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Allograft Compared with Autograft Infection Rates in Primary Anterior Cruciate Ligament Reconstruction

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Background: Injuries to the anterior cruciate ligament are the most common surgically treated knee ligament injury. There is no consensus regarding the optimal graft choice between allograft and autograft tissue. Postoperative septic arthritis is an uncommon complication after anterior cruciate ligament reconstruction. The purpose of this study was to compare infection rates between procedures with use of allograft and autograft tissue in primary anterior cruciate ligament reconstruction.

Methods: A combined prospective and retrospective multicenter cohort study was performed over a three-year period. Graft selection was determined by the individual surgeon. Inclusion and exclusion criteria were equivalent for the two groups (allograft and autograft tissue). Data collected included demographic characteristics, clinical information, and graft details. Patients were followed for a minimum of 5.5 months postoperatively. Our primary outcome was intra-articular infection following anterior cruciate ligament reconstruction.

Results: Of the 1298 patients who had anterior cruciate ligament reconstruction during the study period, 861 met the criteria for inclusion and formed the final study group. Two hundred and twenty-one patients (25.6%) received an autograft, and 640 (74.3%) received an allograft. There were no cases of septic arthritis in either group. The 95% confidence interval was 0% to 0.57% for the allograft group and 0% to 1.66% for the autograft group. The rate of superficial infections in the entire study group was 2.32%. We did not identify a significant difference in the rate of superficial infections between autograft and allograft reconstruction in our study group.

Conclusions: While the theoretical risk of disease transmission inherent with allograft tissue cannot be eliminated, we found no increased clinical risk of infection with the use of allograft tissue compared with autologous tissue for primary anterior cruciate ligament reconstruction.

Level of Evidence: Therapeutic Level II. See Instructions to Authors for a complete description of levels of evidence.

Anterior cruciate ligament injuries are the most common surgically treated knee ligament injury. With an estimated 250,000 new anterior cruciate ligament ruptures occurring in the United States each year[1,2], more than 100,000 anterior cruciate ligament reconstructions are performed annually[3-6]. While the optimal graft choice remains controversial, the use of allograft tissue for anterior cruciate ligament reconstruction has increased steadily over the past decade[7,8]. In 2002, approximately one million musculoskeletal allografts were distributed in the United States compared with 350,000 in 1990[7,8], and the use of allografts has since continued to rise. Allograft options for anterior cruciate ligament reconstruction include bone-patellar tendon-bone, Achilles tendon, anterior tibial tendon, posterior tibial tendon, hamstring tendon, and fascia lata grafts.

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There are well-documented advantages and disadvantages to each graft type. The autogenous bone-patellar tendon-bone graft is considered the gold standard for anterior cruciate ligament reconstruction[9-14], with no risk of disease transmission or immunogenic response. Conversely, the use of allograft tissue allows for decreased donor-site morbidity, larger and predictable graft sizes, decreased operative time, decreased postoperative pain and stiffness, improved cosmesis, and earlier rehabilitation. These advantages must be weighed against the risk of disease transmission, slower graft incorporation, availability, local bone resorption, potential immunologic response, and cost[15-18].

Despite the differences between allograft and autograft tissues, the use of both is supported in the literature. Most clinical studies comparing the two show little difference in long-term outcomes[9,10,19-24].

Postoperative septic arthritis is an uncommon complication after anterior cruciate ligament reconstruction, with a reported prevalence of between 0.14% and 1.70%[25-33]. Bacterial infection of musculoskeletal allograft tissue occurs even less frequently[34]. We are aware of only one study specifically addressing the influence of graft selection with regard to septic arthritis as a postoperative complication after anterior cruciate ligament reconstruction[32].

The potential for disease transmission and infection with allograft tissue makes selection of this graft type a concern for some clinicians. The purpose of this study was to compare infection rates between procedures with use of allograft and autograft tissue in primary anterior cruciate ligament reconstruction. Our hypothesis was that there would be no difference in infection rates between the two tissue types.

Materials and Methods

After institutional review board approval, a combined retrospective and prospective multicenter cohort study was performed. Six centers were included in the study. Each surgeon in the study used allograft tissue from the same tissue bank (Musculoskeletal Transplant Foundation, Edison, New Jersey). This requirement was instituted in order to eliminate tissue bank variability. Musculoskeletal Transplant Foundation tissue is processed with use of aseptic processing methods designed so that the natural function of the graft is not altered during processing. The disinfection of tissue is accomplished through an extended antibiotic solution soak-agitation validated process, followed by a thorough, controlled purified water rinse. In order to maintain tissue integrity, terminal sterilization agents such as high dose (>2.5-Mrad [>25 kGy]) gamma irradiation or ethylene oxide are not used in the process. Approximately 65% of all recovered unprocessed tissue is exposed to a low dose (12 to 18 kGy) of gamma irradiation in a frozen state prior to aseptic processing. The Musculoskeletal Transplant Foundation utilizes this low-dose irradiation pretreatment step to decontaminate tissue prior to aseptic processing. All tissue processing and packaging is performed under aseptic conditions[35,36].

Patients were followed prospectively at four of the centers from January 1, 2005, through January 1, 2008. Additionally, two centers performed retrospective chart reviews on patients covering the same time interval. Charts were reviewed to identify the presentation of injury, operative procedure, type of graft, and results at the time of the latest follow-up. Operative variables (antibiotic, tourniquet, and drain usage) and patient demographics were also recorded.

The choice between allograft and autograft tissue and the specific graft type was made individually by the surgeon. Inclusion criteria for this study included otherwise healthy patients presenting with an anterior cruciate ligament injury requiring a primary reconstruction. The individual surgeons determined nonsurgical compared with surgical treatment and the timing of the operation. Exclusion criteria for this study included any known risk factors for surgical site infection[37,38] (diabetes mellitus, rheumatoid arthritis, immunosuppression, history of septic arthritis, or radiation to the knee), or risk factors for Clostridium species infection[39,40] (intravenous drug use or hematologic cancer). Revision anterior cruciate ligament reconstruction and retained hardware in the joint also were exclusion criteria, as they have been identified as risk factors for postoperative infections and septic arthritis[28-30,32,33].

Preoperative antibiotic prophylaxis was used for each patient undergoing anterior cruciate ligament reconstruction. All centers had a similar protocol: antibiotics were administered thirty to sixty minutes prior to incision. Intravenous administration of 1 g of cefazolin was used for patients weighing ≤80 kg, and 2 g was used for those weighing >80 kg. Intravenous administration of 600 mg of clindamycin was used for patients with cephalosporin allergy. The surgical technique included standard knee portals for arthroscopic surgery and additional incisions, depending on the type of graft (allograft or autograft). The procedures and techniques were similar to those described in standard orthopaedic textbooks, and no breaks in sterile techniques were reported[41]. Two of the six centers used a tourniquet as necessary. The maximum tourniquet pressure was 300 mm Hg, and the maximum tourniquet time was 120 minutes. No drains were used postoperatively by any surgeon. The postoperative dressing was changed at the first follow-up visit, generally within seven days of surgery. The postoperative rehabilitation protocol was similar for all centers: weight-bearing and range-of-motion exercises as tolerated immediately postoperatively, with specific anterior cruciate ligament rehabilitation exercises performed under the guidance of a physical therapist starting after the first postoperative visit. At the discretion of the surgeon, patients wore a range-of-motion brace until adequate quadriceps strength was achieved (typically, four to six weeks).

Patients were followed for a minimum of 5.5 months postoperatively. Patients unavailable to return for a follow-up evaluation completed questionnaires by telephone interview or mail. Infections were classified as superficial or intra-articular (deep). A superficial infection was one that resolved with simple wound care and oral medication. A case of intra-articular infection was defined as any culture-proven infection at the site of implantation occurring within six months of implantation[42]. The patients were screened for standard symptoms and signs of infection[43] (fever, increased pain, swelling, erythema, drainage,

TABLE I Demographics

	Allograft (N = 640)	Autograft (N = 221)
Sex		
Female	238 (37.2%)	66 (29.9%)
Male	402 (62.8%)	155 (70.1%)
Age* *(yr)*	31.2 ± 11.4 (30.4)	25.4 ± 9.0 (22.3)
Body-mass index* *(kg/m²)*	27.2 ± 5.4 (26.5)	26.1 ± 5.0 (25.6)
Follow-up time* *(mo)*	11.7 ± 6.4 (9.7)	11.6 ± 7.3 (8.8)

*The values are given as the mean and the standard deviation, with the median in parentheses.

or warmth at the surgical site) during the follow-up. Any suspicion of infection resulted in a workup for infection, including laboratory testing (white blood-cell count, erythrocyte sedimentation rate, and/or C-reactive protein level), joint aspiration with cultures, and blood cultures. The workup and treatment protocols for infection were performed at the discretion of the attending physician.

Statistical Analysis

Summary statistics were calculated for categorical variables with use of frequency tables, and descriptive statistics such as the mean and standard deviation were calculated for numeric variables. The allograft and autograft groups were compared with each other relative to certain demographic characteristics. Chi-square tests for homogeneity of proportions were used with categorical variables, and two-sample t tests were used for continuous variables of age, height, weight, body-mass index, and follow-up time. The rate of septic arthritis in each group was described by the observed proportion and by a confidence interval.

Source of Funding

Funding from the Musculoskeletal Transplant Foundation supported data collection and analysis for this study.

Results

Data from 1298 anterior cruciate ligament reconstructions were collected prospectively and retrospectively over the three-year period from January 1, 2005, to January 1, 2008. Screening according to inclusion and exclusion criteria excluded eighty-eight patients. An additional 349 patients did not meet the minimum 5.5-month follow-up, leaving 861 patients (66.3%) who formed the final study population. The mean length of follow-up was 11.7 months (range, 5.5 to 53.9 months) for the allograft group and 11.6 months (range, 5.5 to 41 months) for the autograft group. Five and a half months, rather than six months, is reported because several patients had follow-up visits one to two weeks prior to their exact six-month follow-up date. The patients had a mean age (and standard deviation) of 29.9 ± 10.9 years (range, 12.5 to 61.5 years) and a mean body-mass index of 27.2 ± 5.4 kg/m² (range, 15.4 to 48.4 kg/m²). A total of 557 patients (64.7%) were male and 304 were female. There were significant differences in sex, age, and body-mass index between the autograft and allograft groups. The autograft group had a higher percentage of male patients, a younger mean age, and a lower mean body-mass index than the allograft group (Table I).

Of the 861 patients, 221 (25.6%) received an autograft and 640 (74.3%) received an allograft. The tissue used in the patients in the allograft group was from bone-patellar tendon-bone (39.5%), Achilles tendon (31.1%), anterior tibial tendon (27.3%), and posterior tibial tendon (0.94%). The tissue used in the patients in the autograft group was from bone-patellar tendon-bone (77.4%) and the hamstrings (20.8%). (The graft type could not be determined for 1.1% of the patients in the allograft group and for 1.8% in the autograft group.) Half (49.8%) of the total number of grafts were bone-patellar tendon-bone (Table II).

There were no cases of septic arthritis in either group. Although the observed deep infection rates were zero, we calculated 95% confidence interval estimates, which were found to be 0% to 0.57% for the allograft group and 0% to 1.66% for the autograft group. The fact that the confidence interval is somewhat wider for the autograft group simply reflects the fact that the sample size was smaller (221 compared with 640 patients). Further, a 95% confidence interval estimate for the difference in rates between the autograft group and the allograft group was –0.47% to 1.81%.

The rate of superficial infections in the entire study population was 2.32% (95% confidence interval, 1.42% to 3.56%). These twenty superficial infections resolved with oral antibiotics or simple wound care. There was no significant difference in the rate of superficial infection between the autograft group (three of 221 patients; 1.36% [95% confidence interval, 0.28% to 3.92%]) and the allograft group (seventeen of 640 patients; 2.66% [95% confidence interval, 1.55% to 4.22%]). The 95% confidence interval estimate for the difference in rates between the autograft group and the allograft group was –3.14% to 1.43%. Graft type analysis revealed no significant differences in the superficial infection rate between the different graft types. Superficial infection rates per graft type were 2.83% (95% confidence interval, 1.47% to 4.89%)

TABLE II Graft Type

Graft Type	Allograft (N = 640)		Autograft (N = 221)	
	Patients	Percentage	Patients	Percentage
Achilles tendon	199	31.1	0	0
Bone-patellar tendon-bone	253	39.5	171	77.4
Hamstring	0	0	46	20.8
Anterior tibial tendon	175	27.3	0	0
Posterior tibial tendon	6	0.94	0	0
Unknown*	7	1.1	4	1.8

*Graft type could not be determined despite review of patients' medical records.

for bone-patellar tendon-bone grafts, 2.17% (95% confidence interval, 0.06% to 11.53%) for hamstrings, 2.01% (95% confidence interval, 0.55% to 5.07%) for Achilles tendon grafts, and 1.71% (95% confidence interval, 0.35% to 4.93%) for anterior tibial tendon grafts.

Discussion

Judd et al., in a retrospective review of 1615 anterior cruciate ligament reconstructions, identified eleven (0.68%) that had a postoperative intra-articular infection[26]. When the time frame of the investigation was narrowed, they found that eleven (2.6%) of 418 anterior cruciate ligament reconstructions had an infection. All of the intra-articular infections were found in reconstructions performed with hamstring autografts; however, only eight allografts were used overall during the entire study period. A prior anterior cruciate ligament reconstruction was especially noted to be an important risk factor. In the current study, we eliminated this variable by only considering primary anterior cruciate ligament reconstructions.

In the same study, Judd et al. also performed a literature review and identified fifty patients who had septic arthritis after anterior cruciate ligament reconstruction. The average number of days to presentation was 15.4 (range, two to seventy-nine days). Two recent additional series presented a total of twenty-two cases of septic arthritis after anterior cruciate ligament reconstruction[25,44]. All patients presented within eight weeks (mean, seventeen days) after surgery, excluding one very late presentation at fifteen months.

The study by Indelli et al.[32] is the only one we are aware of prior to ours that investigated graft selection with regard to infection rates. The study's purpose was to assess treatment options and outcomes for septic arthritis following anterior cruciate ligament reconstruction. Autografts were used in 40% of the 3500 anterior cruciate ligament reconstructions and allografts were used in 60%. Five (0.14%) of the reconstructions had a postoperative deep infection, two of which were with allograft tissue. Primary and revision cases were not differentiated. No difference was found in the postoperative infection rates in a comparison of allograft and autologous tissues. The results of our investigation are comparable with those reported by Indelli et al.

We did not observe any cases of intra-articular infection in either study group, and thus we did not observe a significant difference between the two groups in our sample. The 95% confidence interval was 0% to 0.57% in the allograft group and 0% to 1.66% in the autograft group. On the basis of our sample, we are 95% confident that the true infection rate among anterior cruciate ligament reconstructions is no more than 0.57% for those performed with allografts and 1.66% for those performed with autografts. Further, since a 95% confidence interval estimate for the difference in rates between the autograft group and the allograft group is –0.47% to 1.81%, we can be confident that if there is a difference in rates, it would be no more than 1.81%.

Despite the absence of postoperative deep infections in our study with the use of allograft tissue, the potential for disease transmission and infection remains. Tissue banks perform standard tissue-recovery procedures that screen for high-risk donor behavior and test for infections[15]. Nevertheless, there have been several cases of viral disease transmission following reconstruction with allograft tissue: a single case of human immunodeficiency virus (HIV) transmission in 1985, and two cases of hepatitis C, the most recent of which was reported in 2002[45-50]. The American Association of Tissue Banks (AATB) recommends serologic screening for HIV, human T-cell leukemia virus, hepatitis B, hepatitis C, aerobic and anaerobic bacteria, and syphilis. The risk for HIV transmission with connective tissue allografts is estimated to be one in 1.6 million[1,51,52]. In our current study, there were no cases of viral transmission through allograft donor tissue.

After the reported death of a recipient of an allograft contaminated with Clostridium species[53], the Centers for Disease Control and Prevention (CDC) initiated an investigation into allograft-associated infections. From January 1998 to March 2002, it received twenty-six reports of bacterial infections associated with musculoskeletal tissue allografts[42,53,54]. Thirteen of the patients were infected with Clostridium species; fourteen were associated with a single

tissue processor. All allografts were processed aseptically but did not undergo terminal sterilization. Additional evidence implicated the allograft as the source of infection in eleven of the thirteen cases, likely contaminated hematogenously by donor bowel flora prior to tissue harvesting. On the basis of its investigation, the CDC made specific recommendations to tissue banks to decrease the risk of bacterial contamination[42]. All of our allograft tissue came from a single tissue processor, which processes tissues in accordance with current Good Tissue Practices of the U.S. Food and Drug Administration[55] and AATB standards[56] and is an accredited member of AATB.

Unfortunately, the use of aseptic technique during donor tissue harvesting does not protect against in situ microorganisms, and the only definitive mechanism of microorganism elimination is sterilization. The adverse effects of secondary sterilization, including irradiation and chemical processing, are well outlined in the literature and are not reviewed in the present study[1,7,15,57-61]. Culturing of allograft tissue prior to anterior cruciate ligament reconstruction has been suggested, but the report by Guelich et al. on 321 consecutive allograft anterior cruciate ligament reconstructions challenges this recommendation[62]. Their results call into question the utility of routinely culturing allograft tissue, as positive results did not correlate with infectious complications.

The FDA oversees tissue-processing practices, and together with the CDC and the AATB, provides specific recommendations for tissue procurement, preparation, and distribution. The FDA has established Good Tissue Practice guidelines, and the number of tissue banks accredited by AATB has doubled since 2001[62]; however, it is estimated that nearly 43% of all tissue banks are neither members of nor adhere to the standards of the AATB, which may increase the risk of infection[15]. A recent review of allograft risks and recalls noted that as few as 10% of those tissue facilities involved with musculoskeletal allografts were accredited[63].

There were several limitations to our investigation. First, it is limited by the relatively short period of follow-up. The 5.5-month minimum was established as a reasonable balance between adequate follow-up and concerns regarding loss of patients to follow-up, given the transitory nature of this patient group. Furthermore, to the best of our knowledge, all infections after anterior cruciate ligament reconstruction that have been documented in the literature have presented within three months after surgery, with the exception of one patient[25,27,44]. Second, our results can only be applied to a fairly healthy population, as we excluded subjects who were at higher risk for a surgical site infection. Third, our current series involved multiple centers with a diversity of surgical practices, by necessity creating a number of confounding variables that cannot be controlled. However, all of the surgeons in our study obtained their allograft tissue from the same tissue bank. Last, because the decision on graft choice was made by the individual surgeon, a certain amount of selection bias could exist. This selection bias might explain some of the differences we noted with regard to the demographic data. However, these differences should be interpreted with caution. Although some of the differences are significant, due in part to the large sample sizes, they may not be of clinical importance.

In conclusion, while the theoretical risk of disease transmission inherent to allograft tissue cannot be eliminated, we found no increased clinical risk of infection with use of allograft tissue compared with autologous tissue for primary anterior cruciate ligament reconstruction. The surgeon should have thorough knowledge about the tissue bank he or she uses. Furthermore, we suggest obtaining allograft tissue from tissue banks that follow the recommendations set forth by the CDC and the FDA and that are accredited by the AATB. ■

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