[Orthopaedic Surgery]

Infections in Anterior Cruciate Ligament Reconstruction

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Context: Anterior cruciate ligament (ACL) reconstruction is a safe, common, and effective method of restoring stability to the knee after injury, but evolving techniques of reconstruction carry inherent risk. Infection after ACL reconstruction, while rare, carries a high morbidity, potentially resulting in a poor clinical outcome.

Evidence Acquisition: Data were obtained from previously published peer-reviewed literature through a search of the entire PubMed database (up to December 2012) as well as from textbook chapters.

Results: Treatment with culture-specific antibiotics and debridement with graft retention is recommended as initial treatment, but with persistent infection, consideration should be given to graft removal. Graft type likely has no effect on infection rates.

Conclusion: The early diagnosis of infection and appropriate treatment are necessary to avoid the complications of articular cartilage damage and arthrofibrosis.

Keywords: anterior cruciate ligament; infection; graft type

nterior cruciate ligament (ACL) rupture is the most frequent ligamentous injury of the knee.³² It is frequently injured in young athletes performing cutting and pivoting sports and predisposes the knee to subsequent injuries, as well as the potential for earlier onset of osteoarthritis.^{8,25,40} Arthroscopic ACL reconstruction is a common and effective method of restoring stability to the knee after injury, with more than 400,000 ACL reconstructions performed annually in the United States.^{11,18,19,29,30,31,33,35,36,50,60} Like any surgical procedure, a number of potential complications have been recognized that may affect functional outcome.^{3,7,31,43,53} Specifically, infection after ACL reconstruction can be a devastating complication. Overall, infection rates are low (0.14%-1.7%) after ACL reconstruction.44 Despite the theoretical risk of disease transmission and higher graft failure in irradiated grafts, the use of allograft tissue continues to gain popularity for a number of reasons.

ALLOGRAFT VERSUS AUTOGRAFT: INCIDENCE OF SEPSIS

Allograft tissue has become an acceptable graft choice for ACL reconstruction, raising considerable questions regarding the risk of viral and bacterial transmission from contaminated tissue. Although the risk is low (0.14%-1.7%), these confirmed cases

represent a major medical and surgical challenge. To date, there have been 3 reported cases of viral disease transmission from bone-patellar tendon-bone allografts used to reconstruct the ACL. One case of HIV was reported in 1995, and 2 cases of hepatitis C have been reported.^{17,20,57,58,61} The American Association of Tissue Banks (AATB) recommends routine serologic screening for HIV, human T-cell leukemia virus, hepatitis B, hepatitis C, aerobic and anaerobic bacteria, and syphilis. Overall, the risk of HIV transmission with connective tissue allografts is estimated to be 1 in 1.6 million.^{10,12,19}

The Centers for Disease Control and Prevention (CDC) reported 26 cases of bacterial infections associated with musculoskeletal tissue allografts after the death of a recipient of an allograft (femoral condyle) contaminated with *Clostridium*.¹⁷ Thirteen cases were infected with *Clostridium*, and 14 were associated with a single tissue processor. All were processed aseptically, but none underwent terminal sterilization. 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.^{16,17} Completed sterilization techniques were confirmed from the Texas-based tissue bank, but sterilization procedures were mistakenly not performed on the tissue from the Floridabased tissue bank. Tissue bank regulation has increased

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Study (year)	Autograft infections/ Total (%)	Allograft infections/ Total (%)	
Barker et al (2010) ⁵	12 of 177 (0.44%)	6 of 1349 (0.68%)	
Indelli et al (2002) ³⁴	4 of 1400 (0.29%)	2 of 2100 (0.10%)	
Greenberg et al (2010) ²⁶	0 of 221 (0%)	0 of 640 (0%)	
Garras et al (2012) ²⁴	2 of 253 (0.79%)	4 of 535 (0.74%)	
Katz et al (2008) ³⁹	2 of 170 (1.2%)	4 of 628 (0.63%)	
Wang et al (2009)66	20 of 3978 (0.50%)	1 of 90 (1.11%)	
Crawford et al (2005) ²¹	0 of 41 (0%)	11 of 290 (3.8%)	
Total	40 of 7840 (0.51%)	28 of 5632 (0.49%)	Overall: 68 of 13,472 (0.50%)

Table 1. Infection rate by graft type

dramatically since these transmissions were documented. As of May 2005, all tissue banks in the United States are required to conform to the FDA's "Good Tissue Practice" guidelines, which permit inspection of tissue bank facilities and specify minimum standards for tissue recovery, testing, and processing.³⁷

Septic arthritis remains a rare but devastating complication following ACL reconstruction; reports show an incidence of 0.14% to 1.70%.^{13,23,34,45,65,67} Reports evaluating the difference in the rates of postoperative infection with allografts versus autografts are limited, and the current literature provides conflicting data (Table 1). Some papers have suggested no difference in infection rates between allograft and autograft. Barker et al reviewed 3126 ACL reconstructions with 1777 autografts and 1349 allografts and found infection rates of 0.44% in allografts and 0.68% in autografts.⁵ Although their infection rates were lower, Indelli et al also found no significant difference between allograft and autograft³⁴ or in 3500 arthroscopic ACL reconstructions (0.29% [1400] for bonetendon-bone [BTB] autograft and 0.1% [2100] for allograft). Greenberg et al examined 861 patients and found no infections in either group.²⁶ In 788 ACL reconstructions (535 allograft and 253 autograft), infection rates of 0.74% (4 patients) and 0.79% (2 patients), respectively, were reported.²⁶

Conversely, several studies have reported differences in the rates of infection associated with graft type. Katz et al showed an increased rate of infection among autografts (1.2%) versus allografts (0.63%), but it was not statistically significant.³⁹ Explanation for this trend toward a higher infection rate in the autograft population included longer surgical time, more invasive tissue dissection, and longer preparation of the graft. Furthermore, the same type of "tube-within-a-tube" tissue harvester suspected by Tuman et al as a source of contamination when not disassembled during sterilization was

used during their study.⁶² Meanwhile, data reported by both Wang et al⁶⁶ and Crawford et al²¹ suggested a higher rate of infection in allograft tissue (1.11% vs 0.5%⁶⁶ and 3.8% vs 0%²¹). Both of these studies have flaws. In the study by Wang et al, the 1 infection in 90 allograft reconstructions skewed their results when compared with 20 infections in 3978 autografts. Crawford reported 11 infections in 290 allografts (3.8%), in which none of the allografts underwent sterilization procedures, and 0 infections in 41 autografts.²¹ These 7 studies combined represent the largest series comparing infection rates in allografts with autografts (Table 1). These data include over 13,000 reconstructions, with infection rates for autograft and allografts of 0.51% and 0.49%, respectively (Table 1).

Although it has been hypothesized that allograft contamination has the potential for disease transmission, the link between contaminated grafts and clinical infections has been called into question. Guelich et al evaluated the utility of culturing allografts, demonstrating a positive bacterial culture rate of 9.7% (24 of 247 allografts).²⁷ These patients did not receive antibiotics in addition to the routine use of preoperative prophylactic antibiotics, and none developed septic arthritis or wound complications. Likewise, Diaz-de-Rada et al had 24 positive cultures from 181 allograft implantations analyzed; no patients showed clinical infection during follow-up.²² Hence, culture-positive evidence of allograft contamination did not correlate with infectious complications.¹⁴

AUTOGRAFT: BONE-PATELLA TENDON-BONE VERSUS HAMSTRING INCIDENCE OF SEPSIS

Some reports suggest an increased rate of infection with hamstring tendon autograft as compared with BTB autograft. Barker et al noted 18 cases of septic arthritis after ACL reconstruction out of a total population of 3126 patients. There was a statistically significant increased risk of infection with hamstring tendon autograft (1.44%) compared with BTB autograft (0.49%).⁵ Other studies have demonstrated a trend toward increased risk with hamstrings but none that have achieved statistical significance.^{13,38,39,66} In one of the largest reports, Wang et al reviewed 21 cases of infection from a population of 4068 patients with ACL reconstruction.⁶⁶ The majority of reconstructions were performed using autografts, and 20 (0.57%) infections occurred among 3536 patients reconstructed with hamstrings; no infections occurred among 442 BTB autografts. Judd et al found similar results in a review of 217 BTB autografts and 192 hamstring autografts, where all 11 intra-articular infections occurred in the hamstring group.³⁸

DIAGNOSIS OF INFECTION

Prompt diagnosis and treatment of a septic joint is necessary for infection control and to achieve the best long-term clinical outcomes. Postoperative infections are classified as either acute (<2 weeks), subacute (2 weeks to 2 months), or late (>2 months).67 Most patients have acute or subacute presentation of symptoms.^{5,9,13,23,34,38,39,45,54,56,64-67} The most consistent findings include increased pain, inflammation, and moderate effusion, whereas fevers, chills, erythema, and drainage are not consistently present.34,38,54,67 Typical postoperative pain usually lasts for only 1 to 2 days, and pain lasting longer than this should be suggestive of septic arthritis; there is a high degree of patient variability, with infected patients generally having more pain than expected.² The diagnosis of septic arthritis can be difficult to make in the early postoperative period as knee swelling, inflammation, and stiffness may be interpreted as normal, making laboratory data crucial to establishing the diagnosis. Laboratory values including erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are recommended to confirm diagnosis, since they have high negative predictive values.^{13,34,45,54,64-67} Wang et al used ESR, CRP, and fibrinogen (FIB) levels more than 50 mm/h, 6 mg/mL, and 800 mg/mL, respectively, for septic arthritis.66 CRP may be a more accurate predictor of postoperative complications than ESR, as both can be elevated postoperatively, but CRP rises and falls more rapidly than ESR levels.42 A sustained elevation of CRP beyond 2 weeks or new rise should prompt investigation to rule out infection.42 Complete CRP level normalization is generally seen after 2 to 12 weeks.64

Synovial fluid aspirate is still the best diagnostic test for infection.¹³ Progressively higher synovial white blood cell counts are seen with septic arthritis; polymorphonuclear cells greater than 90% are highly predictive.³⁴ Findings on imaging can include joint effusion, synovitis, bone erosions, edema of adjacent soft tissues and bone marrow, sinus tracts, and soft tissue abscesses.⁵²

RISK FACTORS FOR INFECTION

Several risk factors common for infection following ACL reconstruction include intra-articular corticosteroid injection, systemic corticosteroids, immunocompromised state, prior

or concomitant procedures on the same knee, and history of previous knee infection.^{1,38,47,67} More recent literature suggests other possible risk factors, including graft type, operative time, tourniquet time, foreign body load, and drains.34,13,44,45,53,54,56,65,67 Individual reports have implicated methods of sterilization of instrumentation and hardware used for graft fixation.38,62,66 Wang et al noted that flash sterilization of instrumentation was correlated with high rates of infection.⁶⁶ Tuman et al suggested that failure to disassemble a "tube-within-a-tube" hamstring harvester may lead to unsatisfactory sterilization, providing a potential source for contamination.⁶² Judd et al found a higher incidence of infection (11 of 193 [5.6%] in hamstring vs 0 of 217 in patellar tendon) associated with post/washer/braided suture construct in hamstring autograft fixation.³⁸ This may be related to soft tissue injury during hamstring harvesting combined with relatively subcutaneous positioning of the metallic construct.³⁸ Eight of 11 patients had concomitant extra-articular wound infection at this site, with cultures positive for the same causative organism.38

Many different microorganisms have been cultured from synovial fluid of septic arthritis, but the most common pathogen is *Staphylococcus aureus*.⁶⁴ Causative bacteria also include coagulase-negative Staphylococcus, 5,13,34,38,39,45,54,56,62,65-67 Propionibacter acnes, 5,38,39 Peptostreptococcus, 9,23,67 Enterobacter, 20,38,39 Enterococcus, 64,66 Pseudomonas aeruginosa,¹³ Escherichia coli,⁹ Klebsiella,²³ and Methicillinresistant Staphylococcus aureus (MRSA).5,41,64 More unusual organisms have also been identified in case reports, including Mycobacterium fortuitum,⁵¹ Mycobacterium tuberculosis,⁴⁹ Staphylococcus lugdenesis,⁴⁶ Erysipelothrixrhusio pathiae,⁶³ fungal species Rhizopus Microsporus,48 and Candida albicans.48 Establishing the causative organism in an intraarticular infection is crucial to predicting prognosis and commencing appropriate treatment. MRSA is a virulent organism that typically presents acutely and entails greater need for lavage and graft removal.⁴¹ Given that the majority of infections present with skin flora and are associated with concomitant extra-articular sites for infection, inoculation may occur at the time of surgery or shortly thereafter,^{38,45} including concomitant inside-out meniscus repair.45,67 In subacute or late septic knee arthritis, the tibial or femoral sites may be infected and spread to the knee joint from hematoma collection in the subcutaneous tissue.9,23,34,38

TREATMENT OF INFECTION

Suspected joint infection is an emergency situation with 2 main treatment goals: protecting the articular cartilage and the graft. In an animal model, more than half the glycosaminoglycan in cartilage and collagen were lost within 7 days from the onset of infection.⁵⁹ Prompt intravenous antibiotic therapy to cover the most common organisms (*Staphylococcus aureus* and coagulase-negative *Staphylococcus*) should be given as soon as laboratory studies and joint fluid have been obtained. A third-generation cephalosporin or vancomycin is recommended.^{34,38,45,54,65,67} When there is strong clinical

suspicion, antibiotic therapy should be continued even if synovial fluid cultures are negative.^{34,54,65}

There are several options for treatment of postreconstruction infection of the knee.³⁵ Barrett and Field recommended joint debridement with graft and hardware removal.⁶ Burks et al recommend arthroscopic graft removal with 6 weeks of antibiotics, followed by early reimplantation within 6 weeks of completing antibiotic treatment.¹³ Open arthrotomy with removal of hardware and curettage of tunnels has been recommended.⁶⁸ Staging treatment with multiple initial debridements followed by placement of antibiotic-pregnated polymethylmethacrylate (PMMA) beads and final reimplantation at 6 to 8 months may be best.⁵⁶ A full course of antibiotic treatment may proceed with arthroscopic debridement in cases of persistent clinical or abnormal laboratory findings.⁶⁵ There is an algorithm for the treatment of infections based on a series of 7 infections in 2500 ACL reconstructions.⁶⁷

A survey of sports medicine fellowship program directors regarding a standard of care for infections found 85% use culture-specific antibiotics and surgical irrigation of the joint with graft retention as the initial treatment for infected patellar tendon autografts and 64% for infected allografts.⁴⁴ For cases resistant to initial treatment, the most common treatment (39%) favored continuing intravenous antibiotics with repeated surgical irrigation and graft retention. Thirty-one percent of respondents recommended a combination of intravenous antibiotics, hardware removal, and graft removal in resistant cases. Overall, graft removal was not considered the standard of care for initial treatment; it was chosen for 6% of autografts and 33% of allografts.⁴⁴ After graft removal, the earliest time interval for a revision procedure was 6 to 9 months.⁴⁴

OUTCOMES AFTER INFECTION

The outcomes of deep infection after ACL reconstruction are mixed.38,45,54,55,65 Complications include pain, stiffness, arthrofibrosis, articular cartilage degeneration, and graft weakening or failure.^{2,9,34,55,66} While patients can generally perform pain-free activities in daily living, knee function following infection is impaired, and results are much less satisfactory.38 A full return to athletic activities was not certain, and pain followed by arthrofibrosis was the most common cause of unsatisfactory results.³⁸ In 13 knees treated with antibiotics initially, of which only 2 had positive cultures, 6 patients failed to improve and underwent arthroscopic irrigation and debridement.⁶⁵ Of these 13, 4 had pain with stair climbing, 3 had slight impairment with squatting exercises, and 3 had anterior knee pain with activities of daily living. In contrast, clinical outcomes inferior to control subjects without infection appeared to be secondary to articular cartilage degeneration.55 Four infections with the most significant functional limitations had severe bicondylar focal articular surface irregularities noted using magnetic resonance imaging (MRI) upon final follow-up at a mean of 36 months (range, 28-42 months). These patients averaged 12.25 days of inpatient hospital stay for these infections.

Recently, a long-term follow-up after infection on 4 of 831 patients that developed septic arthritis postoperatively required an average of 2.75 additional procedures for eradication.⁵⁵ At a mean 17.9-year follow-up (range, 17.1-18.6 years), each patient had a decline in SF-36, Lysholm, and IKDC scores and increase in KT-1000 arthrometer displacement. Radiographic and MRI studies showed progression of arthritis in all patients as compared with their 36-month follow-up.

CONCLUSION

Patients should be educated about the signs of infection, and surgeons should always err on the side of caution to provide early treatment. Management with antibiotics and debridement with graft retention is usually the recommended initial treatment. While infection after reconstruction has significant morbidity, eradication of infection can usually produce a functional knee with a much higher likelihood of osteoarthritis.

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