Long-Term Outcomes of Allograft Reconstruction of the Anterior Cruciate Ligament

Injuries of the anterior cruciate ligament (ACL) are common. Good to excellent long-term results are generally expected in more than 90% of ACL reconstructions. Although our knowledge of the biomechanics, kinematics, and long-term outcomes of ACL reconstruction is extensive, the ideal graft choice for ACL reconstruction is still up for debate.

Historically, both quadruple-stranded hamstring tendon and bone-patellar tendon-bone (BPTB) autografts have been the most popular graft options for operative reconstruction of the ACL. Recently, allograft tissues have become increasingly popular as a graft source. Proponents of allograft ACL reconstruction have cited several advantages over autograft reconstruction, including decreased donor-site morbidity, shorter operative times, and quicker postoperative recovery. Nevertheless, some authors have recently reported higher rates of both reoperation and graft failure after allograft ACL reconstruction.

To evaluate the long-term outcomes of allograft ACL reconstruction, we retrospectively reviewed the cases of all patients who underwent allograft or autograft ACL reconstruction by 2 senior surgeons at a single institution over an 8-year period. We hypothesized that the reoperation and revision surgery rates for allograft ACL reconstruction would not be higher than those reported for autograft reconstruction. We also hypothesized that allograft ACL reconstruction failure rates would not be higher for patients younger than 25 years than for patients who are older and less active.

Materials and Methods

This study was approved by the Institutional Review Board at the University of Arizona College of Medicine. We retrospectively reviewed the cases of all patients who underwent primary endoscopic ACL reconstruction at the University of Arizona College of Medicine over an 8-year period (2000–2008). All ACL reconstructions were performed by 2 senior, fellowship-trained sports medicine specialists, including Dr. William A. Grana. Patients
were identified from the *Current Procedural Terminology (CPT)* code for ACL reconstruction. Both autograft and allograft reconstructions were included in the study. Patients undergoing revision ACL reconstruction and patients with multi-ligamentous knee injuries were excluded. All available medical records were reviewed for patient demographics and any concomitant knee pathology. We included patients of all activity levels, patients with acute ACL tears, and patients with chronically ACL-deficient knees. We identified a separate cohort of Division I varsity athletes from the University of Arizona for evaluation. These patients were identified from the injury surveillance system in the athletic training facility of the University of Arizona.

ACL reconstructions at our institution during this 8-year period were performed with both allograft and autograft soft tissue. Allograft tendons were most commonly used. Tibialis anterior allograft was used in the majority of those knees. Tibialis posterior and semitendinosus allografts were used in a small subset of patients. Autograft reconstruction was performed with quadruple-stranded semitendinosus and gracilis tendons. We reviewed operative reports to determine type of graft used for reconstruction.

Patients were assessed clinically by telephone interview and/or mailed survey. They were specifically asked whether there had been any postoperative complications. We reviewed all operative and postoperative follow-up notes for postoperative complications. Objective clinical assessment involved use of the International Knee Documentation Committee (IKDC) Subjective Knee Evaluation Form, the Tegner-Lysholm Knee Scoring Scale, and the Tegner Activity Scale.

**Operative Technique**

A standard, transtibial arthroscopically assisted ACL reconstruction was performed in all patients. For autograft reconstruction patients, both the semitendinosus and gracilis tendons were harvested through a small anteromedial incision and prepared to form a quadruple-stranded graft. All allograft tendons were obtained from the Musculoskeletal Transplant Foundation (MTF). Tibialis anterior and tibialis posterior allografts were folded in half to form a double-stranded graft. Alternatively, 2 semitendinosus allografts were prepared in the same fashion as that described for autograft hamstring tendons. The tibial tunnel was placed into the center of the ACL tibial footprint. With use of a transtibial approach, an endoscopic offset guide was used to place the femoral tunnel at the 10- and 2-o'clock positions in the right and left knees, respectively. In almost all cases, the graft was secured on the femoral side with a cortical fixation button. Tibial fixation was obtained with a bioabsorbable interference screw.

After ACL reconstruction, each patient participated in the standard accelerated rehabilitation outlined by Shelbourne and Gray. Guided rehabilitation was instituted within 1 week after surgery under the guidance of a physical therapist. Range-of-motion exercises and closed-chain strengthening exercises were begun at this time. The protocol emphasized early return of full terminal extension and normalization of gait patterns. Patients were allowed to return to play only after meeting specific criteria, about 6 months after surgery. Many athletes in our Division I university population are allowed to return to play 5 to 6 months after surgery, after meeting return-to-play criteria.

**Statistical Analysis**

We used Minitab 14 (Minitab, State College, Pennsylvania) to perform all statistical analyses, unpaired Student *t* tests to compare IKDC and Tegner-Lysholm results between allograft and autograft groups, and *χ*² tests to compare revision and reoperation rates between groups. Significance was set at *P* = .05.
Results

We identified 362 patients who underwent ACL reconstructions at our institution between 2000 and 2008. Of these patients, 302 met the study inclusion criteria. One-hundred twenty-three (40.7%) of the 302 were available for follow-up by telephone interview and/or mailed questionnaire. This follow-up group consisted of 67 males and 56 females. Mean age at surgery was 29 years (range, 17-53 years). Mean follow-up was 50.3 months (range, 11-111 months). Of the 123 patients, 99 underwent allograft ACL reconstruction, and 24 underwent autograft ACL reconstruction. Seventeen (17%) of the 99 allograft cases required additional surgery (Table 1). The reoperation rate for patients under age 25 years (30.8%) was higher than the rate for patients older than 25 years (Table 2). Regarding patients who underwent additional surgeries, mean scores were lower with allograft (Tegner-Lysholm, 59; IKDC, 54) than with autograft (Tegner-Lysholm, 83; IKDC, 79) (Ps = .0025 and .006, respectively).

Revision rates were 10.1% (allograft group) and 4.2% (autograft group) (Table 1). This difference was not statistically significant (P = .18). In the allograft group, the revision rate was higher for patients younger than 25 years (20.5%) than for patients older than 25 years (3.3%) (Table 2). In comparison, in the autograft group, the revision rate was only 4% for patients younger than 25 years. For younger patients, the higher rate of revision with allograft (vs autograft) was statistically significant (P = .038). For older patients, allograft and autograft revision rates did not differ significantly (P = .19). No patient younger than 25 years required revision reconstruction after autograft ACL reconstruction.

IKDC and Tegner-Lysholm outcome scores for allograft and autograft groups are shown in Table 3. In patients 25 years or younger, IKDC scores were 75.18 after allograft reconstruction and 85.34 after autograft reconstruction—a significant difference (P = .045). In addition, Tegner-Lysholm scores were significantly higher after autograft reconstruction (91.58) than allograft reconstruction (78.19) in these younger patients (P = .003).
(Table 3). IKDC and Tegner-Lysholm scores were not significantly different for older patients ($P_s = .241$ and .211, respectively).

The study also included a subset of 19 primary ACL reconstructions (13 allograft, 6 autograft) performed on Division I athletes from the University of Arizona. (Nineteen [91%] of the 21 athletes in our Division I cohort were available for follow-up.) All these patients were younger than 25 years. All autograft reconstructions were performed with quadruple-stranded gracilis and semitendinosus tendons. ACL graft failure occurred in 8 (62%) of the 13 allograft cases; there were no failures in the autograft group (Table 4). One of the 5 allograft cases that did not fail required multiple surgical débridement procedures for infection, but the graft was ultimately retained. There were no infections among the 6 autograft cases.

Discussion

The ideal graft for ACL reconstruction is still a matter of intense debate. There are many graft options for ACL reconstruction. Both BPTB and hamstring autografts are associated with various graft-specific comorbidities. Anterior knee pain, knee extensor weakness, extension loss, patella fracture, patellofemoral crepitance, and infrapatellar nerve injury have been described with BPTB autografts.\(^{13-17}\) In a meta-analysis of 11 studies comparing BPTB autografts with hamstring autograft, Goldblatt and colleagues\(^{17}\) found more extension loss, kneeling pain, and patellofemoral crepitance in the BPTB group.

Knee flexion weakness, knee flexion loss, increased knee laxity, and saphenous nerve injury have all been described with use of hamstring autografts.\(^{16-19}\) Goldblatt and colleagues\(^{17}\) demonstrated a significant flexion loss in the hamstring group in their meta-analysis as well as increased laxity with both the Lachman test and the pivot shift test. They also found that the hamstring autograft group exhibited side-to-side differences of more than 3 mm on KT-1000 testing when compared with the BPTB autograft group.
Proposed advantages of allograft reconstruction include elimination of donor-site morbidity and/or pain from a less invasive procedure, faster initial recovery, more sizing options, and shorter operative times.\textsuperscript{4-7} In a 5-year follow-up of patients who had ACL reconstruction with either Achilles allograft or BPTB autograft, Poehling and colleagues\textsuperscript{7} demonstrated overall similar long-term outcomes between the groups. However, the allograft patients reported less pain 1 and 6 weeks after surgery; better function 1 week, 3 months, and 1 year after surgery; and fewer activity limitations throughout the follow-up period. Lamblin and colleagues\textsuperscript{20} also found no difference between nonirradiated allograft and autograft tissue in ACL reconstruction in a 2013 meta-analysis of ACL studies published over a 32-year period.

Despite the proposed advantages of allograft ACL reconstruction, several recent studies have demonstrated poorer outcomes in both younger patients and more active patients after allograft reconstruction.\textsuperscript{8-11,21} In a 2007 meta-analysis, Prodromos and colleagues\textsuperscript{11} compared a series of allograft reconstructions with previously published data sets of both BPTB and hamstring autografts. They found that allograft reconstructions had significantly lower stability rates than autograft reconstructions. In a case–control study by Borchers and colleagues,\textsuperscript{21} 21 patients with ACL graft failure were identified over a 2-year period, and surgical outcomes were compared with those of 42 age- and sex-matched controls. The authors found higher activity level and allograft use to be risk factors for subsequent graft failure after ACL reconstruction. More important, they showed a multiplicative interaction between higher activity level after ACL reconstruction and allograft use—an interaction that greatly increased the odds for ACL graft failure. Last, in a retrospective review, Singhal and colleagues\textsuperscript{8} evaluated the outcomes of ACL reconstruction using tibialis anterior tendon allograft and reported a 23.1% revision rate. In addition, 37.7% of patients required repeat surgery. The failure/reoperation rate was 55% for patients 25 years or younger and 24% for patients older than 25 years. The authors recommended not using tibialis anterior allografts in patients 25 years or younger and in patients who frequently engage in level I ACL-dependent sports.

The poor outcomes reported by Singhal and colleagues\textsuperscript{8} may be related to use of irradiated soft-tissue allografts. In a comparison of nonirradiated BPTB allograft and BPTB autograft in patients 25 years or younger, Barber and colleagues\textsuperscript{22} found equivalent outcomes at 2-year follow-up. They actually found a higher rate of failure for autograft reconstruction (9.4%) than allograft reconstruction (7.1%). A potential critique of their study is the significant difference between the patient groups’ mean ages: 18.6 years (autograft) versus 20.1 years (allograft). Despite this selection bias, Barber and colleagues\textsuperscript{22} argued that nonirradiated BPTB allograft is equivalent to BPTB autograft for ACL reconstruction.

Our study is one of the largest allograft studies with a comparison group. The principal findings of this study demonstrate that overall reoperation and revision rates after irradiated soft-tissue allograft ACL reconstruction are higher than those historically quoted for autograft ACL reconstruction. Specifically, allograft patients younger than 25 years had a reoperation rate of 30.8% and a revision rate of 20.5%. (Allograft patients older than 25 years had lower rates of reoperation, 8.3%, and revision, 3.3%.) After revision surgery, autograft patients’ subjective outcomes (IKDC and Tegner-Lysholm scores) were significantly improved compared with those of allograft patients ($P_s = .0017$ and $.0031$, respectively). Most compelling, however, is the unexpected and quite concerning 62% failure rate in our high-level Division I intercollegiate athletes.

There are multiple hypotheses regarding the higher failure rates of allograft tissues versus autograft tissues in ACL reconstruction. Processing methods, exposure to ionizing radiation, and the incorporation/ligamentization process have all been cited as possible reasons for allograft failure. All the allograft tendons used in the present study were obtained from MTF, which uses a proprietary “aseptic” processing system that includes washing in buffered saline impregnated with antibiotics (imipenem/cilastatin, amphotericin B, gentamicin) followed by final rinsing in phosphate-buffered saline. The majority of grafts are subjected to low-level irradiation (<2 Mrad/20
kGy) based on the outcomes of MTF’s stringent donor-selection process. Although the washing process has not been shown to alter the structural integrity of donor grafts, multiple studies have outlined the detrimental effects of higher levels of gamma radiation on allograft tissues. Although lower levels are effective against potential bacterial contaminants, a radiation level of 4 Mrad is necessary to kill the human immunodeficiency virus (HIV). Thus, a dose of 4 Mrad or higher is needed to truly “sterilize” a graft. This higher dose is an issue, as it has been known for some time that higher levels of ionizing radiation can have adverse effects on the biomechanical strength of soft-tissue allografts. In fact, ionizing radiation has dose-dependent effects. Schwartz and colleagues showed in a caprine model that radiation exposure at 4 Mrad significantly decreased the biomechanical strength of ACL allografts at 6 months. Balsly and colleagues found in a biomechanical study that radiation doses of 18 to 22 Mrad did not significantly affect the mechanical integrity of soft-tissue allografts. Conversely, in an in vivo study, Rappe and colleagues showed that Achilles allografts irradiated at a dose of 2.0 to 2.5 Mrad had a failure rate (33%) much higher than that of nonirradiated allografts (2.4%). The radiation dose used by MTF is less than 2 Mrad. Although more than needed to kill bacterial contaminants, this dose is considered by MTF to be below the threshold for biomechanical alterations. Only a minority of grafts is treated without irradiation.

It is possible that any level of radiation affects ligamentization of allograft tissues. Multiple studies have outlined the ligamentization process of autograft tendons in vivo. Patellar tendon autografts undergo central degeneration 2 to 6 weeks after reconstruction, but, by 6 to 12 months, these tendons have structural properties similar to those of the native ACL. Findings are similar for hamstring autografts. Goradia and colleagues found that, by 52 weeks, semitendinosus autografts transform into a histologic structure similar to that of the normal ACL. Remodeling of allograft tendons has been described as occurring at a much slower rate. Bhatia and colleagues demonstrated faster remodeling in autograft tissues versus allograft tissues at early time points in an in vivo rabbit model. Ultimately, differences in graft incorporation and ligamentization may be a primary factor in the higher failure rates of allograft ACL reconstruction. Current rehabilitation protocols may not take into account the longer ligamentization process for allograft tissues. These protocols are largely based on our current understanding of the ligamentization process after autograft reconstruction. It is possible that the rehabilitation program and return-to-play schedule for allograft reconstruction need to be altered to help avoid higher failure rates. The return-to-play protocol at the authors’ institution scheduled most varsity athletes to return to play 6 months after surgery. In some cases, the timetable was shortened, and some athletes were returned to play 5 months after surgery, after meeting all return-to-play criteria. Based on the findings of the present study, this return-to-play schedule may be much too aggressive for high-level athletes after allograft reconstruction. It is possible these allografts have not reached “maturity,” as their autograft counterparts have, and thus are not ready for unrestricted return to play.

Our study had multiple strengths. All reconstructions were performed by 2 senior surgeons with extensive clinical experience. The autograft and allograft reconstructions used the same techniques and rehabilitation protocols. This is one of the largest studies of outcomes of allograft ACL reconstruction and one of the largest studies that used a comparison group of autograft reconstructions. Having a comparison group effectively allowed us to contrast the differences between allograft and autograft tissues. Last, this study evaluated a subgroup of high-level NCAA Division I athletes. Follow-up in the overall study was 40.7%, but follow-up in this subgroup was 91%. The very high follow-up rate in the university population helped us validate the overall results of the study. Study results reinforced the fact that irradiated soft-tissue allograft may not be indicated for ACL reconstruction in a younger, more active patient population and led to a change in approach to ACL reconstruction for Division I intercollegiate athletes at the University of Arizona. Allograft ACL reconstruction is no longer recommended for the intercollegiate athletes at the University of Arizona.

Our study had its limitations. First, it had the inherent biases of a retrospective study. Second, many patients were
lost to follow-up. We contacted and surveyed 40.7% of the patients who met the inclusion criteria. We tried reaching them in multiple ways—through US mail, all listed phone numbers, family members, and so forth. Tucson, Arizona is a college town and has a larger transient population, which may have added to the difficulty in contacting patients.

**Conclusion**

Given the high rates of reoperation and revision surgery with allograft reconstruction in younger patients in this study, we recommend against routine use of irradiated soft-tissue allograft tissue for ACL reconstruction in patients 25 years or younger. In our clinical practices, we prefer using autograft tissue for ACL reconstruction in younger, more active individuals. Irradiated soft-tissue allograft ACL reconstruction is a viable option in the older, less active patient population. Although the overall reoperation rate in this cohort study is acceptable, the revision rate for patients younger than 25 years is concerning and should be taken into account when considering use of irradiated soft-tissue allograft for ACL reconstruction in these younger patients.

**Key Info**

**Figures/Tables**

**References**


Multimedia

Product Guide

Product Guide

- Med4 Elite™
- GRPro 2.1®
- Shoulder Wrap
- Knee Wrap

Citation