A Meta-analysis of Patellar Tendon Autograft Versus Patellar Tendon Allograft in Anterior Cruciate Ligament Reconstruction

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Purpose: Studies have suggested good long-term success rates with bone–patellar tendon–bone (BPTB) autograft and BPTB allograft in anterior cruciate ligament (ACL) reconstruction, but the numbers reported in available prospective studies may be underpowered to elucidate significant differences between the two groups. Here, we present a meta-analysis to compare the results of BPTB autograft and BPTB allograft in primary ACL reconstruction. **Methods:** A systematic review of prospective trials using BPTB autograft and BPTB allograft tissue for ACL reconstruction with a minimum 2-year follow-up was performed. Summary odds ratios (ORs), confidence intervals, and *P* values were calculated. **Results:** Of 548 studies, 6 fulfilled our inclusion criteria, with 256 patients in the autograft and 278 patients in the allograft group. Allograft patients were more likely to rupture their graft than autograft patients (OR, 5.03; $P = .01$) and more likely to have a hop test less than 90% of the nonoperative side (OR, 5.66; $P < .01$). When irradiated and chemically processed grafts were excluded from analysis, no significant differences were found between allograft and autograft patients with respect to graft rupture, rate of reoperation, normal/near normal IKDC scores, Lachman exam, pivot shift exam, patellar crepitus, hop test, or return to sport. **Conclusions:** In this meta-analysis, ACL reconstruction with BPTB autograft was favored over BPTB allograft for graft rupture and hop test parameters. However, when irradiated and chemically processed grafts were excluded, results were not significantly different between the two graft types. **Level of Evidence:** Level III, systematic review of prospective nonrandomized cohort studies. **Key Words:** Allograft—Anterior cruciate ligament—Autograft—Bone–patellar tendon–bone—Meta-analysis.

Bone–patellar tendon–bone (BPTB) autograft is widely used for reconstruction of the anterior cruciate ligament (ACL)–deficient knee. It is often chosen because of its excellent initial fixation, biomechanical properties, durability, and success at long-term follow-up.[1] However, studies have shown that the harvesting of the central third of the patellar tendon has associated donor site morbidity. Specifically, patellofemoral osteoarthritis, scar formation with shortening of the patellar tendon, loss of terminal knee extension, and patellofemoral pain have been reported.[2-4]

BPTB allograft has been used as an alternative graft choice in ACL reconstruction. Its potential advantages include less chance of harvest-related patellofemoral symptoms, shorter operative time, availability of larger grafts, superior cosmesis, and the possibility for multiple ligament reconstructions.[5] Potential drawbacks include delayed graft incorporation,[6] disease transmission,[7] potential immune reactions,[8] and altered mechanical properties caused by sterilization.[9-11]

Both BPTB autografts and BPTB allografts have shown satisfactory long-term results,[1,10] but the current literature does not consistently favor either graft in ACL reconstruction. In fact, several prospective studies have failed to identify significant differences in any clinical outcome.[12] We hypothesized that by

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using a meta-analysis technique, effective for incorporating results of several primary trials while utilizing methods to control for error and bias, clinically meaningful differences between BPTB autograft and allograft might be elucidated if present. We therefore conducted a meta-analysis of available evidence in order to evaluate the efficacy of BPTB autograft compared to BPTB allograft in ACL reconstruction.

METHODS

Literature Search

We searched the published literature using MEDLINE, EMBASE, Scopus (January 1985 to April 2006), and Web of Science (January 1993 to April 2006) databases, not restricted to English-language articles. We used the following subject headings and key words in separate searches: anterior cruciate ligament, surgery, reconstruction, allograft, or autograft. Five hundred and forty-eight relevant abstracts were reviewed. All potentially pertinent articles were retrieved and reviewed in detail. Additionally, we performed a manual search of the references listed in all relevant papers reviewed.

Selection of Studies

For inclusion, studies were required to be: (1) comparative studies of BPTB autograft with prospective data; (2) a minimum 2-year follow-up; (3) have identical rehabilitation protocols; and have (4) subjective and (5) objective assessment of outcome. Allografts other than BPTB (Achilles, tibialis anterior tendon, etc.) were excluded.

Data Extraction

Each study was carefully analyzed by two reviewers. Any minor inconsistencies between reviewers were re-examined and resolved. From the selected publications, subjective and objective measures included anterior drawer examination, Lachman examination, patellar crepitus, Noyes activity score, Lysholm score, KT-1000 arthrometry measurement, Tegner scores, pre- and postoperative range of motion, thigh circumference, Kujala patellar score, Cybex quadriceps strength, Cincinnati knee score, hop test greater than 90% of nonoperative side, re-operation, International Knee Documentation Committee (IKDC) scores, pivot shift scores, return to sport, time to return to sport, associated injuries, reoperation, and graft failure including re-rupture. We evaluated the following outcomes: graft failure, re-operation, Lachman manual examination, pivot shift scores, patellofemoral crepitus, return to sport, hop test greater than 90% of nonoperative side, and IKDC scores for normal or nearly normal knee. Other outcomes were not evaluable, either because data were reported with inconsistency, or without variance statistics, or as medians, and therefore not amenable to meta-analysis. The odds ratio (OR) for a given outcome was calculated for individual studies, as well as combined for an overall summary odds ratio. ORs were calculated for the odds of a bad outcome for allograft versus autograft, so a value greater than one indicates an outcome favoring BPTB autografts, whereas a value less than one would indicate an outcome favoring allografts. Shifting of the dots to the right favors the autograft outcomes (Fig 1).

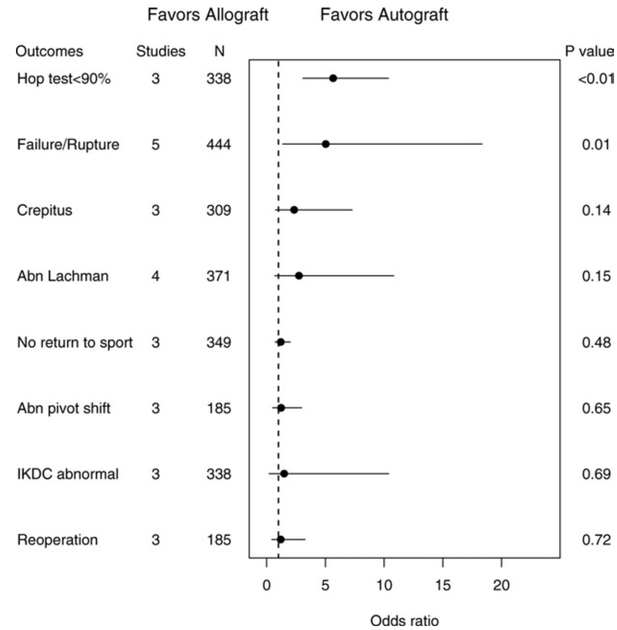

FIGURE 1. Odds ratios for each outcome evaluated, including data from all studies. Odds ratios <1 favor allograft and >1 favor autograft. DerSimonian–Laird estimates of summary odds ratios are represented for each outcome with a circle; the *bars* represent 95% confidence intervals. The *vertical dotted line* is placed at an odds ratio value of 1.0. Shifting of the dots further to the right favors autograft outcomes.

Manual Lachman examination was analyzed in our study by identifying the number of patients in each study with normal tibial translation on clinical examination by the individual study's criteria. Gorschewsky et al.[13] report the number of patients in each of two groups: one with a Lachman of 0 to 2 mm and those with increased laxity. Barrett et al.[14] and Peterson et al.[15] report side-to-side difference using Lachman testing as scores of 1+ and 2+ if increased from the nonoperative side. Kleipool et al.[12] grade Lachman testing as 0, 1, 2, and 3, with 0 being considered a normal examination. To facilitate the calculation of ORs for the meta-analysis, we evaluated the outcomes normal versus abnormal/increased translation (Lachman grade 0 *v* Lachman grade >0).

Data Analysis

Meta-analysis calculations were performed using the DerSimonian and Laird random-effects method to calculate summary ORs.[16] A distinct advantage of the DerSimonian and Laird random-effects model used in meta-analysis is the ability to evaluate heterogeneity between studies.[16] Sources of heterogeneity were explored and sensitivity analyses performed as necessary. Mantel–Haenszel fixed effects estimates were also calculated to assess the sensitivity of modeling assumptions on the results but were not reported, as they did not differ substantively from DerSimonian and Laird estimates except where heterogeneity was an issue, in which case the two methods agreed well in sensitivity analyses that excluded the heterogenous study. Statistical tests for the presence of significant heterogeneity were performed using the Mantel–Haenszel Q-statistic.[17]

Results are presented as summary ORs with 95% confidence intervals (CIs) and *P* values. Q statistics are also presented with *P* values. All results are reported such that an OR more than 1 favors autograft over allograft. $P < .05$ was considered statistically significant. For outcomes with no observed events in a particular group, Yate's continuity correction was used to allow for OR estimation.[18] Forest plots of summary ORs and CIs for each outcome were created. Data analysis was performed using R (version 2.2.1) statistical software[19] and the package rmeta.[20]

RESULTS

Literature Review

Of 548 studies initially identified, 6 studies fulfilled our inclusion criteria, including manuscripts by Gorschewsky et al.,[13] Barrett et al.,[14] Peterson et al.,[15] Kleipool et al.,[12] Harner et al.,[21] and Victor et al.[22] Of note, Peterson et al. and Shelton et al. reported data from a 2-year follow-up,[11] and later on the same group of patients at 5 years follow-up, respectively.[15] We chose to include only the 5-year follow-up data, to specifically assess any long-term issues with use of allografts. Gorschewsky et al.[13] present both 2- and 6-year follow-up data in their paper. We included only the 6-year data for the same reason. No additional articles were identified by the manual review of the bibliographies of relevant articles.

Patient Characteristics

From the 6 studies, 534 patients were evaluated. Of these, 256 patients underwent primary ACL reconstruction with BPTB autograft and 278 patients with BPTB allograft. Overall, there was no significant difference in age or gender of the patients between the allograft and autograft groups for any individual study. Table 1 summarizes the individual studies with respect to patient characteristics.

Surgical Procedure

The surgical technique with regard to implant fixation was varied somewhat among studies, although relatively consistent within each study, and fixation consisted primarily of interference screw fixation (Table 1).

Postoperative Treatment

The postoperative management of patients varied, but was consistent within individual studies. Rehabilitation generally included early weightbearing and range of motion exercises with return to full activity between 6 and 12 months.

Graft Failure/Re-rupture

One study did not list graft rupture or failure as an outcome.[21] The authors of this study were contacted for further information, but the data were unavailable. The remaining studies reported data for graft rupture including 444 patients (214 allograft, 230 autograft). The meta-analysis summary OR for graft failure was 5.03, demonstrating significantly more graft ruptures in the allograft group (95% CI, 1.38-18.33; $P = .01$; Q-statistic = 4.14; $P = .25$; Fig 1).

Rate of Reoperation: Three studies[12,14,15] reported data for reoperation (distinct from graft rupture), including 185 patients (104 allograft, 81 autograft). Overall, 13 allograft patients and 8 autograft patients had a subsequent surgery for hardware removal, meniscectomy, or notchplasty for cyclops lesion. The meta-analysis summary OR of 1.20 was not significant (95% CI, 0.44-3.27; $P = .72$; Q-statistic = 0.11; $P = .95$).

Lachman Examination: Four studies[12-15] reported data on the manual Lachman test, totaling 371 patients (189 allograft, 182 autograft). For the meta-analysis,

TABLE 1. *Study Descriptions*

	Gorschewsky et al.[13]	Barrett et al.[14]	Peterson et al.[15]	Harner et al.[21]	Victor et al.[22]	Kleipool et al.[12]
Country	Switzerland	U.S.A.	U.S.A.	U.S.A.	Belgium	Netherlands
Year	2005	2005	2001	1996	1997	1998
Study quality	Prospective, pts randomized to surgeon, independent examiner	Prospective, pts nonrandomized, 1 surgeon, examined by surgeon	Prospective, pts nonrandomized, 1 surgeon, examined by surgeon	Prospective, pts nonrandomized to 2 surgeons, examined by surgeons	Prospective, nonrandomized to 1 surgeon, independent examiner	Prospective, nonrandomized to 1 surgeon, independent examiner
Graft allocation	Chronologic division	Patient preference	Patient preference	Patient preference	Allograft availability	Allograft availability
No. patients enrolled (allo/auto)	132/136	38/25	30/30	64/26	25/48	36/26
Average age allo	*	47.13	25	23.9†	28† (18-43)	28 (16-38)
Average age auto	*	44.52	28	23.9†	28† (18-43)	28 (14-43)
Allo patient gender (M/F)	*	20/18	14/16	35/29	*	17/19
Auto patient gender (M/F)	*	15/10	19/11	15/11	*	9/7
Trauma-operative interval	No difference between groups	Allo 25 d, auto 28 d	Allo 9 <3 mos, 16> 3 mos; Auto 21 <3 mos, 14 >3 mos	43 pts <4 wks, 201 pts >4 wks	No difference between groups	Auto 30 (1-128 mos), Allo 55 (0.25-240 mos)
Surgical technique	Single-incision arthroscopic-assisted	Single-incision arthroscopic-assisted	Single-incision arthroscopic-assisted	Two-incision arthroscopic-assisted	Single-incision arthroscopic-assisted	Single-incision endoscopic technique
Fixation	Absorbable IS	IS or EndoButton	IS	IS	IS	IS
Average follow-up (mos)	71	41.2	63	36-60	24	Allo 46, auto 52

Abbreviations: allo, BPTB allograft; auto, BPTB autograft; IS, interference screw; pts, patients.
*Values not available, but no significant difference noted.
†No distinction available between groups.

we evaluated the outcomes of Lachman grade 0 versus Lachman grade greater than 0. The meta-analysis showed a summary odds ratio of 2.75, which was not statistically significant (95% CI, 0.70-10.81; $P = .15$; Q-statistic = 17.4: $P < .01$; Fig 1).

Pivot Shift Examination: Three studies[12,14,15] reported quantitative data on pivot shift testing, in a total of 185 patients (104 allograft, 81 autograft). There were no significant differences found between the two groups in any of the studies. The meta-analysis summary OR for an abnormal pivot shift (pivot shift > 0) was 1.23 for allograft versus autograft (95% CI, 0.51-2.98; $P = .65$; Q-statistic = 1.9; $P = .39$), showing similar performance between the two groups (Fig 1).

Patellofemoral Crepitus: Three studies[13-15] reported data for patellofemoral crepitus, for a total of 309 patients (153 allograft, 156 autograft). As evaluation of this outcome varied, our analysis of these data examined the presence of crepitus versus the absence of patellofemoral crepitus. The meta-analysis summary OR was 2.34, which was not statistically significant (95% CI, 0.76-7.27; $P = .14$; Q-statistic = 5.14; $P = .08$; Fig 1).

Return to Pre-injury Activity Level: Three studies[13,21,22] reported data for return to original sport, including 349 patients (174 allograft, 175 autograft). There were no significant differences between the two groups in any of the studies. The meta-analysis summary OR for not returning to sport was 1.2 (95% CI, 0.72-2.0; $P = .48$; Q-statistic = 0.22; $P = .90$), showing similar results for both groups (Fig 1).

Hop Test: Three studies[12,13,21] reported data for the hop test including 338 patients (185 allograft, 153 autograft). The meta-analysis summary OR for hop test was 5.66, significantly favoring BPTB autograft when compared to BPTB allograft (95% CI, 3.09-10.36; $P < .01$; Q-statistic = 1.6; $P = .45$; Fig 1).

IKDC Scores: Three studies[12,13,21] reported data for IKDC scores, including 338 patients (185 allograft, 153 autograft). For this meta-analysis, the calculation of ORs was normal or nearly normal versus outcomes worse than this (IKDC A and B versus IKDC C and D). The meta-analysis summary OR for an IKDC score of a normal or nearly normal knee was 1.49 for autograft compared with allograft, revealing no significant difference (95% CI, 0.21-10.38; $P = .69$; Q-statistic = 26.7; $P < .01$; Fig 1).

Heterogeneity Between Included Studies

When analyzing the OR for each individual study, it was evident that the Gorschewsky et al.[13] study had results dissimilar to the other studies for several outcomes. Statistical tests of heterogeneity using the Q-statistic were significant for the outcomes of abnormal IKDC ($P < .0001$) and abnormal Lachman ($P = .0006$) and showed a trend for crepitus ($P = .08$) when the Gorschewsky study was included. When comparing the methods used in the Gorschewsky et al. study to the other five studies included for meta-analysis, the main difference in technique related to preparation and sterilization of the BPTB allografts with radiation and acetone drying process. When these data were excluded, the statistically significant heterogeneity was no longer present for any outcome (Q-statistic P values ranging from .32 to .97), and the meta-analysis then shows that BPTB autografts were not significantly favored over BPTB allografts with respect to graft rupture ($P = .37$) or hop test greater than 90% of unoperated side ($P = .34$). In addition, the remaining outcomes—Lachman exam, pivot shift exam, patellar crepitus, return to sport, IKDC score, and reoperation—showed similar results between the two groups with no statistically significant differences identified.

DISCUSSION

Although BPTB autografts are widely used for primary ACL reconstruction, donor site morbidity remains a significant limitation.[2-4] BPTB allografts maintain some advantages of the BPTB autograft, including bone to bone fixation, and improve on the morbidity associated with harvesting the central third of a healthy, asymptomatic patellar tendon. However, the potential decrease in tensile properties with allograft sterilization[23] as well as the risk of inflammatory reaction has been a concern.[8] Several studies with relatively small patient numbers have attempted to identify differences in outcomes between the two graft choices, but none have been consistently established. In an effort to clarify the clinical results in primary ACL reconstruction, we performed a meta-analysis of prospective trials comparing BPTB autograft with BPTB allograft and found that hop test and graft rupture were significantly better with BPTB autograft. However, when irradiated and chemically processed grafts were excluded, no significant differences were found in any of the measurable outcomes.

Studies in the literature have shown allograft rupture rates from 7% to 13%,[9] and autograft rupture rates between 5% and 7%.[1,24] Salmon et al.[25] report that risk factors for ACL graft rupture include return to competitive side-stepping, pivoting, or jumping sports, and the contact mechanism of the index injury.[25] Additionally, poorly positioned grafts are thought to be a leading cause of failure.[26] In our meta-analysis, two studies reported more failures in the allograft group.[13,22] The authors of the Gorschewsky et al.[13] study postulated that increased failures were caused by both the sterilization process and perhaps a higher percentage of patients participating in contact sports.[13] The second study cited possible lack of revascularization of the graft as a cause for more failures of allograft.[22] The results of our meta-analysis suggest that graft rupture is higher among BPTB allografts, when compared with BPTB autografts. Because it is possible that the sterilization process used in the Gorschewsky et al.[13] study impacted failure rate, we feel it is important to point out that when those grafts that had undergone irradiation and chemical processing (including acetone drying) were excluded, there was no significant difference between the allograft and autograft groups.

The stability of reconstruction with allograft has been another question of active debate. In our meta-analysis, no significant differences existed between the two groups, with respect to Lachman or pivot shift testing. Recent histologic studies show that the morphology and ligamentization of autograft tendon are more favorable than that of allograft at the sixth post-operative month.[27] In our meta-analysis, all included studies used rehabilitation protocols that entailed return to full activity in 6 to 12 months. We submit that if patients adhere to established rehabilitation protocols similar to those in this meta-analysis, there is likely no difference in graft stability between allograft and autograft reconstructions. However, Barret et al.[14] suggest that allograft patients may be more active earlier after surgery, secondary to less pain, and therefore stress their grafts earlier than patients undergoing reconstruction with BPTB autograft. Thus, for the reasons outlined above, it is conceivable that reconstructions with allograft should use a less aggressive rehabilitation protocol because of delayed graft incorporation.

Functional outcome of the ACL reconstruction is extremely important to athletes who desire to return to their sport. Previously, authors suggested compromised quadriceps strength and functional capacity with the use of patellar tendon autograft,[28,29] raising the question of whether harvesting the patellar tendon should be avoided in athletes. In our meta-analysis, similar numbers in each group returned to sport, and athletes actually performed better on the hop test in the autograft group. However, quadriceps strength was not analyzed in our study. Firm conclusions therefore cannot be made regarding the impact of allograft versus autograft on functional outcome. Additionally, direct evaluation of donor site morbidity is limited in this meta-analysis as there was no standardized method of reporting these data between studies. With respect to patellofemoral crepitus, we found no difference between autograft and allograft patients. However, several of the studies included did not assess patellofemoral symptoms, underscoring a need for standardized outcomes for assessing harvest site morbidity in future studies.

An advantage of the DerSimonian and Laird method of meta-analysis is evaluation of heterogeneity between included studies.[16] Gorschewsky et al.[13] report similar patient demographics, patient selection, surgical technique including fixation, and postoperative rehabilitation when compared to the other prospective studies. The main difference, however, was in sterilization of the allograft. In contrast to fresh frozen allografts, the Gorschewsky[13] study allografts were sterilized with a combination of radiation (1.5 Mrad and 15 kGy) and acetone solvent drying. It is certainly possible that this sterilization process negatively affected the outcome of the allograft group in the Gorschewsky et al.[13] study.

We recognize several limitations of the present study. First, a meta-analysis is only as good as the studies it examines. None of the studies included are randomized, possibly introducing patient selection bias. However, no significant differences in patient demographics were found within individual studies, and randomized data between autograft and allograft are largely unavailable. Second, methodologic flaws are common within meta-analyses in the orthopaedic surgery literature.[30] As suggested by Bhundari et al.,[30] each point identified by the Oxman and Guyatt scoring system (a measure of scientific quality of review articles published in the literature)[31] was appropriately addressed in the present study, thereby attempting to control such errors. Third, by excluding irradiated graft data, the power to detect significant differences between groups is somewhat reduced. Nevertheless, our sample size remains the largest currently available in the literature.

CONCLUSIONS

In this meta-analysis, graft failure and functional outcome as measured by single-leg hop test favored ACL reconstruction with BPTB autograft over BPTB allograft. However, when irradiated and chemically processed grafts were excluded, no significant differences were found in all measurable outcomes.

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