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Infections in Anterior Cruciate Ligament Reconstruction

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Abstract:

**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 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 generally more effective than graft removal, but with persistent infection consideration should be given to graft removal. Graft type likely has no effect on infection rates.
**Conclusions:** 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

**Introduction**

Anterior cruciate ligament (ACL) rupture is the most frequent ligamentous injury of the knee (42). It is frequently injured in the young athletes performing cutting and pivoting sports, and predisposes the knee to subsequent injuries, as well as the potential for earlier onset of osteoarthritis (15, 35, 51). 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 U.S. (18, 40, 39, 26, 38, 43, 45, 46, 65, 79, 27). Like any surgical procedure, a number of potential complications have been recognized that may affect functional outcome (41, 57, 12, 3, 69). Specifically infection after ACL reconstruction can be a devastating complication. Overall, infection rates are low after ACL reconstruction (58). Despite 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 vs. Autograft: Clinical Outcomes**

Graft material has received a significant amount of attention when focusing on surgical variables (14). The ideal graft would have low infection rates, low cost, low donor-site morbidity, fast incorporation, and wide availability. Autograft reconstruction remains the gold standard for younger patients, and despite the frequency of reconstruction surgery there is considerable controversy and variability in graft selection. No perfect graft exists. The use of
allografts in ACL reconstruction has increased significantly as both surgeons and patients desire limited donor-site morbidity, ease of use, decreased operative time, lower incidence of postoperative arthrofibrosis, low residual muscle weakness, availability and variety of graft sizes, decreased postoperative pain, improved cosmetic appearance, and commencement of earlier rehabilitation with faster return to work (27, 80, 70, 11, 67). Autograft harvest is not a completely benign event and has potential short and long-term morbidity, limiting options during procedural complications of graft harvest and revision reconstruction (5). Desire to avoid the sacrifice of autologous tissue, as well as to minimize surgical trauma and postoperative donor-site morbidity, has promoted consideration and increased use of allograft tissue. Tissue autografts amenable for use include central third bone-patellar tendon-bone (BTB), semitendinosus-gracilis graft from the hamstring (HS), or quadriceps tendon graft. Allograft tissues include the tibialis anterior or posterior, BTB, Achilles tendon with bone plug, fascia lata, peroneus longus, HS, and quadriceps tendons. Ultimately, graft selection is influenced by preoperative physical exam, patient age and activity level, as well as by the surgeon’s preference, experience, and bias (28). A number of studies have demonstrated allograft efficacy in improving stability and function, and clinical outcomes comparable to reconstruction with autologous tissue, making them an acceptable alternative to autografts (32, 75, 52, 47, 81, 13, 21). Yet, other studies have suggested higher failure rates with allograft tissue (8, 55, 60, 16, 7, 53, 71). While no consensus exists, allografts have been recommended for patients over 45 because they permit quicker recovery when morbidity associated with graft procurement is eliminated (80).

Allograft vs. 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, these confirmed cases represent a major medical and surgical challenge. To date there have been three reported incidences of viral disease transmission from bone-patellar tendon-bone allografts used to reconstruct the ACL. One case of HIV was reported in 1995, and two cases of hepatitis C have been reported (82, 29, 76, 77, 25). 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 one in 1.6 million (19, 17, 27).

The Center for Disease Control (CDC) and Prevention reported 26 cases of bacterial infections associated with musculoskeletal tissue allografts after the reported death of a recipient of an allograft (femoral condyle) contaminated with Clostridium. Thirteen of the cases were infected with Clostridium, and fourteen were associated with a single tissue processor. All were processed aseptically, but none underwent terminal sterilization. The CDC also described two cases of septic arthritis following allograft ACL reconstructions from a common donor at a Texas-based tissue bank, and two from a common donor at a Florida-based tissue bank (23, 24). Completed sterilization techniques were confirmed from the Texas-based tissue bank, but sterilization procedures were mistakenly not performed on the tissue from the Florida-based tissue bank. Tissue bank regulation has increased dramatically since the occurrence of these documented transmissions, and as of May 2005, all tissue banks in the United States were 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 (48).

Septic arthritis remains a rare but devastating complication following ACL reconstruction. Reports in the literature show an incidence of 0.14% to 1.70% (20, 33, 44, 59, 86, 88). Reports evaluating the difference in the rates of postoperative infection with allografts versus autografts are limited, and the current literature provides conflicting data. Using the PubMed database we sought to study the largest available trials that specifically investigated the incidence of infection in allograft and autograft ACL reconstruction (Table 1). Some papers have suggested no difference in infection rates between allo- and autograft. Barker et al. reviewed 3,126 ACL reconstructions with 1,777 autografts and 1,349 allografts, finding infection rates of 0.44% in allografts and 0.68% in autografts (6). Although their infection rates were lower, Indelli et al also found no significant difference between allograft and autograft (44). They reviewed 3,500 arthroscopic ACL reconstructions and found infection rates of 0.29% (4/1,400) for BTB autograft and 0.1% (2/2,100) for allograft. Greenberg et al examined 861 patients and found no infections in either group (36). Our research has also suggested no difference as well (34). We looked at 788 ACL reconstructions, 535 allograft and 253 autograft, with infection rates of 0.74% (four patients) and 0.79% (two patients), respectively.

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 (50). 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 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 (83). Meanwhile, data reported by both Wang et al and Crawford et al suggested a higher rate of infection in allograft tissue than autograft tissue (Wang 1.11% versus 0.5%; Crawford 3.8% versus 0%, respectively) (87, 30). Both of these studies have their flaws. In the study by Wang et al, the one infection in 90 allograft reconstructions skewed their results when compared to 20 infections in 3,978 autografts. The Crawford et al study reported 11 infections in 290 allografts (3.8%) in which none of the allografts had undergone sterilization procedures, and no infections in 41 autografts. These seven studies represent the largest series comparing infection rates in allografts with autografts. As shown in Table 1, pooling these data together to include over 13,000 reconstructions shows infection rates for autograft and allografts to be 0.51% and 0.49%, respectively.

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) (37). These patients did not receive antibiotics in addition to the routine use of preoperative prophylactic antibiotics, and none went on to develop 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 (31). Hence, culture positive evidence of allograft contamination did not correlate with infectious complications (22).

Autograft: Bone-patella tendon-bone vs. hamstring incidence of sepsis
Some reports suggest an increased rate of infection with hamstring tendon autograft as compared with BTB autograft. Barker et al had 18 cases of septic arthritis after ACL reconstruction, there was a statistically significant increased risk of infection with hamstring tendon autograft (1.44%) compared with BTB autograft (0.49%) (6). Other studies have demonstrated a trend toward increased risk with hamstrings, but have not achieved statistical significance. In one of the largest reports, Wang et al reviewed 21 cases of infection from a population of 4,068 patients with ACL reconstruction (87). 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 post BTB autografts. A possible explanation included the frequent use of flash sterilization that was correlated with the occurrence of infections. 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 (49). The high rate of infection among hamstring autografts was attributed to the choice of graft fixation or additional soft-tissue dissection rather than the graft itself. Katz et al also had two of 118 hamstring autograft infections and 0 of 52 BTB (50). Burks et al reported eight postoperative ACL infections from a population of 1,918 arthroscopic ACL reconstructions, including seven hamstring tendon autografts and only one BTB autograft (20). One explanation for this trend was the relatively short length of hamstring graft places suture material inside the joint, which acts as a foreign body predisposing the joint to infections (10).

Diagnosis of infection

Prompt diagnosis and treatment of a septic joint is necessary for infection control and to achieve best long-term clinical outcomes. Postoperative infections are classified as either
acute (<two weeks), subacute (two weeks to two months) or late (>two months). Most patients have acute or subacute presentation of symptoms (20, 33, 44, 59, 86, 88, 6, 50, 87, 49, 10, 85, 74, 72). The most consistent findings include increased pain, inflammation and moderate effusion, whereas fevers, chills, erythema and drainage are not consistently present (44, 88, 49, 72). While Armstrong et al state that typical postoperative pain usually lasts for only 1-2 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 as they have high negative predictive values. 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 (87). Margheritini et al believe CRP to 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. A sustained elevation of CRP beyond two weeks or new rise should prompt investigation to rule out infection (56). Complete CRP levels normalization is generally seen after 2-12 weeks. Synovial fluid aspirate is still the best diagnostic test for infection (20). Progressively higher synovial WBC counts are seen with septic arthritis; polymorphonuclear cells greater than 90% are highly predictive (44). Magnetic Resonance Imaging (MRI) can substantiate the diagnosis of infection in uncertain scenarios, and it can further determine the extent of the infection and detect any specific fluid collection. Findings on imaging can include joint effusion, synovitis, bone
erosions, edema of adjacent soft tissues and bone marrow, sinus tracts, and soft tissue abscesses (68).

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 (88, 49, 62, 1). More recent literature suggests other possible risk factors including graft type, operative time, tourniquet time, foreign body load, and usage of drains (3, 69, 20, 59, 86, 88, 74, 72, 58, 4). Individual reports have implicated methods of sterilization, instrumentation, and specific hardware used for graft fixation. Wang et al noted that flash sterilization of instrumentation was correlated with high rates of infections (87). 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 (83). Judd et al found a higher incidence of infection associated with post/washer/braided suture construct in hamstring autograft fixation. This may be related to soft tissue injury during hamstring harvesting combined with relatively subcutaneous position of the metallic construct (49). Eight of 11 patients had concomitant extra-articular wound infection at this site with cultures positive for the same causative organism.

Many different microorganisms have been cultured from synovial fluid of with septic arthritis, but the most common pathogen is Staphylococcus aureus. Causative bacteria also include coagulase-negative Staphylococcus, Propionibacter acnes, Peptostreptococcus, Enterobacter, Enterococcus, Pseudomonas aeruginosa, Escherichia coli, and Klebsiella (20, 33, 44, 59, 86, 88, 6, 50, 87, 49, 10, 85, 74, 72). Methicillin-resistant Staphylococcus aureus
(MRSA) were also cultured among patients. (Au: Reference needed.) More unusual organisms have also identified in case reports, including *Mycobacterium fortium*, *Mycobacterium tuberculosis*, *Staphylococcus lugdenesis*, *Erysipelothrix rhusiopathiae*, and fungal species Rhizopus, Microsporus and Candida albicans (61, 84, 63, 66, 64). Establishing the causative organism in an intra-articular infection is crucial to predicting prognosis and commencing appropriate treatment. MRSA joint fluid is a virulent organism which typically presents acutely and entails greater need for lavage and for graft removal (54). Given that the majority of infections are with skin flora and are associated with concomitant extra-articular sites for infection, inoculation may occur at the time of surgery or shortly thereafter (59, 49) including concomitant inside-out meniscus repair (59, 88). 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 (49, 10, 33, 44).

Treatment of infection

Suspected joint infection is an emergency with the two main treatment goals: protecting the articular cartilage and the graft. In an animal study cartilage test, more than half its glycosaminoglycan and collagen within seven days from the onset of infection (78). 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 (44, 59, 86, 88, 49, 72). When there is a strong clinical suspicion, antibiotic therapy should be continued even if synovial fluid cultures are negative (44, 86, 72).
There are several options for treatment of post-reconstruction septic arthritis of the knee (45). Barrett and Field recommended joint debridement with graft and hardware removal (9). Burks et al recommend arthroscopic graft removal with six weeks of antibiotics, followed by early re-implantation within six weeks of completing antibiotic treatment (20). Open arthrotomy with removal of hardware and curettage of tunnels has been recommended (89). Staging treatment with multiple initial debridements followed by placement of antibiotic-pregnated polymethylmethacrylate (PMMA) beads, and final re-implantation at 6-8 months may be best (74). A full course of antibiotic treatment may proceed with arthroscopic debridement in case of persistent clinical or abnormal laboratory findings (86). There is an algorithm for the treatment of infections based on a series of seven infections in 2,500 ACL reconstructions (88).

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 (58). For cases resistant to initial treatment, the most common treatment (39%) favored continuing IV antibiotics with repeated surgical irrigation and graft retention. Thirty-one percent of respondents did recommend a combination of IV 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. After graft removal, the earliest time interval for revision procedure is was 6 to 9 months. Since there was no consensus in the literature, Matava et al concluded that primary infection can be treated with culture-specific intravenous antibiotics and surgical joint irrigation with graft retention as the initial treatment.
Outcomes after infection

The outcomes after deep infection after ACL reconstruction are mixed. Complications include pain, stiffness, arthrofibrosis, articular cartilage degeneration, and graft weakening or failure. While patients can generally perform pain-free activities of daily living, knee function following infection is impaired and results are much less satisfactory than for patients without postoperative infections (49). A full return to athletic activities was not certain, and pain followed by arthrofibrosis was the most common causes of unsatisfactory results (49). In 13 knees, of which only two had positive cultures, all treated with antibiotics initially, six patients failed to improve underwent arthroscopic irrigation and debridement (86). Of these 13, four had pain with stair climbing, three had slight impairment with squatting exercises, and three anterior knee pain with activities of daily living. In contrast, clinical outcomes inferior to control subjects without infection appeared to be secondary to damage to the articular cartilage from the infection (59). Four infections with the most significant functional limitations had severe bicondylar focal articular surface irregularities at MRI final follow-up. These patients averaged 12.25 days of inpatient hospital stay for these infections.

Recently, a long-term follow-up after infection on four of 831 patients that developed septic arthritis postoperatively required an average of 2.75 additional procedures for eradication (73). At 17.9 year average follow-up each patient had a decline in SF-36, Lysholm, and IKDC scores, and increase in KT-1000 displacement. Radiographic and MRI studies showed progression of arthritis in all patients, as compared to 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 treatment. While the diagnosis of an infection after reconstruction has significant morbidity, eradication of infection can usually be attained and patients may still have a functional knee with a much higher likelihood of osteoarthritis.

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74.


<table>
<thead>
<tr>
<th>Study (year)</th>
<th>Autograft (infections / total)</th>
<th>Allograft (infections / total)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barker et al (2010)</td>
<td>12/177 = 0.44%</td>
<td>6/1349 = 0.68%</td>
</tr>
<tr>
<td>Indelli et al (2002)</td>
<td>4/1400 = 0.29%</td>
<td>2/2100 = 0.10%</td>
</tr>
<tr>
<td>Greenberg et al (2010)</td>
<td>0/221 = 0%</td>
<td>0/640 = 0%</td>
</tr>
<tr>
<td>Garras et al (2012)</td>
<td>2/253 = 0.79%</td>
<td>4/535 = 0.74%</td>
</tr>
<tr>
<td>Katz et al (2008)</td>
<td>2/170 = 1.2%</td>
<td>4/628 = 0.63%</td>
</tr>
<tr>
<td>Wang et al (2009)</td>
<td>20/3978 = 0.50%</td>
<td>1/90 = 1.11%</td>
</tr>
<tr>
<td>Crawford et al (2005)</td>
<td>0/41 = 0%</td>
<td>11/290 = 3.8%</td>
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<tr>
<td><strong>TOTAL</strong></td>
<td>40/7840 = 0.51%</td>
<td>28/5632 = 0.49%</td>
</tr>
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Overall: 68/13472 = 0.50%