Allograft Versus Autograft Decision for Anterior Cruciate Ligament Reconstruction: An Expected-Value Decision Analysis Evaluating Hypothetical Patients

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Purpose: The purpose of this study was to determine the optimal decision between autograft and allograft for patients undergoing anterior cruciate ligament (ACL) reconstruction. **Methods:** An expected-value decision analysis with sensitivity analysis was performed to systematically quantify the clinical decision. We evaluated 100 randomly selected individuals aged 16 to 70 years with regard to the following variables: age, sex, activity level (International Knee Documentation Committee form), and visual analog scale regarding potential outcome preferences. Patients with prior ACL injury were excluded. A decision tree was constructed (allograft *v* autograft potential outcomes), and a literature review determined probabilities of potential outcomes. Statistical fold-back analysis calculated optimal treatment. Sensitivity analysis determined the effect of changing the outcome probabilities on the decision. **Results:** Of the subjects, 88 met the study inclusion criteria. The mean age was 44 years (range, 16 to 66 years), 67% of subjects were female, and the mean activity level was moderate. The expected value for autograft reconstruction was 11.22 versus 8.42 for allograft. Increasing the probability of complications associated with autograft (sensitivity analysis) decreased the expected value of autograft reconstruction. Significant limitations include that (1) decision analysis does not investigate actual patients in whom discussion of graft options between doctor and patient highly influences the decision and (2) patient decision largely depends on the information provided. **Conclusions:** Decision analysis shows that autograft is preferred over allograft for ACL surgical reconstruction. **Clinical Relevance:** Patients' aversion to allograft tissue in general, and specific aversion to risk of disease transmission, results in a decision for ACL autograft, independent of expected outcomes.

Although anterior cruciate ligament reconstruction (ACLR) is one of the most commonly performed orthopaedic procedures, with a reported success rate approaching 90%,[1] the decision regarding the ideal anterior cruciate ligament (ACL) graft choice is controversial. Advantages of autograft include earlier incorporation[2] and avoidance of potential risks of non-host tissue.[3-5] Conversely, the advantages of allograft include a lack of donor-site morbidity[6] and shorter operative time. Two recent systematic reviews have shown comparatively similar clinical outcomes with ACLR performed with autograft and allograft tissue.[7,8]

Expected-value decision analysis is an evidence-

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based medicine tool that integrates published literature with patient values to determine a clinical decision. Using this method, investigators combine clinical evidence with quantitative determination of outcome utilities (patient's values with regard to how strongly he or she would prefer or not prefer a specific treatment outcome) and outcome probabilities (published probabilities of various potential outcomes).[9] Of note, by design, expected-value decision analysis methods evaluate hypothetical patients, to minimize bias that real patients might develop as a result of discussions with their health care providers or other parties.[9,10]

The purpose of this study was to determine the optimal decision between autograft and allograft for patients undergoing ACL reconstruction. The null hypothesis is that there is no difference in the expected value for autograft and allograft ACLR.

METHODS

Our methods followed the 5 steps of expected-value decision analysis as described in the orthopaedic literature by Kocher et al.[10] and previously summarized[9]: (1) structuring the decision problem, (2) determining outcome probabilities, (3) determining outcome utilities, (4) performing fold-back analysis, and (5) performing sensitivity analysis.

Step 1: Decision Structure

First, a decision tree was created to give structure to our decision problem. Our first decision was defined as ACLR using either allograft or autograft tissue. Then, each decision was defined as having 5 further, potential outcomes: well, reinjury, mild complication, moderate complication, or major complication (Table 1).

Step 2: Outcome Probabilities

A literature review was performed by use of the Medline database (1966-2010) to determine outcome probabilities. Search terms included ACL, reconstruction, autograft, allograft, versus, meta-analysis, and complications. We included articles that directly compared allograft and autograft and any meta-analyses or systematic reviews of similar articles. In addition, we searched the cited references in each included article. Outcome probabilities were identified based on established criteria for each potential outcome (Table 1). When not explicitly defined, "well" patients were

Table 1. *Potential Outcomes of Autograft or Allograft Tissue ACL Reconstruction*

Potential Outcome	Description
Well	No complication; no instability; low chance of reinjury; full return to activity
Reinjury	Second knee injury with possible pain, swelling, or laxity; possible meniscus injury; possible need for repeat surgery
Mild complication	
Autograft	Postoperative knee stiffness without need for repeat surgery; possible donor-site pain or morbidity; possible wound problem without need for hospitalization
Allograft	Postoperative knee stiffness or laxity without need for repeat surgery; possible incision-site pain; possible wound problem without need for hospitalization
Moderate complication	
Autograft	Postoperative wound problem or infection with need for hospitalization but without need for repeat surgery; lost time from work or inability to return to prior level of function because of persistent postsurgical knee complaints
Allograft	Postoperative wound problem or infection with need for hospitalization but without need for repeat surgery; lost time from work or inability to return to prior level of function because of persistent postsurgical knee complaints; postoperative laxity requiring bracing for athletic activity but not normal activities of daily living
Major complication	
Autograft	Postoperative serious health risk of deep venous thrombosis with possible pulmonary embolism requiring hospitalization; possible severe knee infection or stiffness with need for repeat surgery; significant lost time from work and/or inability to return to activity
Allograft	Postoperative serious health risk of deep venous thrombosis with possible pulmonary embolism requiring hospitalization; possible severe knee infection or stiffness with need for repeat surgery; significant lost time from work and/or inability to return to activity; graft-versus-host immune response resulting in graft failure and need for immune response suppression; disease transmission from graft tissue to host resulting in major infection (e.g., human immunodeficiency virus, hepatitis B, or hepatitis C).

identified as those who had not sustained reinjury or moderate to major complications at final postoperative follow-up. Cumulative mean probabilities were calculated from available probabilities identified in each study. Probabilities in studies including irradiated allograft tissue or indeterminate secondary sterilization methods were documented but not included in cumulative calculations.

Step 3: Outcome Utilities

One hundred randomly selected individuals completed our survey and were evaluated with regard to the following demographic variables: age, sex, International Knee Documentation Committee (IKDC) subjective level of activity (Table 2), and prior ACL injury. Study exclusion criteria were age younger than 16 years or older than 70 years and prior ACL injury.

Subject's values with regard to how strongly he or she would prefer or not prefer each specific potential treatment outcome (Table 1) were determined by use of a 10-cm visual analog scale, where 0 represented the worst possible medical outcome conceived by the patient and 10 represented the best possible outcome. These numerical evaluations of potential outcomes were subsequently averaged to determine outcome utilities. Of note, subjects completed the written surveys without assistance from, or discussion with, a health care provider.

Of significance, in addition to the potential outcomes described in Table 1, subjects were educated in writing with the following survey introduction:

> The ACL is like a rope that prevents knee buckling. The ACL can be surgically reconstructed with a graft using either your OWN TISSUE or DONOR TISSUE from a cadaver. Using your OWN TISSUE, there are 10-20 minutes of additional knee surgery required to remove your own tissue from your knee, resulting in a more noticeable scar. Using DONOR TISSUE, even though the tissue is carefully tested, there *is* a rare risk of getting a disease from the donor tissue.

Table 2. *IKDC Subjective Levels of Activity*

IKDC Subjective Level of Activity	Type of Activity
Very strenuous	Jumping or pivoting as in basketball or soccer
Strenuous	Heavy physical work, skiing, or tennis
Moderate	Moderate physical work, running, or jogging
Light	Walking, housework, or yard work
Unable	None of the previously mentioned activities because of knee pain

Step 4: Fold-Back Analysis

Fold-back analysis was performed. In decision analysis, fold-back analysis is used to calculate the optimal graft selection by combining the outcome probability data with the outcome utility data to compute the expected value of the various treatment options. The expected value is the product of the utility of an uncertain outcome (outcome utility) and the probability of the occurrence of that outcome (outcome probability). The optimal graft selection is the graft type with the higher expected value.[11]

Step 5: Sensitivity Analysis

Sensitivity analysis was performed. In decision analysis, sensitivity analysis is performed to establish the effect of varying the outcome probability data or the outcome utility data to determine how such changes would affect the treatment strategy decision. Ultimately, sensitivity analysis allows clinical scientists to ensure against sampling bias by allowing scrutiny of the data using quantitatively different outcome probabilities or outcome utilities. For example, if the probability of a postoperative complication increases, the decision to pursue operative treatment would be expected to decrease. Sensitivity analysis requires a series of calculations where either the outcome utility or the outcome probability is varied and the range of expected values is calculated.[11]

Statistical Methods

Methods for fold-back analysis and sensitivity analysis are described in the previous sections and were performed with use of Microsoft Office Excel 2003 (Microsoft, Redmond, WA). Mean outcome probabilities and mean outcome utilities were also assessed with this software.

RESULTS

Demographics

This study included 88 subjects after the exclusion of 12 subjects for age outside the study inclusion range (n = 6), incomplete survey information (n = 5), or prior history of ACL injury (n = 1). Mean age was 44 years (range, 16 to 66 years). Female subjects comprised 67% of included subjects, and male subjects comprised 33%. With regard to IKDC subjective

TABLE 3. *Probability of Potential Outcomes of Autograft or Allograft Tissue for ACL Reconstruction*

			Well		Reinjury	
Source	Graft Type	Population	Autograft	Allograft	Autograft	Allograft
Poehling et al.[22]	Achilles allograft, BPTB autograft	General	NR	NR	NR	NR
Harner et al.[25]	BPTB*	General	24/26 (92.3%)	61/64 (95.3%)	1/26 (3.8%)	0/26 (0%)
Chang et al.[23]	BPTB	General	30/33 (90.9%)	33/46 (76.7%)	0/33 (0%)	3/46 (6.5%)
Prodromos et al.[21]	Mixed	Meta-analysis	53/56 (94.7%)	15/17 (88%)	0/56 (0%)	0/17 (0%)
Mascarenhas et al.[30]	BPTB	High-demand athletes	15/19 (78.9%)	17/19 (89.5%)	0/19 (0%)	0/19 (0%)
Mehta et al.[12]	BPTB	General	141/142 (99.2%)	28/31† (90.3%)	1/142 (0.8%)	3/31†
Edgar et al.[26]	4HS	General	34/37 (91.9%)	45/47 (95.8%)	3/37 (8.1%)	2/47 (4.2%)
Kleipool et al.[27]	BPTB	General	18/26 (70%)	23/36 (64%)	0/26 (0%)	0/36 (0%)
Victor et al.[14]	BPTB	Athletes	45/48 (93.7%)	22/25† (88%)	0/48 (0%)	3/25† (12%)
Peterson et al.[29]	BPTB	General	29/30 (96.7%)	29/30 (96.7%)	1/30 (3.3%)	1/30 (3.3%)
Barrett et al.[31]	BPTB	High-/low-demand athletes aged <40 yr	367/411 (89.3%)	59/78 (75.6%)	44/411 (10.7%)	19/78 (24.4%)
Barrett et al.[24]	BPTB	Patients aged >40 yr	25/25 (100%)	37/38 (97.4%)	0/25 (0%)	1/38 (2.6%)
Gorschewsky et al.[11]	BPTB	General	95/101 (94.1%)	47/85† (55.3%)	6/101 (5.9%)	38/85† (44.7%)
Stringham et al.[13]	BPTB	General	40/47 (85.1%)	28/31† (90.3%)	4/47 (8.5%)	6/31† (19.4%)
Kustos et al.[28]	BPTB	Athletes	52/53 (98.1%)	24/26 (92.3%)	1/53 (1.9%)	2/26 (7.7%)

Abbreviations: 4HS, quadruple-looped hamstring graft; NR, not reported.
*Included 4 Achilles allografts.
†Included or may have included irradiated grafts or indeterminate sterilization methods.

level of activity, 7% of subjects participated in very strenuous activity on a regular basis, 16% participated in strenuous activity, 38% participated in moderate activity, 37% participated in light activity, and 2% were unable to participate in such activities.

Literature Review

We identified 17 published articles reporting potential outcomes of ACLR comparing autograft and allograft. Two reviews[7,8] included substantial data from the remaining articles. These are considered in the discussion, but data from these reviews were not tabulated and extracted for anaysis.

From the remaining 15 articles (Table 3), we extracted the outcome probabilities for autograft and allograft reconstruction of the ACL. Probabilities in studies including irradiated allograft tissue[12-14] or indeterminate secondary sterilization methods[15] were documented but not included in cumulative calculations.

Outcome Probabilities

From our literature review, we calculated the mean probabilities of the potential outcomes of ACLR using autograft and allograft. For reconstruction with an autograft, the probabilities were as follows: well, 0.92; reinjury, 0.06; mild complication, 0.33; moderate complication, 0.04; and major complication, 0.06. For reconstruction with an allograft, the probabilities were as follows: well, 0.86; reinjury, 0.07; mild complication, 0.11; moderate complication, 0.06; and major complication, 0.06 (values recorded beneath potential outcomes in Fig 1).

Patient Utilities

Patients' values (where 0 represents the worst possible medical outcome and 10 represents the best possible outcome) with regard to how strongly they would prefer or not prefer each specific potential treatment outcome were as follows: well, 9.34 for autograft and 8.2 for allograft; reinjury, 6.88 for autograft and 6.65 for allograft; mild complication, 5.75 for autograft and 5.93 for allograft; moderate complication, 4.4 for autograft and 4.36 for allograft; and major complication, 2.6 for autograft and 1.27 for allograft (values recorded to right of potential outcomes in Fig 1).

Table 3. *Continued*

Mild Complication		Moderate Complication		Major Complication	
Autograft	Allograft	Autograft	Allograft	Autograft	Allograft
NR (31-68%)	NR (0-43%)	NR	NR	NR	NR
NR	NR	1/26 (3.8%)	2/64 (3.1%)	0/26 (0%)	1/64 (1.6%)
3/33 (9.1%)	9/46 (19.6%)	3/33 (9.1%)	9/46 (19.6%)	0/33 (0%)	1/46 (2.2%)
NR	NR	3/56 (5.3%)	2/17 (12%)	NR	NR
NR	NR	4/19 (21.1%)	2/19 (10.5%)	0/19 (0%)	0/19 (0%)
NR	NR	NR	NR	NR	NR
NR	NR	0/37 (0%)	0/47 (0%)	0/37 (0%)	0/47 (0%)
NR	NR	NR	NR	8/26 (30%)	13/36 (36%)
20/48 (41.7%)	10/25 (40%)	3/48 (6.3%)	2/25 (8%)	NR	NR
16/30 (53.3%)	2/30 (6.7%)	0/30 (0%)	0/30 (0%)	0/30 (0%)	0/30 (0%)
NR	NR	NR	NR	NR	NR
1/25 (4%)	1/38 (2.6%)	0/25 (0%)	0/38 (0%)	0/25 (0%)	0/38 (0%)
50/101 (49.5%)	0/85† (0%)	3/101 (3%)	0/85† (0%)	NR	NR
6/47 (12.8%)	4/31† (12.9%)	0/47 (0%)	0/31 (0%)	7/47 (14.9%)	3/31† (9.7%)
NR	NR	0/53 (0%)	0/26 (0%)	0/53 (0%)	0/26 (0%)

Decision Analysis

Fold-back analysis showed that autograft ACLR was the optimal graft choice for treatment. The expected value or utility for autograft use was 11.22, whereas the expected value for allograft use was 8.42 (values recorded in rectangular boxes in Fig 1).

Sensitivity Analysis

To address the possibility of sampling bias, 1-way sensitivity analysis was performed to vary the probability of particular outcomes with autograft and allograft ACLR. Sensitivity analysis of moderate complications with autograft ACLR is shown in Fig 2. As the probability of moderate complications increases with a reciprocal decrease in the probability of a well outcome, the expected value for autograft ACLR diminishes. In this case allograft ACLR is favored when the probability of moderate complications with autograft exceeds 60%.

DISCUSSION

In this study the null hypothesis was rejected. Our results show a clear difference in expected values according to graft type, and autograft was identified as the preferred graft choice for ACLR. Despite similar descriptions of the expected outcome utilities for many of the potential outcomes (Table 1), the study population preferred the autograft outcome at every utility (except mild complications). This result is likely influenced by the survey introduction (described earlier in the "Methods" section) where patients are educated that, "Using DONOR TISSUE, even though the tissue is carefully tested, there *is* a rare risk of getting a disease from the donor tissue."

According to our systematic review of the literature, the probabilities of doing well, having a reinjury, or having a complication after autograft or allograft reconstruction are similar (with the exception of mild complications, which are 3 times higher after autograft reconstruction because of the possibility of donor-site morbidity). Analysis of the results of this investigation shows that strong differences in patient utilities (preferences) for autograft, rather than outcome probabilities (small differences in outcome after either autograft or allograft reconstruction), determine the optimal decision.

In reality, the overall rationale for graft choice decision is complex. Previous studies have emphasized the

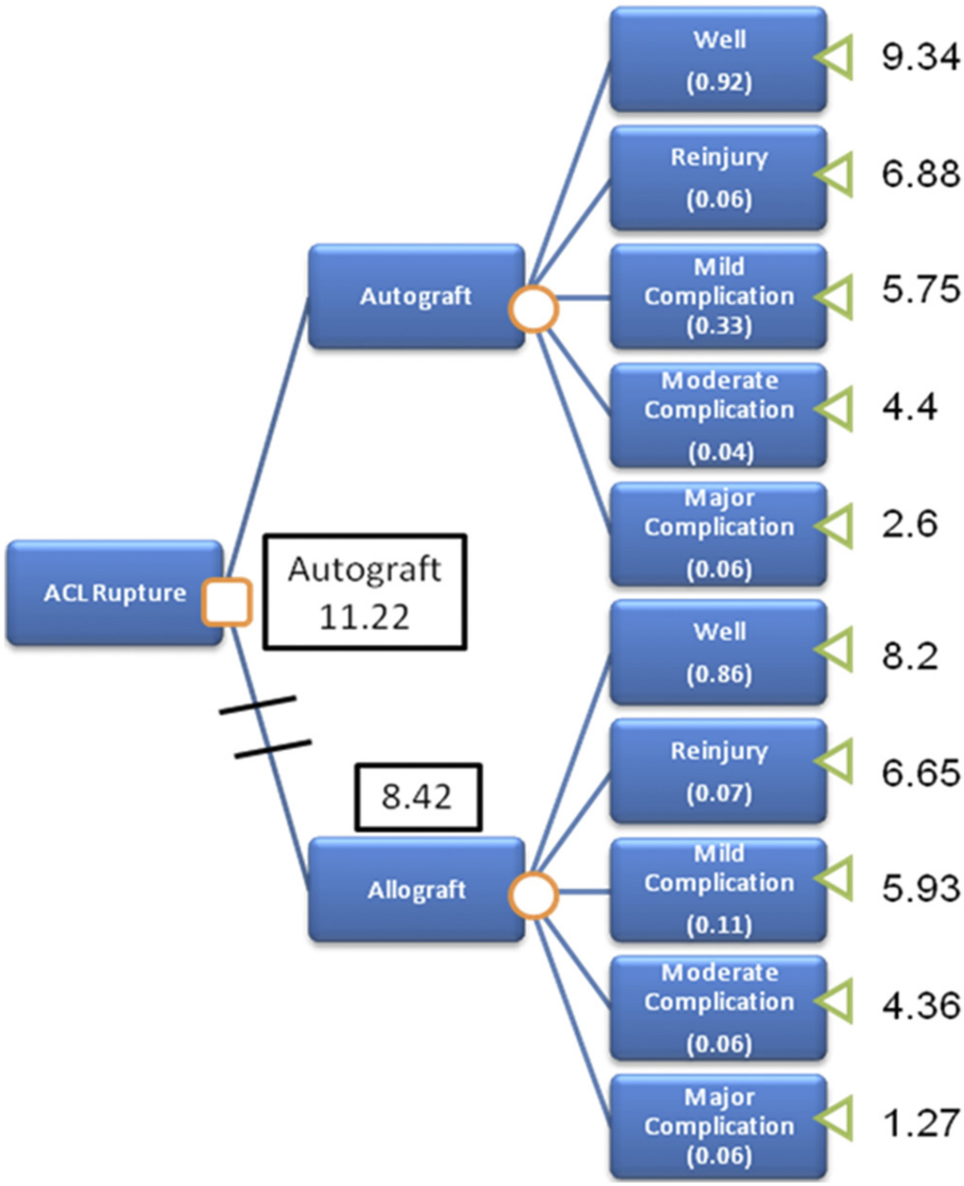

FIGURE 1. Decision tree structuring treatment options (first decision node: autograft *v* allograft), potential outcomes (terminal outcome nodes: well, reinjury, mild complication, moderate complication, and major complication), and mean probabilities of potential outcomes of autograft versus allograft ACL reconstruction (outcome probabilities) (values recorded beneath potential outcomes) plus outcome utilities (patients' values with regard to how strongly they would prefer or not prefer each potential outcome) (values recorded to right of potential outcomes). The optimal treatment strategy is the treatment strategy with the higher expected value (recorded in rectangular boxes). As opposed to allograft choice for ACLR (indicated by double slashed line), autograft is the treatment decision.

importance of physician recommendation in graft selection for ACLR, where over two-thirds of patients identified this as the leading factor in their decision.[16] However, other factors also do contribute to the decision, including an aversion to cadaveric tissue in general and specific concerns regarding disease transmission.[17] In addition, allograft concerns regarding slower biologic incorporation or perceptions regarding time until return to full activity, residual knee laxity, or cost may influence the decision to choose autograft versus allograft tissue.[18-20]

Three recent reviews compare allograft with autograft outcomes after ACLR, including 2 meta-analyses and 1 systematic review. Krych et al.[8] performed a meta-analysis focusing on bone–patellar tendon–bone (BPTB) allograft versus autograft. The results showed no difference between autograft and allograft reconstruction outcomes with respect to graft rupture, hop test, increased laxity, or return to sport. The investigators did find that when irradiated and chemically processed allograft tissue was included, allograft outcomes were worse. Carey et al.[7] performed a systematic review of ACLR with autograft compared with allograft. Originally, 9 studies were included that compared allograft and autograft. However, allograft tissue in 1 study was sterilized with a unique chemical process that resulted in a

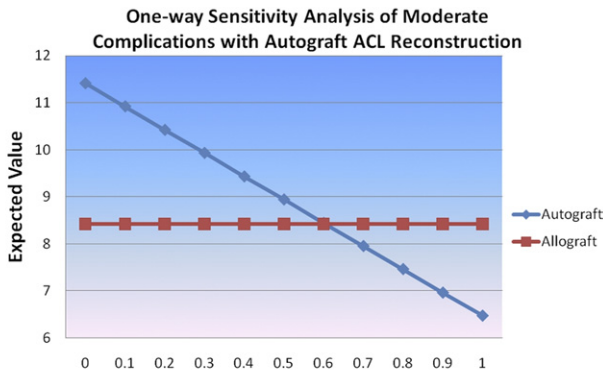

FIGURE 2. Sensitivity analysis. As the probability of a moderate autograft complication increases, the expected value of autograft ACL reconstruction decreases.

45% failure rate. When the results from that study were removed, the remaining 8 studies yielded Lysholm scores, instrumented laxity measurements, and clinical failure rates that were not significantly different. Prodromos et al.[21] studied the stability of autograft compared with allograft ACLR and showed increased laxity and higher rupture rates with allograft tissue. However, the allograft studies used in this meta-analysis included investigations with tissue prepared by irradiation or chemical sterilization.

Several studies have compared the outcomes of allograft with autograft tissue for ACLR. Poehling et al.[22] analyzed the outcomes at 5 years, comparing postoperative pain, subjective knee function, and laxity. They found that pain and subjective function were better in the allograft group despite increased laxity on KT-1000 testing (MEDmetric, San Diego, CA). Chang et al.[23] studied outcomes of allograft versus autograft BPTB grafts at 2 years postoperatively. Their results showed similar outcomes in terms of subjective function and return to preinjury activity level. There was a slight increase in flexion loss and 3 traumatic reruptures in the allograft cohort, but none occurred in the autograft population. Barrett et al.[24] focused their study on ACLR in patients aged older than 40 years. The results show no difference in Tegner activity level, range of motion, pain scores, or KT-1000 laxity measurements. The allograft group returned to sports more quickly than the autograft patients, but by 1 year, this difference was not statistically significant. Harner et al.[25] evaluated 3- to 5-year outcomes after autograft and allograft ACLR with both BPTB and Achilles graft and showed no statistically significant differences in laxity or knee scores. A higher incidence of loss of terminal extension was noted in the autograft group. In 1 of the few studies of soft-tissue grafts, Edgar et al.[26] found no differences in rates of graft failure or Tegner, Lysholm, KT-1000, or IKDC scores at 3 to 6 years' follow-up. Additional review of the literature does not support clinically significant subjective or objective differences between autograft and allograft outcomes.[27-29]

More recently, authors have attempted to evaluate the outcomes of autograft and allograft BPTB in a younger, more high-demand athletic population. In their analysis at 3 to 14 years' follow-up, Mascarenhas et al.[30] showed no difference in multiple patient-reported or objective outcome measures, including IKDC scores, return to activity, physical examination findings, reported and measured laxity, and radiographic outcomes. In contrast, Barrett et al.[31] also investigated high- and low-demand patients aged under 40 years undergoing ACLR with BPTB autograft and allograft. Subjective visual analog scale reports and Lysholm and Tegner scores were almost uniformly better in the autograft group, whereas no significant differences were noted in objective measures. However, nearly a quarter of allograft patients (24.4%) had graft failure, and high-demand individuals receiving allograft ACLR were at a 2.7- to 4.2-fold greater risk of graft rupture than those receiving autograft. Borchers et al.[32] also reported that allograft use in high–activity level patients increased the odds of graft failure.

In summary, review of the literature indicates similar results of autograft or allograft ACLR, when irradiated or chemically treated grafts are excluded, yet allograft use in high-demand, young patients requires additional investigation and cannot be summarily recommended.

The primary limitation of our study is that decision analysis methods evaluate hypothetical patients who complete a standardized survey. This is required, by convention, in decision analysis, to minimize bias, because patients who have already had the clinical problem (ACL injury) may have biased outcome utilities based on their prior decisions and experiences.[10] In addition, a standardized, written survey minimizes bias that could be introduced if potential outcomes including risks were verbally discussed with study subjects. This limitation has specific relevance regarding ACLR graft choice, where surgeon recommendation is the evidence-based, primary determinant of patient graft choice decision.[16] To reiterate this limitation, decision analysis methods, by convention, eliminate the primary and vital determinant of patient decision regarding graft selection, which is the doctor-patient discussion and associated surgeon recommendation of graft choice.

In fact, we disclose that, in direct contrast to our study finding, the preferred graft choice of the senior author (J.H.L.) for an ACLR patient of our study mean age (44 years) is allograft. Although our study methods (decision analysis) eliminate this author bias, these methods do have limitations as discussed.

Another major limitation is that the research subjects' values (hypothetical patients' utilities) depend on the information provided. As discussed, the major influence on subjects' decision to prefer autograft tissue may be the information that, "even though the (allograft) tissue is carefully tested, there *is* a rare risk of getting a disease from the donor tissue." It is possible that, despite the use of the word "rare," the risk of disease transmission has been overemphasized, (especially in the context of absence of surgeon-patient discussion as noted earlier). Furthermore, Poehling et al.[22] have reported faster return to activity or shorter rehabilitation using allograft tissue. Our literature review did not derive this finding as a quantifiable outcome probability, yet had we included "slower recovery" as a minor or moderate complication of autograft, patients may have reported different preferences. In summary, had subjects been provided different information, subjects may have reported different preferences.

Other limitations exist. We surveyed 100 patients, by convention, and 88 were included after application of exclusion criteria. Survey of different, or other, populations could yield different results. In addition, patient level of education was not evaluated. Survey of populations with different levels of education could yield different results.

CONCLUSIONS

Decision analysis shows that autograft is preferred over allograft for ACL surgical reconstruction.

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