factors for an infection after ACLR. Candidate variables for the regression analysis included age, sex, BMI, comorbidity index, graft type, and revision versus primary surgery. Age, sex, BMI, and comorbidity index were chosen a priori. Additional variables were included if they were found to be significantly associated with a postoperative infection in the univariate analysis. Findings from the logistic regression model are reported as odds ratios (ORs) and 95% CIs. All analyses were performed using 2-sided testing, with statistical significance defined as a *P* value of ≤.05. Statistical analyses were performed using SAS 9.4 (SAS Institute) and RStudio 1.2.5042 (RStudio).

RESULTS

Characteristics of the ACLR Cohort

In the 9-year study period (2010-2018), a total of 11,451 ACLR cases were identified. Of these, 6384 (55.8%) were in male patients. The mean age was 30.0 ± 12.3 years, and the mean BMI was 25.2 ± 4.4. There were 10,305 patients (90.0%) who underwent primary ACLR and 1146 patients (10.0%) who underwent revision ACLR. Overall, 81.2% of grafts used were autologous, with BPTB autografts being most commonly used (46.3% of total cohort), followed by hamstring tendon autografts (33.2% of total cohort). The most common type of allograft used was Achilles tendon allograft (12.7% of total cohort), followed by hamstring tendon allograft (2.7% of total cohort). The mean Elixhauser Comorbidity Index was 0.2 ± 0.5. Additionally, 588 (5.1%) patients had a documented history of smoking, 55 (0.5%) had diabetes, and 243 (2.1%) were obese (Table 1).

With regard to graft utilization trends for this cohort during the period of 2010 to 2018, hamstring tendon autograft use increased from 97 per 1000 cases to 379 per 1000 cases, and allograft use decreased from 326 per 1000 cases to 112 per 1000 cases. Overall, BPTB autografts were the most commonly used at 468 per 1000 cases during 2018 (Figure 1).

Risk Factors Associated With an Infection

The overall infection rate was 0.42% (48/11,451). The infection rate according to graft type was 0.71% (27/3798) for hamstring tendon autografts, 0.23% (12/5306) for BPTB autografts, 0.59% (1/169) for quadriceps tendon autografts, and 0.37% (8/2156) for allografts (Table 2). The infection rate for revision cases was 1.05% (12/1146). There were significant differences in patient age (26.0 ± 12.0 vs 30.0 ± 12.3 years, respectively; $P = .023$) and graft type ($P = .005$) used between infection cases and noninfection cases. No significant differences were found for the BMI ($P = .498$), Elixhauser Comorbidity Index ($P = .694$), or history of smoking ($P > .999$) (Table 1).

In the multivariable logistic regression model for the risk of infections after ACLR, revision surgery (OR, 3.13 [95% CI, 1.55-6.32]; $P = .001$), allografts compared with BPTB autografts (OR, 5.27 [95% CI, 1.81-15.35]; $P = .002$), and hamstring tendon autografts compared with BPTB autografts (OR, 4.39 [95% CI, 2.15-8.96]; $P < .001$) increased the risk of infections. Younger age was found to be associated with an infection (OR, 1.06 [95% CI, 1.02-1.10]), with every year increase in age associated with a decreased likelihood of infections (OR, 0.94 [95% CI, 0.91-0.98]; $P = .001$) (Table 3).

Infection Group

Of 48 patients with postoperative infection, the graft was retained in 33 patients (68.8%). Patients with 3 I&D procedures were more likely to have their graft removed ($P = .028$). The median time from index surgery to the initial I&D procedure was 29 days (IQR, 16-36 days). The median time between symptom onset and the initial I&D procedure was 5 days (IQR, 2-7.5 days). During the initial hospital admission, 29 (60.4%) underwent 1 I&D procedure, 14 (29.2%) underwent 2 I&D procedures, and 5 (10.4%) underwent 3 I&D procedures. Also, 13 (27.1%) underwent concomitant procedures at the time of index surgery. These procedures included the following: meniscal repair (n = 7), additional ligament reconstruction (n = 2), microfracture to articular surfaces (n = 2), and lateral augmentation procedures (n = 2). Coagulase-negative staphylococci (12/48 [25.0%]) were the most common infecting organism. In addition, there were 9 (18.8%) culture-negative cases. The only statistically significant difference between patients whose graft was ultimately removed and patients whose graft was retained was the number of I&D procedures (higher rate for >2 procedures in graft removal group) (Table 4).

TABLE 1
Patient Characteristics of ACLR Cohort[a]

	Total (N = 11,451)	Noninfection (n = 11,403)	Infection (n = 48)	*P* Value
Age, y	30.0 ± 12.3	30.0 ± 12.3	26.0 ± 12.0	**.023**[b]
Body mass index	25.2 ± 4.4	25.2 ± 4.4	24.7 ± 4.5	.498[b]
Elixhauser Comorbidity Index	0.2 ± 0.5	0.2 ± 0.5	0.2 ± 0.4	.694[b]
Female sex	5067 (44.2)	5050 (99.7)	17 (0.3)	.217[c]
Graft type				.701[c]
Autograft	9295 (81.2)	9255 (99.6)	40 (0.4)	**.005**[c]
BPTB	5306 (46.3)	5294 (99.8)	12 (0.2)	
Hamstring tendon	3798 (33.2)	3771 (99.3)	27 (0.7)	
Quadriceps tendon	169 (1.5)	168 (99.4)	1 (0.6)	
Allograft[d]	2156 (18.8)	2148 (99.6)	8 (0.4)	
Index procedure				**.001**[c]
Primary	10,305 (90.0)	10,269 (99.7)	36 (0.3)	
Revision	1146 (10.0)	1134 (99.0)	12 (1.0)	
Laterality				.074[c]
Left	5823 (50.9)	5792 (99.5)	31 (0.5)	
Right	5628 (49.1)	5611 (99.7)	17 (0.3)	
History of smoking	588 (5.1)	586 (99.7)	2 (0.3)	>.999[e]
Diabetes	55 (0.5)	55 (100.0)	0 (0.0)	>.999[e]
Inflammatory arthritis	26 (0.2)	26 (100.0)	0 (0.0)	>.999[e]

[a]Data are presented as mean ± SD or n (%). ACLR, anterior cruciate ligament reconstruction; BPTB, bone–patellar tendon–bone. Bolded p values represent statistical significance (<0.05).
[b]*P* values were calculated using the Mann-Whitney *U* test.
[c]*P* values were calculated using the chi-square test.
[d]Allografts included 1454 Achilles tendons, 304 hamstring tendons, 269 tibialis tendons, 120 patellar tendons, and 9 quadriceps tendons.
[e]*P* values were calculated using the Fisher exact test.

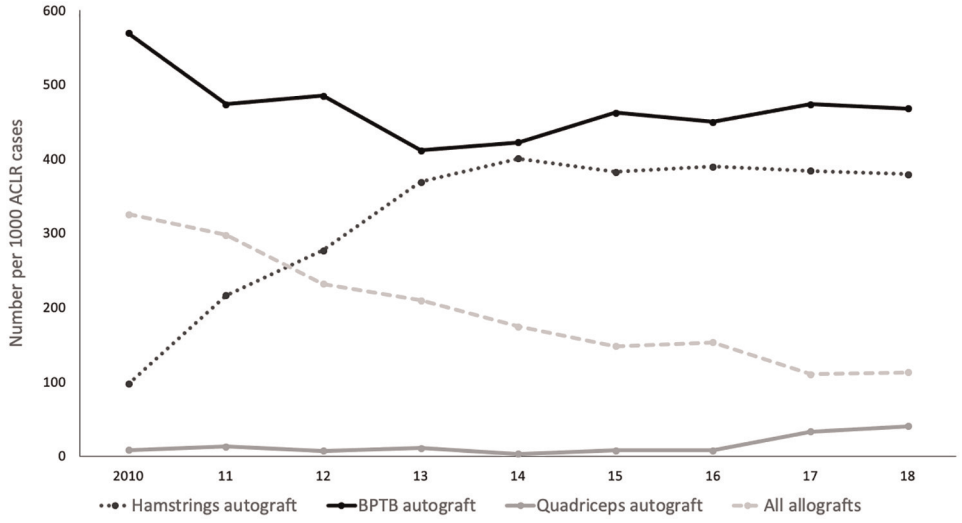

Figure 1. Graft utilization trends between 2010 and 2018 at our institution. ACLR, anterior cruciate ligament reconstruction; BPTB, bone–patellar tendon–bone.

DISCUSSION

Septic arthritis after ACLR remains a rare complication that is challenging to manage. To our knowledge, this study represents the largest series of infection cases after ACLR originating from a single center in the literature. The most important finding of this study is that patients with both hamstring tendon autografts and allografts had a higher incidence of infections after ACLR when separately compared with patients with BPTB autografts (OR, 4.39 and 5.27, respectively). While multiple studies[2,3,6,20,23] have reported on the higher incidence of infections with the use of hamstring tendon autografts compared with BPTB autografts (OR range, 3.34[3] to

TABLE 2
Patient Characteristics and Rate of Infections by Graft Type[a]

	Total (N = 11,451)	Hamstring Tendon Autograft (n = 3798)	BPTB Autograft (n = 5306)	Quadriceps Tendon Autograft (n = 169)	Allograft (n = 2156)
Age at surgery, y	30.0 ± 12.3	32.3 ± 11.8	23.9 ± 8.6	23.6 ± 11.4	41.5 ± 11.1
Body mass index	25.2 ± 4.4	25.2 ± 4.3	25.0 ± 4.1	23.1 ± 4.2	26.4 ± 5.2
Sex					
Male	6384 (56)	2013 (53)	3216 (61)	94 (56)	1043 (48)
Female	5067 (44)	1785 (47)	2090 (39)	75 (44)	1113 (52)
Infection	48 (0.42)	27 (0.71)	12 (0.23)	1 (0.59)	8 (0.37)

[a]Data are presented as mean ± SD or n (%). BPTB, bone–patellar tendon–bone.

TABLE 3
Multivariable Logistic Regression Analysis for Risk of Infections After ACLR[a]

Factor	Odds Ratio (95% CI)	*P* Value
Age (younger)[b]	1.06 (1.02-1.10)	**.001**
Body mass index[b]	0.98 (0.91-1.06)	.596
Female sex	0.54 (0.29-1.01)	.056
Hamstring tendon autograft vs BPTB autograft	4.39 (2.15-8.96)	**<.001**
Allograft vs BPTB autograft	5.27 (1.81-15.35)	**.002**
Revision surgery	3.13 (1.55-6.32)	**.001**
Elixhauser Comorbidity Index	0.88 (0.43-1.80)	.728

[a]ACLR, anterior cruciate ligament reconstruction; BPTB, bone–patellar tendon–bone. Bolded p values represent statistical significance (<0.05).
[b]Continuous variable.

8.24[23]), the most recent literature did not show an increased risk with the use of allografts compared with BPTB autografts.[3,12,20,23] Other studies have reported no differences in the risk of infection between the use of allografts and autografts[18] in general or between the use of BPTB autografts and all other grafts.[2] Conversely, Brophy et al[6] reported on an increased infection risk for a mixed group of allografts and allografts plus autografts compared with BPTB autografts (OR, 4.29); however, this was not a direct comparison between allografts and BPTB autografts. In fact, no previous study has shown a statistically significant increase in the infection rate with the use of allografts compared with BPTB autografts as we report in this study, and we believe that those studies may have been underpowered to detect these differences, with insufficient sample sizes of both total ACLR cases and infection cases for both types of grafts.

Despite the overall low incidence of infections after ACLR, the considerably lower risk of infections with the use of BPTB autografts, compared with both hamstring tendon autografts and allografts, is clinically relevant. The reasons for these graft-based differences in the infection rate are unknown. Several authors have proposed various theories, including the deeper dissection required for the harvest of hamstring tendon autografts with a potential for local hematoma, which may promote infections in close proximity to the tibial graft tunnel[23]; the use of multiple multifilament sutures for hamstring tendon graft preparations, which may harbor bacteria[23]; the bony components being intrinsic protective factors for BPTB autografts compared with soft tissue–only grafts[6]; and the longer graft harvest and preparation time for hamstring tendon autografts, which may increase the exposure to contamination.[13] For allografts, several studies[7,10,14] have reported on positive cultured grafts during ACLR, with rates ranging from 4.8% to 13.3%; however, this was not proven to be associated with infections after ACLR.

This study also found younger age and revision surgery to be independently associated with a higher risk of infections (OR, 1.06 [95% CI, 1.02-1.10] and 3.13 [95% CI, 1.55-6.32], respectively). Schuster et al[28] reported on a higher risk of infections for revision ACLR (OR, 2.5). Conversely, Baron et al[4] did not find a statistically significant higher risk of infections for revision ACLR versus primary ACLR; however, they reported on only 11 infections in 1640 ACLR cases, which raises the possibility that the study was underpowered for detecting statistical significance. Age was investigated by Brophy et al[6] and Maletis et al[23] and was not found to be independently associated with a higher risk of infections. However, in both studies, the mean age of the ACLR cohort was younger (27 and 29 years, respectively, compared with 30 years in our study). Our findings merit further research on these possible contributing factors to infections after ACLR.

Overall, the incidence of deep infections after ACLR in this study (0.42%) falls in the range of published literature (0.12%-1%).[2-6,11,20,21,23] Additionally, the bacterial profile in our cohort, with coagulase-negative staphylococci being most commonly isolated, followed by methicillin-susceptible *Staphylococcus aureus*, also supports the findings of a recently published large-scale meta-analysis performed by Kuršumović and Charalambous.[20] The similar microbiological pathogens in deep infections after ACLR and most other postoperative orthopaedic infections suggest the likelihood that the etiological origins of infections are also similar, with an introduction of cutaneous flora (often endogenous to the patient rather than introduced). Our data do not suggest the bacterial contamination of allograft material with environmental organisms as a significant concern. The implications of soaking the graft with vancomycin was not explored in this trial; however, considering the

TABLE 4
Patient Characteristics of Infection Group[a]

	Total (n = 48)	Graft Retained (n = 33)	Graft Removed (n = 15)	*P* Value
Age, y	26.0 ± 12.0	23.7 ± 9.7	30.9 ± 15.0	.054[b]
Female sex	17 (0.35)	14 (0.42)	3 (0.2)	.196[c]
Body mass index	24.7 ± 4.5	23.9 ± 4.2	26.4 ± 4.7	.076[b]
Elixhauser Comorbidity Index	0.2 ± 0.4	0.2 ± 0.4	0.2 ± 0.4	.752[b]
Synovial white blood cell count (× 1000)	47.0 (13.8-70.8)	41.1 (16.3-67.5)	60.8 (8.0-141.0)	.057[d]
Erythrocyte sedimentation rate	53.5 (31.0-70.0)	51.5 (34.5-76.0)	62.0 (14.3-69.8)	.944[d]
C-reactive protein level	4.3 (2.3-14.9)	4.3 (2.3-12.7)	6.3 (1.6-20.7)	.567[d]
Time from index ACLR to symptom onset, d	24.0 (10.0-34.5)	24.0 (8.0-30.0)	27.0 (12.3-67.8)	.345[d]
Time from symptom onset to first I&D procedure, d	5.0 (2.0-7.5)	5.0 (2.0-8.0)	4.5 (2.0-8.0)	.863[d]
Time from index ACLR to first I&D procedure, d	29.0 (16.0-36.0)	28.0 (14.5-35.0)	30.0 (21.0-63.0)	.361[d]
Time from index ACLR to first I&D procedure				.367[e]
<30 d	27 (56.2)	20 (60.6)	7 (46.7)	
≥30 d	21 (43.8)	13 (39.4)	8 (53.3)	
No. of I&D procedures				**.028**[e]
1-2	43 (89.6)	32 (97.0)	11 (73.3)	
3	5 (10.4)	1 (3.0)	4 (26.7)	
Graft type				.279[e]
Hamstring tendon autograft	27 (56.2)	19 (57.6)	8 (53.3)	
BPTB autograft	12 (25.0)	10 (30.3)	2 (13.3)	
Allograft	8 (16.7)	4 (12.1)	4 (26.7)	
Index procedure				>.999[c]
Primary	36 (75.0)	25 (75.8)	11 (73.3)	
Revision	12 (25.0)	8 (24.2)	4 (26.7)	
History of smoking	2 (4.2)	0 (0.0)	2 (13.3)	.101[c]
Concomitant procedure at index surgery	13 (27.1)	10 (30.3)	3 (20.0)	.727[c]
Bacterial profile				.796[e]
Culture-negative case	9 (18.8)	7 (21.2)	2 (13.3)	
Coagulase-negative staphylococci	12 (25.0)	7 (21.2)	5 (33.3)	
Methicillin-susceptible *Staphylococcus aureus*	11 (22.9)	7 (21.2)	4 (26.6)	
Polymicrobial infection	5 (10.4)	4 (12.1)	1 (6.6)	
Corynebacterium acnes	4 (8.3)	2 (6.1)	2 (13.3)	
Methicillin-resistant *Staphylococcus aureus*	3 (6.3)	2 (6.1)	1 (6.6)	
Methicillin-resistant *Staphylococcus epidermidis*	3 (6.3)	3 (9.1)	0 (0.0)	
Gram-positive other	1 (2.1)	1 (3.0)	0 (0.0)	

[a]Data are presented as mean ± SD, median (interquartile range), or n (%). ACLR, anterior cruciate ligament reconstruction; BPTB, bone–patellar tendon–bone; I&D, irrigation and debridement. Bolded p values represent statistical significance (<0.05).
[b]*P* values were calculated using the independent-samples *t* test.
[c]*P* values were calculated using the Fisher exact test.
[d]*P* values were calculated using the Mann-Whitney *U* test.
[e]*P* values were calculated using the chi-square test.

recent published evidence supporting a reduction in the incidence of infections after ACLR by soaking ACL grafts in vancomycin,[4,20,26,27] surgeons may consider applying this precaution routinely when using higher risk grafts.

The median time to the onset of deep infection symptoms was 24 days (IQR, 10-34.5 days). A similar median time of 20 days (IQR, 12-30 days) to an infection was reported in a large multicenter registry-based cohort by Maletis et al.[23] A shorter duration was described by studies reporting on the mean time to the onset of symptoms. Judd et al[17] reported a mean time of 14.2 days (range, 6-34 days) for their cohort of 11 infections of 1615 ACLR cases. A similar duration was also reported by Abdel-Aziz et al[1] for 24 infections of 2560 ACLR cases (mean, 12.4 days [range, 5-45 days]).

The recommended treatment for septic arthritis after ACLR includes arthroscopic I&D and intravenous antibiotics (or high-dose oral antibiotics in specific antibiotics), with a preference to retain the ACL graft if possible.[11,24,32] In 4 recent systematic reviews, graft retention rates ranged from 63% to 100% following this treatment strategy.[19,21,22,31] We report a 69% graft retention rate for our infection group. Our algorithm of treatment was outlined in previously published studies, and this protocol has been in use for >25 years.[3,33] The ability to retain the ACL graft was based on a gross inspection of the graft at the time of I&D combined with the patient's clinical symptoms and laboratory findings in response to the treatment. There is limited information in the literature on factors associated with ACL graft retention versus removal. In this series, older age, higher BMI, and larger synovial white blood cell count (in initial joint aspirations) were reported in the ACL graft removal group (*P* = 0.054-

0.076); however, statistical significance was not reached. These findings suggest that despite the large number of infection cases, our study was still underpowered to detect factors associated with retention versus removal of the ACL graft. The only statistically significant difference that was found was the number of arthroscopic I&D procedures, with >2 I&D procedures more commonly performed in the ACL graft removal group, suggesting that the need for a third I&D procedure indicated that the surgeon was more likely to decide the graft should be removed. There were no differences in bacterial profile, revision versus primary surgery, concomitant procedures, graft type, and time from the onset of symptoms to I&D between the groups.

The majority of patients in our cohort received a course of oral antibiotic suppression after the initial 4- to 6-week treatment course was completed. Oral antibiotic suppression was typically continued for a duration of ≥12 weeks from I&D to when the graft was further vascularized and incorporated.[8] Our infectious disease specialists recommend antibiotic suppression therapy pending healing of the tendon graft. This approach is comparable with the use of antibiotic suppression therapy in the treatment of infected fractures at our institution, where suppressive antibiotics are given until osseous fracture healing has occurred. If antibiotic therapy for infections after ACLR is stopped before acceptable healing of the graft, the patient may be at risk for persistent infections in the avascular graft, which would ultimately result in destruction of the graft and failure of the reconstruction site. Previous published studies have not systematically assessed the need for a longer course of antibiotics in ACLR infections; however, because biofilm-based chronic infections of grafts and implants frequently benefit from suppressive therapy, because such therapy is generally well tolerated, and because randomized controlled trials of antibiotic treatment in ACLR infections are not possible owing to their low incidence, we believe that such therapy is advisable when infected ACL grafts are retained.

This study included several limitations. ACLR procedures included in this study were performed by 20 surgeons operating at our institution, utilizing a variety of surgical techniques, graft types, graft preparation methods including the use of antibiotic soaking, and postsurgical rehabilitation protocols. However, when an infection was suspected, it was managed with the close involvement and consultation of our institution's infectious disease specialists while applying standard institutional treatment and management protocols. A total of 9 infection cases yielded negative bacterial cultures. Similar rates of negative bacterial cultures were reported in previous studies.[4,23] In all 9 culture-negative cases, patients had infection-related symptoms of fever, chills, knee pain, and/or swelling. Further, in 8 of 9 cases, patients had elevated C-reactive protein levels; 4 of 9 an elevated synovial white blood cell count (>50,000); and 7 of 9, an elevated erythrocyte sedimentation rate. Additionally, each of these cases required intra-articular I&D and intravenous antibiotics for treatment and were therefore counted as infections in this study. An additional limitation relates to the possible heterogenicity of the overall ACLR cohort in terms of concomitant procedures performed with ACLR. Data on concomitant procedures were not available for this cohort. However, concomitant procedures for the infection cases were provided and are based on chart reviews. We acknowledge the possibility of infections that were not included in the study if the patients did not return to our institution for evaluations and treatment or were diagnosed with an infection >90 days after index surgery or if infections were not classified with infection-related diagnosis codes. We recognize the limitation of the possible influence of a relatively small number of infection cases on our regression model, which may be subjected to being overparameterized if one were to follow the rule of 10 events per variable. However, it has been shown[30] that in simulation models, there is less bias when increasing the number of nonevents, which in our study is a large number of noninfection cases in our study population. Last, we acknowledge that the clinical significance of the results related to the increased risk of infections with the use of specific grafts should be taken with consideration of the overall small absolute risk of infections, which stems from the rare nature of this outcome.

In conclusion, this study's results suggest that higher rates of infections after ACLR can be expected with the use of hamstring tendon autografts or allografts compared with BPTB autografts. Revision ACLR and younger age may also be associated with a higher infection rate. Larger infection groups are needed to determine more factors associated with graft salvage versus removal.

AUTHORS

Niv Marom, MD (Department of Orthopaedic Surgery, Meir Medical Center, Kfar Saba, Israel; Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel); Milan Kapadia, BS (Division of Infectious Disease, Department of Medicine, Hospital for Special Surgery, New York, New York, USA); Joseph T. Nguyen, MPH (Biostatistics Core, Hospital for Special Surgery, New York, New York, USA); Brittany Ammerman, MBS (Pennsylvania State University College of Medicine, Hershey, Pennsylvania, USA); Caroline Boyle, BA (Sports Medicine Institute, Hospital for Special Surgery, New York, New York, USA); Isabel Wolfe, BS (Sports Medicine Institute, Hospital for Special Surgery, New York, New York, USA); Kristin C. Halvorsen, BS (Stanford University School of Medicine, Palo Alto, California, USA); Andy O. Miller, MD (Division of Infectious Disease, Department of Medicine, Hospital for Special Surgery, New York, New York, USA); Michael W. Henry, MD (Division of Infectious Disease, Department of Medicine, Hospital for Special Surgery, New York, New York, USA); Barry D. Brause, MD (Division of Infectious Disease, Department of Medicine, Hospital for Special Surgery, New York, New York, USA); Jo A. Hannafin, MD (Sports Medicine Institute, Hospital for Special Surgery, New York, New York, USA); Robert G. Marx, MD (Sports Medicine Institute, Hospital for Special Surgery, New York, New York, USA); and Anil S. Ranawat, MD (Sports Medicine Institute, Hospital for Special Surgery, New York, New York, USA).

ORCID iDs

Niv Marom https://orcid.org/0000-0001-5393-6134
Joseph T. Nguyen https://orcid.org/0000-0003-1686-3911
Michael W. Henry https://orcid.org/0000-0002-0217-1546
Anil S. Ranawat https://orcid.org/0000-0002-3634-4871

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