Do Anterior Cruciate Ligament Allograft Culture Results Correlate With Clinical Infections?

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**Purpose:** In 1998, four cases of contaminated allografts for anterior cruciate ligament (ACL) reconstruction resulted in *Clostridium* infection, and a patient with *Clostridium* infection from a femoral condylar allograft died. It was subsequently published that implanting surgeons should culture ACL allografts so that action could be taken should highly pathogenic bacteria be encountered. The purpose of this study is to test the hypothesis that ACL allograft cultures correlate with clinical infections. **Methods:** Since October 2003, a single surgeon performing ACL reconstruction prospectively cultured all allografts in the operating room before implantation. After culture, grafts were thawed in warm saline mixed with bacitracin. All patients received a single dose of preoperative antibiotics. Final culture results were obtained in all patients, and all patients were followed for a minimum of 90 days to evaluate for postoperative infection. The cost of cultures was determined by multiplying hospital charges by the hospital cost-to-charges ratio. **Results:** Two hundred and ten cases were included. Ten allografts (4.8%) had positive culture results (6 coagulase-negative Staphylococci, 1 alpha-Streptococcus-not-group-B, 1 Enterobacter, 1 Clostridium, and 1 polymicrobial [Klebsiella, Escherichia coli, and Enterococcus]). None of these patients had signs of infection; the three positive highly pathogenic bacteria (Enterobacter, Clostridium, and polymicrobial) graft recipients were treated with antibiotics. The others were observed. One patient with negative cultures developed *Staphylococcus aureus* infection. Mean culture cost was $127 (USD). **Conclusions:** Our results demonstrate that ACL allograft cultures do not correlate with clinical infections. **Level of Evidence:** Level I, diagnostic study (testing of previously developed diagnostic criteria [culture]) in a series of consecutive patients (with universally applied reference gold standard [clinical evaluation for knee sepsis]). **Key Words:** Allograft—Anterior cruciate ligament—Infection—Culture—Complication—Outcome.

Orthopaedic surgical use of musculoskeletal allografts is increasing at a dramatic rate, and allograft tissue is a popular choice for anterior cruciate ligament (ACL) reconstructive surgery, with outcomes reported to be similar to that of ACL reconstruction using autograft tissue. The reported advantages of ACL allograft reconstruction include elimination of donor site morbidity with preservation of the knee extensor and flexor mechanisms, decreased operative time, availability of larger graft sources and provision of a source of graft when the patient has none (because of previous or concomitant harvest or harvests), a lower incidence of arthrofibrosis, improved cosmetic appearance, and decreased overall costs. However, a disadvantage of the use of musculoskeletal allografts is the risk of transmission of disease or infection.

In 2002, the United States Centers for Disease Control and Prevention (CDC) published an update on “allograft-associated bacterial infections,” and reported 26 cases that were associated with musculoskeletal tissue allografts (including 13 cases of Clostridium infection and 1 death). Four of these cases were...
from ACL allografts, and in 2003, Barbour et al. reported four additional cases of ACL allograft–associated Clstridium septicum infection, and published the recommendation that implanting surgeons should culture allografts so that action could be taken should highly pathogenic bacteria be encountered.

The purpose of this study is to determine whether ACL allograft culture results correlate with clinical infections. We hypothesize that ACL allograft tissue cultures will correlate with clinical infections.

METHODS

Beginning in October 2003, and with institutional review board approval, a single surgeon (J.H.L.) performing primary ACL allograft reconstruction using fresh frozen tibialis anterior or tibialis posterior allografts from a single tissue bank (DCI Donor Services, Albuquerque, NM) prospectively cultured all allografts before implantation. After aerobic and anaerobic cultures were obtained, the grafts were thawed in a series of three washes consisting of 500 ml of normal saline; in addition, the third wash contained 1 ampule of bacitracin solution. All patients received preoperative intravenous antibiotics. Cephazolin (1 g) was prescribed for the majority of patients, and clindamycin (600 mg) was prescribed for patients with penicillin or cephalosporin allergies.

Final aerobic and anaerobic cultures were obtained in all patients. All patients were followed clinically for a minimum of 90 days to evaluate for postoperative septic arthritis. Finally, the costs of cultures were determined by dividing hospital charges by the hospital cost-to-charges ratio.

RESULTS

Two hundred and ten cases of primary ACL allograft reconstruction patients with a minimum of 90 days follow-up are included in the study. To our knowledge, no patients were immunocompromised. No patients were lost to follow-up.

Positive culture results appeared in 10 allografts (4.8%). Six were infected with coagulase-negative Staphylococci, 1 with alpha-Streptococcus-not-group-B, 1 with Clostridium perfringens, 1 with Enterobacteriaceae, and 1 infection was polymicrobial (Klebsiella pneumoniae, Escherichia coli, and Enterococcus). The three patients with highly virulent culture positive allografts (Clostridium, Enterobacteriaceae, and polymicrobial) were treated with antibiotic prophylaxis. The remaining seven patients were observed. None of the patients who received the culture positive allografts had clinical signs or symptoms of infection.

One patient with negative allograft cultures developed a Staphylococcus aureus infection 88 days postoperatively. Based upon the delay in presentation, complicating medical conditions (dental procedure as well as viral infection complicated by bilateral lower extremity maculopapular rash associated with breaks in the skin), and based upon the negative allograft culture, this patient was counseled that the allograft was not the most likely source of infection. The mean cost was $127 (USD) per culture.

DISCUSSION

In contrast to our hypothesis, our results demonstrate no correlation between ACL allograft culture results and clinical infections.

A review of the literature reveals only one published study with a purpose similar to our investigation. Diaz-de-Rada et al. prospectively cultured 181 ACL allografts before implantation and reported 24 cases of positive allograft culture results (13.3%). No patient developed clinical signs of infection. While we report one case of clinical infection (0.5% compared to 0%), and while we report a positive allograft culture rate of 4.8% compared to 13.3%, our results are similar to the results of Diaz-de-Rada et al. In addition, with regard to the rate of ACL clinical infection, our results (0.5%) and the results of Diaz-de-Rada et al. (0%) are similar to the rate of 1% cited generally in the orthopaedic literature (for both autograft and allograft).

With regard to cost, the mean cost of cultures at our institution was $127 (USD) per culture. This represents less than 1% of the total cost of ACL reconstruction, calculated at our institution as surgeon’s fees plus hospital charges multiplied by the hospital cost-to-charges ratio: [surgeon’s fees + (hospital charges \times hospital cost:charges ratio)]. To facilitate the discussion that follows, the authors interpret this result as a demonstration that the cost of cultures is relatively small.

It is clinically relevant to discuss whether ACL allograft culture results affected patient management. In our investigation, positive culture results changed the management of three patients, because those implanted with highly virulent culture–positive allografts (Clostridium, Enterobacteriaceae, and polymicrobial) were treated with antibiotic prophylaxis. However, a limitation of this discussion is that it is uncertain whether these patients benefited from antibiotic pro-
phylaxis; it is possible that these patients would have had the same outcome (i.e., no clinical infection) without prophylaxis. An additional limitation is that future research is required to determine if the three washes performed after the cultures were obtained were of benefit or affected the results in any of the cases.

In addition, in our investigation, a single patient who developed a clinical infection was counseled that the allograft was not the most likely source of infection based, in part, upon a negative allograft culture. Again, however, this discussion is limited, because it is uncertain whether the allograft was or was not the source of the clinical infection.

More generally, it is clinically relevant to consider that there are four possibilities when considering whether ACL allograft culture results correlate with clinical infection: 1) true negative culture (negative culture, no clinical infection); 2) true positive culture (positive culture, clinical infection); 3) false negative culture (negative culture, clinical infection); 4) false positive culture (positive culture, negative infection). Each possibility bears discussion.

Our results and review of the literature suggest that true negative culture (negative culture, no clinical infection) will be the most common and occur in approximately 87% to 95% of cases. True negative cultures do not effect patient management, are of no obvious benefit, and have a cost as shown above.

True positive cultures (positive culture, clinical infection) did not occur in our investigation but have been described elsewhere. The rate of true positive culture is unknown. A true positive culture has a theoretical benefit of allowing early recognition and treatment of knee sepsis post-ACL allograft reconstruction, including early, organism-specific antibiotic selection. Theoretically, this could increase the chances of graft preservation, which could be of large (albeit theoretical) benefit.

False negative cultures (negative culture, clinical infection) were not observed by Diaz-de-Rada et al., while we report a single case (1 case/200 negative cultures [0.5%]). False negative cultures do not affect patient management and have an economic cost. False negative cultures may allow surgeons to counsel patients that their allograft is not the most likely source of infection, but as above, this statement is uncertain. False negative cultures are therefore of no clinical benefit and have uncertain benefits with regard to patient counseling.

Finally, our results and review of the literature suggest that false positive cultures (positive culture, negative infection) occur in approximately 5% to 13% of cases. Theoretically, antibiotic prophylaxis of patients with a positive allograft culture could prevent clinical infection, which would be of great benefit. However, as above, it is impossible to determine if the three patients managed similarly by Diaz-de-Rada et al. would have had the same outcome (no clinical infection) without prophylaxis. (To best answer this question prospectively, a randomized, controlled trial would require an extremely large number of patients, along the order of magnitude [estimate of size expressed as a power of 10] of 100,000. This could be ethically challenging [to withhold antibiotic prophylaxis in patients implanted with highly virulent culture positive allografts] and may therefore be unrealistic.) In addition, while there is a theoretical, if uncertain, great benefit as described above, it is important to note that because our results and review of the literature reveal that positive cultures occur on an order of magnitude of 10%—while our results and review of the literature reveal that ACL infection occurs on an order of magnitude of only 1%—at least 90% of positive cultures will not correlate with clinical infection, even in the absence of antibiotic prophylaxis. Worse, it is not possible to determine which of the positive cultures will (or will not) correlate with clinical infection until after an infection occurs. Furthermore, false positive cultures have costs and, in the experience of the authors, result in anxiety for both the patient and the surgeon.

Our summary is as follows: 1) true negative cultures are most common (87%-95%) and are of no benefit; 2) true positive cultures are rare (<1%) but could be of large, albeit theoretical, benefit; 3) false negative cultures are rare (<1%), are of no clinical benefit, and are of uncertain benefit with regard to patient counseling; and 4) false positive cultures are somewhat common (5%-13%) and could theoretically allow prevention of clinical infection via antibiotic prophylaxis, but even if future research supports this theory, at least 90% of false positive cultures will be of no benefit. In addition, it is not possible to determine which of these cultures will be of no benefit until it is too late (after infection occurs), and false positive cultures result in great patient and surgeon anxiety.

**CONCLUSION**

In conclusion, while there are theoretical situations where ACL allograft cultures could result in great...
benefit at a relatively small cost, our results demonstrate that ACL allograft cultures do not correlate with clinical infections.

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REFERENCES