A Retrospective Comparison of the Incidence of Bacterial Infection Following Anterior Cruciate Ligament Reconstruction With Autograft Versus Allograft

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Purpose: To compare the incidence of bacterial infection in anterior cruciate ligament (ACL) reconstruction with autograft versus allograft. **Methods:** We completed a retrospective medical record review of ACL reconstructions performed at our institutions between 2001 and 2005. These included 170 autograft, 628 allograft, and 3 combined autograft/allograft reconstructions. Data collection included patient demographics, comorbidities, preoperative antibiotics, fixation type, and the occurrence of deep postoperative infection. **Results:** Of the 801 patients who underwent ACL reconstruction, 6 (0.75%) developed a confirmed deep infection. There were 2 confirmed deep infections in 170 autograft reconstructions (1.2%) compared with 4 confirmed deep infections in 628 allograft reconstructions (0.6%). Multivariate analysis revealed that ACL reconstruction using autograft had a nearly twice the risk of infection compared to allograft reconstructions (adjusted odds ratio, 1.83; 95% confidence interval, 0.16 to 12.94). **Conclusions:** This study failed to find a higher rate of deep bacterial infection in ACL reconstructions when allograft tissue was used. We therefore feel that surgeons should consider allograft tissue as an alternative to autograft when there is a concern about donor-site morbidity, or for revision reconstructions. **Level of Evidence:** Level III, therapeutic retrospective comparative study. **Key Words:** Allograft—Anterior cruciate ligament—Autograft—Infection.

The anterior cruciate ligament (ACL) is the most commonly injured ligament in the knee.[1] Close to 100,000 ACL reconstructions are performed each year in the United States.[2-4] Traditionally, autograft reconstruction with hamstring or patellar tendon has been the technique of choice. However, with these procedures there is concern regarding donor-site morbidity.[1,5-7] This concern has led to the use of alternative grafts, such as allograft tendons.

Allograft tendons have become a useful alternative for ACL reconstruction. They are readily available, avoid donor-site morbidity, and have been shown to result in a decreased operative time.[1,8] It has been argued that allografts have diminished osteoconductive and osteoinductive capacitites and longer incorporation times.[9] Recent literature has failed to show a significant difference in either the biomechanical or clinical results of autograft versus allograft techniques.[1,2,5,10,11] More concerning though, is the potential increased risk of disease transmission when allograft tissue is used.

The Centers for Disease Control and Prevention (CDC) has reported cases of disease transmission following allograft transplantation.[12,13] Based on these reports, there is fear that allograft use may be associated with an increased risk of transmission of bacterial infections and viral infections such as HIV and hep-

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atitis C.[2,12-14] A review of the literature shows 1 report comparing infection rates of allograft versus autograft in ACL reconstructions performed between February 2000 and June 2002.[15] This study found a higher trend toward infection in the allograft group, but it was not found to be statistically significant. None of the allografts associated with an infection had undergone sterilization techniques.

Given the reported cases of allograft-associated infections and the paucity of data in the literature addressing this concern, we chose to investigate the incidence of bacterial joint infection after ACL reconstructions using autograft versus allograft tendons. Our hypothesis, based on reports in the literature, was that the incidence of joint infection is higher in patients in whom allograft tendons are used.

METHODS

Approval from our hospital's institutional review board was obtained before commencement of the study. A retrospective medical record review was completed for all consecutive ACL reconstructions performed in our hospital system between January 1, 2001, and December 31, 2005. These included procedures performed at the main institution (an inpatient, orthopaedic specialty referral hospital) and at 2 other ambulatory surgery centers. Specifically, the medical record database was queried for all cases with Current Procedural Terminology (CPT) code 29888 (arthroscopically aided anterior cruciate ligament repair/augmentation or reconstruction). All qualified charts were reviewed, and any nonreconstructive procedures (e.g., thermal shrinkage) were eliminated.

Procedures were performed by 11 different surgeons, including the senior author (J.C.R.), all of whom are fellowship-trained in sports medicine and perform arthroscopy as the majority of their practice. For all patients who underwent ACL reconstruction, a detailed chart assessment was performed. The following demographic information, which was obtained at the time of surgery, was collected: age, gender, location of surgery (hospital *v* ambulatory facility), body mass, and body mass index. Patient comorbidities, including diabetes, tobacco use, HIV, and chemotherapy or immunosuppressive use, were noted. Surgical details were recorded, including the type and dose of any preoperative antibiotics, the graft source (allograft *v* autograft), the specific graft tissue (e.g., hamstring, bone–patellar tendon–bone [BPTB]), the type of femoral and tibial fixation, and any concomitant procedures that were performed. Finally, the number and type of any previous operative procedures on that knee were documented.

The decision to use an allograft versus an autograft varied amongst the surgeons. Three of the surgeons routinely use an allograft in patients 35 years of age and older, and autograft in patients under 35 years of age. Three surgeons use allograft in patients 35 years of age and older, and use an autograft or allograft in the younger population based on the patient's preference. One surgeon uses BPTB autografts in competitive athletes and allografts in all other patients. The remaining 4 surgeons use allografts in all patients unless an autograft is specifically requested.

Perioperative antibiotic protocol at our institution consists of cefazolin within 30 minutes of incision. If there is a documented cephalosporin allergy, patients receive clindamycin or vancomycin based on surgeon preference. No postoperative antibiotics are administered.

More than 98% of the allograft specimens were obtained from LifeNet Health (Virginia Beach, VA). All of these grafts underwent a sterilization process called Allowash XG. This process involves rigorous cleaning to remove blood and marrow products, disinfection, and rinsing. Finally, grafts are treated with a dose of gamma irradiation as low as 8.3 kGy for terminal sterilization.[16] All grafts were stored frozen. Aseptic procurement and processing of tissue without specific sterilization procedures is an alternate means of graft preparation.[17] This method depends highly upon donor screening to accept or reject allograft tissue. None of the grafts used in this study were processed in this manner.

All patient charts were then assessed for any postoperative infection requiring hospital admission. Superficial cellulitic infections managed on an outpatient basis were not included. Infections were considered to be superficial cellulitis when erythema was localized to the incision site and associated with painless knee range of motion. If a deep infection was in question, further evaluation was performed with joint aspiration to rule out joint sepsis. A diagnosis of deep infection was based on a combination of lab parameters, including the following: elevated white blood cell count (WBC), elevated C-reactive protein (CRP), elevated erythrocyte sedimentation rate (ESR), elevated synovial cell count, and tissue pathology consistent with an infectious process (Table 1). Infections were considered confirmed if bacterial growth was noted on culture. To ensure that all postoperative infections were captured, a database query for CPT codes 29871 (arthroscopy, knee, surgical; for infection, lavage and

TABLE 1. *Laboratory Studies for Patients With Confirmed and Suspected Deep Knee Infections After Anterior Cruciate Ligament Reconstruction*

Patient No.	WBC (normal, 4-11)	CRP (normal, 0-1)	ESR (normal, 0-20)	SCC	Culture
Confirmed infections					
1	13.7	40.4	54	35,500	Coagulase-negative Staphylococcus
2	10.3	17.8	36	42,000	Coagulase-negative Staphylococcus
3	8.2	25.9	48	66,500	Coagulase-negative Staphylococcus and *Staphylococcus aureus*
4	13.5	70.1	30	50,400	Coagulase-negative Staphylococcus and *Proprionobacter acnes*
5	7.3	19.8	58	56,000	Coagulase-negative Staphylococcus
6	7.8	12.7	124	81,000	Coagulase-negative Staphylococcus
Suspected infections					
7*	7.7	5.4	122	54,000	No growth
8	9.6	11.2	54	51,500	No growth

Abbreviations: ACL, anterior cruciate ligament; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; SCC, synovial fluid, white cell count; WBC, white blood cell count.
*Patient was on oral cephalexin at time of studies. Normal laboratory values are noted in parentheses.

drainage) and 27310 (arthrotomy, knee, with exploration, drainage, or removal of foreign body [e.g., infection]) was performed and cross-referenced against all ACL reconstructions. If an intra-articular infection occurred, the date of diagnosis, surgical intervention, graft conservation versus debridement, culture results, and antibiotic type and duration of treatment were recorded.

Statistical Methods: Rates of infection were compared across a series of variables that included femoral fixation, tibial fixation, graft type, preoperative antibiotic, dose of antibiotic, age, number of previous surgeries, and weight. Two-sided *P* values were calculated using *t* tests for continuous variables and the Fisher exact test for categorical variables. Multivariate logistic regression with exact statement was used to determine the effect of graft type and antibiotic choice on infection rate, by computing an odds ratio (OR) and 95% confidence interval (CI). In all analyses, $P < .05$ was considered statistically significant.

RESULTS

Overall, 811 ACL reconstructions were performed at our institution during the period of interest. We were unable to locate the charts for 10 patients, resulting in the inclusion of 801 knees in 782 patients in this study. Patient demographics can be found in Table 2. There was no difference in the 2 patient populations (allograft *v* autograft) in regards to weight, tobacco use, and the incidence of diabetes mellitus. There was a significant difference between the 2 groups in regards to age and number of previous surgeries, with the allograft population being older ($P < .0001$) and having had slightly more previous surgeries ($P = .01$).

Of the 801 cases, 170 used autograft tendons and 628 used allograft. Three cases used a combination of the two. Allografts included tibialis anterior or posterior, Achilles tendon, and BPTB. Autograft reconstructions included 118 cases using semitendinosus–gracilis (STG) hamstrings and 52 using BPTB.

A total of 6 confirmed postoperative infections were found, resulting in an overall infection rate of 0.75% (95% CI, 0.15 to 1.35). Of these, 4 occurred in cases using allografts (0.63% [95% CI, 0.01 to 1.26]), and 2 occurred after autograft use (1.2% [95% CI, 0 to 2.8]). All infections occurring with autograft use occurred in

TABLE 2. *Patient Demographics Comparing Those Who Underwent Allograft With Autograft Anterior Cruciate Ligament Reconstruction*

	Allograft	Autograft	*P*
Mean age, yr (range)	32 (15-61)	27 (15-56)	<.0001*
Mean weight, kg (range)	84 (48-178)	82 (43-190)	.1397*
Mean previous surgeries (range)	0.23 (0-5)	0.12 (0-2)	.0108*
Regular tobacco use	9.71%	7.65%	.4099†
Diabetes mellitus	0.48%	0.59%	>.9999‡

*Two-sided *P* value from *t* test.
†χ^2 test of independence.
‡Two-sided *P* value from the Fisher exact test.

the STG group (2 of 118; 1.69% [95% CI, 0 to 4.02]). No infections occurred after BPTB autograft reconstruction (0 of 52; 0% [95% CI, 0 to 5.77]). All 4 allograft infections involved a soft tissue–only graft.

Results of the multivariate model with exact statement revealed that patients who had ACL reconstruction using autograft tissue had almost twice the risk of infection as compared to those who had ACL reconstruction using allograft tissue (adjusted OR, 1.83; 95% CI, 0.16 to 12.94). This was not found to be statistically significant ($P = .77$; Table 3). No association was noted between infection rate and surgical venue (hospital *v* outpatient facility), femoral fixation type, tibial fixation type, medical comorbidities, BMI, number of previous surgeries, or choice of antibiotic (Table 4).

The average time for presentation of an infection was 16.4 days postoperatively (range, 6 to 33 days), and the resulting additional length of hospitalization averaged 4.9 days (range, 2 to 8 days). Treatment of all 6 patients with infection in our study included surgical lavage and drainage, and in 5 of the 6 (83%) the ACL graft was ultimately preserved. Final culture results showed coagulase-negative Staphylococcus infections in all 6 patients. One patient also grew *Staphylococcus aureus*, and another patient also grew *Proprionobacter acnes*. Antibiotic treatment was based on sensitivities and consisted of 4 to 6 weeks of therapy. The duration of treatment was determined by normalization of laboratory values. Four patients received ceftriaxone and 1 patient received vancomycin. The remaining patient received oral ciprofloxacin and linezolid for 6 weeks because he refused intravenous access.

During the investigative period, 2 additional patients were diagnosed with a deep knee infection based on clinical examination, the presence of fever, and laboratory evaluation including elevated CRP, ESR, and synovial cell count (Table 1). In both cases, culture results yielded no growth. One of these patients was on oral antibiotics (cefalexin) for suspected cellulitis at the time of aspiration, while the other patient had not received any antibiotics. Each of these suspected infections involved autograft STG tendons, and an incision and drainage with graft retention was performed based on clinical suspicion. Empiric intravenous antibiotics were used to treat both of these patients. Cefazolin was chosen for the patient who had previously been on cefalexin under the assumption that the organism was sensitive to this class of antibiotics. Duration of treatment was 4 weeks. The patient that had not been on antibiotics previously was treated with 6 weeks of ertapenem to attain broader spectrum coverage.

If these 2 patients are considered in the data analysis, a total of 8 postoperative infections were found, resulting in an overall infection rate of 1% (95% CI, 0.31 to 1.69). Of these, 4 occurred in cases using allografts (0.63% [95% CI, 0.01 to 1.26]), and 4 occurred after autograft use (2.4% [95% CI, 0.07 to 4.63%]). Again, there was not a statistically significant difference in infection rates between the allograft and autograft groups ($P = .14$; adjusted OR, 3.79; 95% CI, 0.68 to 21.07; Table 5).

Analysis of these 8 patients found no association between infection rate and surgical venue (hospital *v* outpatient facility), femoral fixation type, tibial fixation type, medical comorbidities, BMI, or number of previous surgeries. In addition, an analysis of infection rate as it relates to autograft type found no statistically significant difference between BPTB and

TABLE 3. *Comparison of Graft Type and Antibiotic Type Using Multivariate Logistic Regression With Exact Statement for the 6 Confirmed Infections*

	Odds Ratio (95% Confidence Interval)	*P*
Autograft *v* allograft	1.83 (0.16-12.94)	.765
Clindamycin *v* cefazolin	5.75 (0.51-40.84)	.158

TABLE 4. *Surgical Variables for Patients With a Confirmed Deep Knee Infection Versus Patients With No Infection*

	Infection		
	Yes	No	*P*
n	6 (0.75%)	795 (99.25%)	—
Femoral fixation			
Button	0 (0.0%)	225 (99.6%)	
Screw	0 (0.0%)	166 (100.0%)	
Cross femoral fixation	6 (1.5%)	404 (98.3%)	.052*
Tibial fixation			
Bioabsorbable screw	6 (0.84%)	707 (99.16%)	
Metal screw	0 (0.0%)	85 (100.0%)	>.999*
Surgical venue			
Hospital	5 (0.75%)	656 (99.25%)	
Ambulatory center	1 (0.7%)	139 (99.3%)	>.999*
Mean age, yr (SD)	27.3 (9.1)	31.3 (10.4)	.364†
Mean previous surgeries (SD)	0.4 (0.9)	0.2 (0.5)	.445†
Mean weight, kg (SD)	88.2 (8.1)	83.8 (19.8)	.583†

*Two-sided *P* value from the Fisher exact test.
†Two-sided *P* value from the *t* test.

TABLE 5. *Comparison of Graft Type and Antibiotic Type Using Multivariate Logistic Regression With Exact Statement for the 6 Confirmed and 2 Suspected Infections*

	Odds Ratio (95% Confidence Interval)	*P*
Autograft *v* allograft	3.79 (0.68-21.07)	.14
Clindamycin *v* cefazolin	12.00 (2.16-66.72)	.004

STG autografts ($P = 1$). It was noted that preoperative antibiotic choice was linked to an increased infection rate, with patients receiving clindamycin having a higher rate of infection. Four out of the 63 patients who received clindamycin (6.3%) developed an infection, while 4 of 728 patients who received cefazolin (0.6%) developed an infection ($P = .004$; adjusted OR, 12; 95% CI, 2.16 to 66.72; Table 4).

DISCUSSION

The principal findings of our study show that there is not a higher infection rate when allograft tissue is used for ACL reconstruction when compared to autograft. While the true incidence of disease transmission following the transplantation of all allografts is unknown, it is estimated, based on reports in the literature, to be less than 4 per 1 million cases.[18] In March 2002, the CDC reported 26 documented cases of allograft-associated bacterial infections.[13] Thirteen of these resulted in Clostridia infections, and 8 of the Clostridia infections involved ACL reconstructions. None of these grafts had undergone sterilization procedures. The CDC also described 2 cases of septic arthritis following allograft ACL reconstructions from a common donor at a Texas-based tissue bank, and 2 from a common donor at a Florida-based tissue bank.[12] Completion of sterilization techniques were confirmed from the Texas-based tissue bank, and sterilization procedures were inadvertently not performed on the tissue from Florida.

In our study involving 170 autograft and 628 allograft tendon reconstructions, there were 2 confirmed deep surgical infections in the autograft group and 4 in the allograft group, for an overall infection rate of 0.75%. Our results do not support the hypothesis that infection rates are higher when allograft tendons are used. In fact, there was a higher trend towards infection in the autograft group, which was not found to be statistically significant ($P = .77$). Possible explanations for the trend towards a higher infection rate in the autograft population include the longer surgical time, an occasional separate incision, and the more extensive tissue dissection that is required with autograft procurement. In addition, a case report by Tuman et al[19] hypothesized that failure to disassemble a tube-within-a-tube tendon harvester during sterilization may result in an increased infection rate. This same type of harvester was used for some of the hamstring tendon harvests in our study.

There were 2 additional patients who underwent an incision and drainage because of suspected deep knee infection. A diagnosis of acute bacterial infection was made based on clinical examination, an elevated ESR, CRP, synovial cell count, and pathology findings consistent with fibropurulent exudate. Infection was not confirmed by culture results in these 2 patients. Culture-negative results in patients believed to have acute bacterial arthritis have been reported in the literature to occur in 10% to 20% of cases.[20] Therefore, it is possible that these 2 cases did represent a deep bacterial infection as was suspected. If these 2 patients are included in the data analysis, the suspected overall infection rate is 1%. Both of these suspected infections occurred in patients who underwent autograft STG ACL reconstructions, but statistical analysis still revealed no significant difference in the infection rates between the 2 groups ($P = .14$).

When these 2 additional suspected infections were included in the data analysis, an increased infection rate was noted in the population that received clindamycin preoperatively compared to that which received cefazolin. The explanation for this is unclear. Coagulase-negative Staphylococcus was the bacterium responsible for all of the confirmed infections in our study. Strains of coagulase-negative Staphylococcus have shown resistance to both clindamycin and cefazolin.[20]

In 2005, Crawford et al.[15] reviewed their experience with postoperative ACL infections. Their data revealed 11 infections in 290 allograft procedures (3.8%) and no infections in 41 autograft surgeries. This difference was not found to be statistically significant. They noted that none of the allografts involved in the postoperative infections had undergone sterilization procedures. In contrast, all of our allografts had undergone sterilization procedures. Our lower infection rate in allografts (0.63%) may suggest that sterilization procedures reduce the risk of infection. In Crawford's study,[15] there was a question of an association between infection and type of internal fixation used in the tibia. Our data did not find any correlation between infection and type of tibial or

femoral fixation used, although there was a suggestive trend consistent with this in our study.

To our knowledge, this is the largest patient population in which an association between bacterial infection and graft choice has been studied after ACL reconstruction. Our study has limitations which must be acknowledged. First, results of a post-hoc power analysis showed that we only had 54.4% power to detect a statistically significant difference within our sample. Given the low incidence of infection after ACL reconstruction (0.75%), achieving 80% or higher power would require approximately 2,000 patients. In addition, it is possible that a patient who experienced a postoperative infection chose to follow-up with a surgeon outside of our institution. A prospective study with documented 1 year follow-up of each patient would be helpful in preventing this potential bias. One must also consider whether our study results are applicable to all general practices. In our patient sample, an autograft reconstruction was performed in 21% of patients, while an allograft reconstruction was performed in 78% of patients. This is a high percentage of allograft reconstructions, which may not be representative of other orthopedic practices. Similarly, the low overall rate of infections in our sample may not be representative of other surgical centers. Finally, we did not look at the possibility of viral transmission (HIV, hepatitis B or C) through allograft transplantation. While there has not been a documented case of HIV transmission through musculoskeletal allograft tissue since stringent testing was employed,[21] it is still a lingering concern.

CONCLUSIONS

This study failed to find a higher rate of deep bacterial infection in ACL reconstructions when allograft tissue was used. We therefore feel that surgeons should consider allograft tissue as an alternative to autograft when there is concern about donor-site morbidity, or for revision reconstructions.

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