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## [ Orthopaedic Surgery ]

# Allograft Versus Autograft Anterior Cruciate Ligament Reconstruction: Predictors of Failure From a MOON Prospective Longitudinal Cohort

Christopher C. Kaeding, MD,\*† Brian Aros, MD,‡ Angela Pedroza, MPH,† Eric Pifel, MD,§ Annunziato Amendola, MD,|| Jack T. Andrish, MD,¶ Warren R. Dunn, MD, MPH,# Robert G. Marx, MD,\*\* Eric C. McCarty, MD,†† Richard D. Parker, MD,¶¶ Rick W. Wright, MD,‡‡ and Kurt P. Spindler, MD#

**Background:** Tearing an anterior cruciate ligament (ACL) graft is a devastating occurrence after ACL reconstruction (ACLR). Identifying and understanding the independent predictors of ACLR graft failure is important for surgical planning, patient counseling, and efforts to decrease the risk of graft failure.

**Hypothesis:** Patient and surgical variables will predict graft failure after ACLR.

**Study Design:** Prospective cohort study.

**Methods:** A multicenter group initiated a cohort study in 2002 to identify predictors of ACLR outcomes, including graft failure. First, to control for confounders, a single surgeon's data (n = 281 ACLRs) were used to develop a multivariable regression model for ACLR graft failure. Evaluated variables were graft type (autograft vs allograft), sex, age, body mass index, activity at index injury, presence of a meniscus tear, and primary versus revision reconstruction. Second, the model was validated with the rest of the multicenter study's data (n = 645 ACLRs) to evaluate the generalizability of the model.

**Results:** Patient age and ACL graft type were significant predictors of graft failure for all study surgeons. Patients in the age group of 10 to 19 years had the highest percentage of graft failures. The odds of graft rupture with an allograft reconstruction are 4 times higher than those of autograft reconstructions. For each 10-year decrease in age, the odds of graft rupture increase 2.3 times.

**Conclusion:** There is an increased risk of ACL graft rupture in patients who have undergone allograft reconstruction. Younger patients also have an increased risk of ACL graft failure.

**Clinical Relevance:** Given these risks for ACL graft rupture, allograft ACLRs should be performed with caution in the younger patient population.

**Keywords:** anterior cruciate ligament reconstruction; retear; allograft; autograft

Reconstruction of a torn anterior cruciate ligament (ACL) is a common procedure in active individuals.<sup>1,3,6,13</sup> Tearing an ACL graft is a devastating occurrence after ACL

reconstruction (ACLR). Numerous studies and meta-analyses on hamstring and patellar tendon autograft ACLRs have been published, with average failure rates of 3.6% (95% confidence

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interval, 2.3%-5.3%).<sup>37</sup> There has been a recent increase in the use of allografts in ACLR due to their lack of harvest morbidity, less traumatic surgical technique, decreased postoperative pain, and easier early rehabilitation. Singhal et al recently reported a 23.1% risk of ACL soft tissue allograft failure.<sup>36</sup> A meta-analysis of level 2 and 3 studies comparing primary patellar tendon autograft and allograft ACLRs found 5.03 times higher odds of graft rupture for patients after allograft reconstructions.<sup>18</sup> Similarly, a meta-analysis of 20 studies by Prodromos et al reported a 5% failure rate in autografts, compared with a 14% failure rate in allografts ( $P < 0.01$ ).<sup>28</sup> Two systematic reviews found more failures in allograft ACLRs; however, the limited number of failures within the allograft group left these studies underpowered, and they did not reach statistical significance ( $P > 0.05$ ).<sup>6,11</sup> In one of these reviews, no difference was reported in the entire study group, but the authors did show a statistically significant difference between patellar tendon autografts and allografts, with the allograft group having a higher failure risk.<sup>11</sup> Thus, the prognostic question of whether an allograft ACLR has an increased risk of failure versus an autograft ACLR remains to be determined by either a large prospective randomized trial or a prospective longitudinal cohort with sufficient sample size, including failure events, to provide the highest level of evidence. This analysis is needed to facilitate decision making regarding graft choice for ACLR based on individual patient-expected outcomes with major risk factors (predictors) considered.

Proposed causes of ACLR graft failure include traumatic overload, surgical technical error, infection, and failure of the biological incorporation of the graft. The risk factors for ACLR graft tear are largely unknown, most likely a result of the limited number of failures within the prospective studies on allograft ACLR. In 2 meta-analyses,<sup>6,11</sup> the total number of failures was too low to allow for adequate analysis of potential confounders and risk factors. Identifying and quantifying the modifiable risk factors or predictors of ACLR failure are necessary for 3 major reasons: (1) to assist the surgeon in choosing graft type based on expected risk of re-rupture, (2) to augment preoperative counseling of patients on expected outcomes after ACLR including risk of failure; (3) to spur efforts to mitigate, modify or eliminate these risk factors for ACLR failure. These decisions and discussions with patients should be based on a high level of evidence from a prospective longitudinal cohort. Risk factors associated with native ACL injury have been studied<sup>38</sup> but the multivariable analysis of risk factors (ie, predictors) for rupture of an ACL graft are relatively unexplored.

The MOON (Multicenter Orthopaedic Outcomes Network) consortium began in 2002 and is a prospective longitudinal cohort of ACLR outcomes. The overall multicenter prospective cohort is designed to determine the independent predictors of patient-reported outcomes, symptoms of arthritis, and predictors of ACLR failure. The consortium captured > 95% of all ACLRs performed by its surgeons, and it has an 85% 2-year validated patient-reported outcome follow-up.

<sup>38</sup>References 1, 3, 5, 9, 10, 14, 15, 23, 24, 30

To focus on the impact of graft choice (autograft vs allograft) on the risk of ACLR graft rupture and minimize the impact of potential intraoperative and postoperative confounders, data from a single consortium surgeon were analyzed. The results from the single-surgeon analysis were then compared to the entire group to evaluate for generalizability of the results. We hypothesized that several modifiable patient and surgical variables were risk factors or predictors of graft failure after ACLR, thereby identifying preoperative choices for discussion before ACLR to reduce the risk of ACLR graft failure.

## METHODS

This multicenter research consortium consists of 6 academic medical centers prospectively collecting patient demographic, intra-articular findings, and surgical technique data on > 97% of the ACLRs performed at their institutions, with > 80% 2-year follow-up by patient questionnaire. The goal of the group is to identify predictors of clinical outcomes after ACLR. A further description of the data collected, inclusion criteria, timing, and nature of patient follow-up for this prospective longitudinal cohort has been delineated in a previous study.<sup>40</sup> By using data from a single surgeon—whose surgical technique, postoperative rehabilitation protocol, and return-to-play guidelines were identical for either graft choice—we minimized many potential surgeon-driven confounders. Other potential patient-driven confounders were analyzed as well, such as age, sex, activity level, meniscus status, primary versus revision, and body mass index. The decision of which graft to use was made after discussion with the patient regarding the risks and benefits of both options. The decision to use an allograft was usually driven by the patient's desire to avoid graft harvest morbidity.

Based on 2-year follow-up data from patients enrolled in the multicenter group by a single surgeon and then by the entire group, a model predictive of ACL graft rupture was generated. Using a single surgeon's data to build the initial model allowed control of potential confounders of surgical technique, rehabilitation, and return-to-play guidelines. In the single-surgeon cohort, identical surgical technique for placement and fixation of the soft tissue grafts was used for autografts and allografts. The autografts were quadrupled hamstring grafts, and the allografts were tibialis grafts. Autograft and allograft reconstructions underwent identical rehabilitation and return-to-play protocols. After construction of a predictive model from the single-surgeon data, data from the remainder of the group were then used to validate the model. Summary statistics were used to describe the demographic profile of the patients that provided data for the model building.

### Model Building

Data were evaluated from 281 patients enrolled in the study from January 2002 through December 2003 and treated by a single consortium surgeon. All patients had been contacted

by phone at their 2-year postoperative follow-up and were asked to fill out a questionnaire about the status of their reconstructed knee.

The primary outcome measure for the study was ACL graft tear, which was defined by a patient's having undergone an ACL revision reconstruction by the 2-year follow-up questionnaire and confirmed by phone interview and operative records. Patient characteristics—age, sex, Marx activity score at the time of index tear (the Marx activity score is a 16-point validated activity scale for athletic populations<sup>20</sup>), and body mass index—surgical characteristics of graft type (allograft vs autograft), primary or revision surgery, and meniscal pathology were all considered variables that could influence the primary outcome.

Multivariable logistic regression was calculated with STATA 9.0 (StataCorp LP, College Station, Texas) to determine if the chosen variables were associated with our primary outcome: ACL graft tear. A regression model was created using forward selection. All variables were individually evaluated to determine their association with graft failure. All significant variables were then added to the model. Each variable was then individually removed from the model, and the likelihood ratio test was performed. This analysis involved comparing the output of the model with and without the variable, using a chi-square analysis. A significant likelihood ratio test indicates that a variable adds significant information to the model and cannot be removed. If the likelihood ratio test was not significant, the variable tested was dropped from the model. Testing was repeated until it was determined that the model contained the fewest number of variables and was still predictive of the risk of graft failure. Interactions between all the variables were tested. Any significant interaction would then be added to the model and the likelihood ratio test performed to determine if it significantly improved the model. The point of this analysis was to include any single variable or combination of variables that produced a statistically significant effect on the model's predictive power. Assumptions, colinearity, and outliers were tested and violations reported. Odds ratios and confidence intervals were reported for the variables associated with our outcome.

### Model Validation

Validation testing was performed to confirm that the predictors of failure for the single surgeon were the same as for the entire group. To test the generalizability of the single-surgeon model's ability to predict our primary outcome of ACL graft failure, we validated the model using data from 645 patients of the other surgeons during the same period. We evaluated the percentage change in the  $\beta$  coefficients between the single surgeon's data and the rest of the consortium surgeons' data.<sup>21</sup> The percentage change in  $\beta$  coefficients between the single surgeon and the other surgeons was used to identify variables associated with ACL graft failure, and pooled odds ratios for those variables were reported.

## RESULTS

### Model Building

Of 281 patients from the single surgeon, 22 sustained an ACL graft rupture. In sum, 6 of 123 autograft reconstructions (4.9%) and 16 of 158 allograft reconstructions (10.1%) reported a graft rupture. Of the 8 variables evaluated, graft type and age were significantly associated with our primary outcome: ACL graft tear (Table 1). Marx activity score was also a significant predictor of ACL graft tear but was not included in the model-building process due to its colinearity with age. Age was included in the model because it remains predictable whereas Marx activity scores can increase or decrease over time. The 6 variables not associated with ACL graft rupture were individually added to the model, and a test for effect modification demonstrated that none was an important predictor of our outcome. Interactions among all the variables were also tested, and none was found to be a significant contributor to the model. All assumptions were tested, and no assumptions were violated.

Based on the single surgeon's data, the odds ratios for the final model, predictive of the risk of graft rupture, included age and graft type (Table 2). For the single surgeon's data, the odds of tearing an ACL graft for a patient who underwent allograft ACLR was 2.84 times higher than for a patient who had an autograft ACLR, regardless of age ( $P = 0.04$ ). When graft type is held constant, increasing a patient's age by 10 years confers a 43% reduction in the odds of ACL graft rupture ( $P < 0.01$ ).

### Model Validation

The descriptive statistics for both the single surgeon and the rest of the surgeons are shown in Table 3. Of 645 patients (3.5%) from the other consortium surgeons, 23 reported an ACL graft rupture. In sum, 18 of 568 autograft reconstructions (3.2%) and 5 of 77 allograft reconstructions (6.5%) tore. These data from the other surgeons were placed in the model from the single surgeon, and the difference in the  $\beta$  coefficients was calculated (Table 4). The area under the receiver operator characteristic curve for the other group surgeons was 0.75, and the Hosmer-Lemeshow goodness of fit test was not significant, thereby showing no lack of fit,  $\chi^2(8) = 10.23$ ,  $P = 0.25$ . The area under the curve for the single surgeon model was 0.72. The similarities in the curve between both models demonstrate that the model built from the single surgeon's data was well validated by the larger consortium cohort.

### Pooled Results

Given the similarity of the models, data for the single surgeon and the other surgeons were combined. In total, 24 of 691 patients with autograft reconstructions (3.5%) and 21 of 235 patients (8.9%) with allograft reconstructions reported a graft failure (Figure 1). The highest percentage of graft tears was in the 10- to 19-year age group (Figure 2). The odds of tearing an

Table 1. Variables considered for inclusion in model building used to predict anterior cruciate ligament reconstruction failure.<sup>a</sup>

| Variable                        | n (%)           | $\beta$ | SE   | P    |
|---------------------------------|-----------------|---------|------|------|
| <b>Graft type</b>               |                 |         |      |      |
| Autograft                       | 123 (43.8)      | 0.79    | 0.49 | 0.11 |
| Allograft                       | 158 (56.2)      |         |      |      |
| <b>Sex</b>                      |                 |         |      |      |
| Male                            | 152 (54.1)      | -0.02   | 0.45 | 0.97 |
| Female                          | 129 (45.9)      |         |      |      |
| <b>Primary/revision</b>         |                 |         |      |      |
| Primary                         | 239 (85.1)      | 0.60    | 0.76 | 0.43 |
| Revision                        | 42 (14.9)       |         |      |      |
| <b>Medial meniscal tear</b>     |                 |         |      |      |
| Yes                             | 87 (31.0)       | -0.75   | 0.57 | 0.19 |
| No                              | 194 (69.0)      |         |      |      |
| <b>Lateral meniscal tear</b>    |                 |         |      |      |
| Yes                             | 94 (33.5)       | -0.32   | 0.50 | 0.54 |
| No                              | 187 (66.5)      |         |      |      |
| <b>Mean <math>\pm</math> SD</b> |                 |         |      |      |
| Body mass index                 | 25.6 $\pm$ 4.3  | -0.10   | 0.06 | 0.09 |
| Age, years                      | 27.8 $\pm$ 10.9 | -0.07   | 0.03 | 0.01 |
| Marx score                      | 10.9 $\pm$ 5.1  | 0.19    | 0.07 | 0.01 |

<sup>a</sup>Data from a single surgeon.Table 2. Odds ratio from final model obtained during the model building stage used to predict anterior cruciate ligament reconstruction failure.<sup>a</sup>

| Variable   | Odds Ratio | SE   | P      | 95% Confidence Interval |
|------------|------------|------|--------|-------------------------|
| Graft type | 2.84       | 1.46 | 0.04   | 1.03, 7.80              |
| Age        | 0.92       | 0.03 | < 0.01 | 0.87, 0.97              |

<sup>a</sup>Data from a single surgeon.

allograft ACLR were 4 times (95% confidence interval, 2.08 to 7.60) higher than the odds of a patient tearing an autograft ACLR, holding age constant (Table 5). Across the

entire cohort, the odds of a patient tearing an ACL graft in comparison to a patient 10 years older is 2.3 times higher, controlling for graft type (Table 5). Figure 3 demonstrates the

Table 3. Descriptive statistics for the single surgeon and the other consortium surgeons.

|                  | n (%)           |                     |                 |
|------------------|-----------------|---------------------|-----------------|
|                  | Single Surgeon  | Consortium Surgeons | Total           |
| Sex              |                 |                     |                 |
| Male             | 152 (54.1)      | 363 (56.3)          | 515 (55.6)      |
| Female           | 129 (45.9)      | 282 (43.7)          | 411 (44.4)      |
| Primary/revision |                 |                     |                 |
| Primary          | 239 (85.1)      | 592 (91.8)          | 831 (89.7)      |
| Revision         | 42 (14.9)       | 53 (8.2)            | 95 (10.3)       |
| Graft type       |                 |                     |                 |
| Autograft        | 123 (43.8)      | 568 (88.1)          | 691 (74.6)      |
| Allograft        | 158 (56.2)      | 77 (11.9)           | 235 (25.4)      |
| Mean $\pm$ SD    |                 |                     |                 |
| Age, years       | 27.8 $\pm$ 10.9 | 26.0 $\pm$ 10.9     | 26.6 $\pm$ 10.9 |
| Marx score       | 10.9 $\pm$ 5.1  | 11.3 $\pm$ 5.3      | 11.2 $\pm$ 5.3  |

Table 4. Comparison of the  $\beta$  coefficients between the model-building and model validation data sets.

|            | Consortium   |        | Single Surgeon |        | Difference, % |
|------------|--------------|--------|----------------|--------|---------------|
|            | $\beta$ (SE) | P      | $\beta$ (SE)   | P      |               |
| Age        | -0.09 (0.02) | < 0.01 | -0.08 (0.03)   | < 0.01 | 11.1          |
| Graft type | 1.38 (0.33)  | < 0.01 | 1.05 (0.51)    | 0.04   | 23.9          |

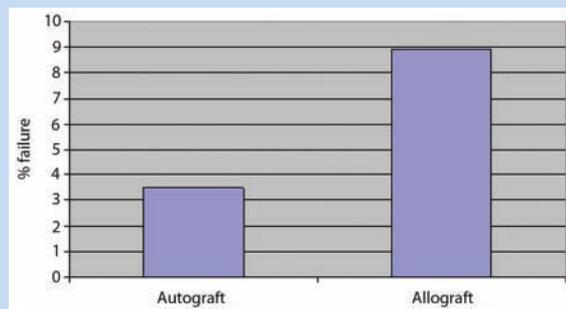


Figure 1. Percentage of graft failures by graft type for the combined consortium cohort.

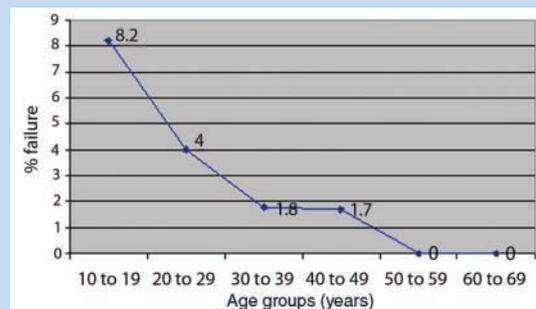


Figure 2. Percentage of graft failures by age groups for the combined consortium cohort.

Table 5. Odds ratios for entire consortium cohort.

|                       | Odds Ratio | SE   | Z     | P      | 95% Confidence Interval |
|-----------------------|------------|------|-------|--------|-------------------------|
| Graft type: allograft | 3.97       | 1.32 | 4.17  | < 0.01 | 2.08, 7.60              |
| Age: 10-year increase | 0.40       | 0.22 | -4.04 | < 0.01 | 0.26, 0.63              |

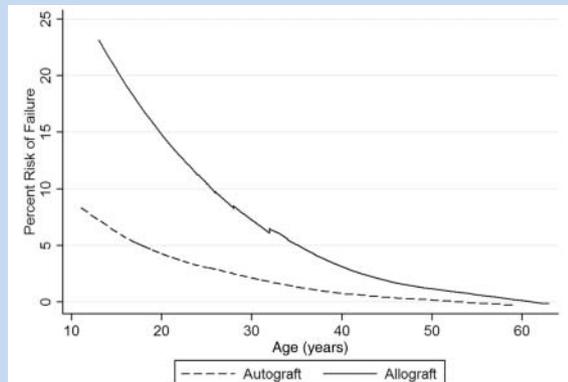


Figure 3. Probability of retear (in percentages on vertical axis) for autograft versus allograft by age for the combined consortium cohort.

impact of age on the risk of graft tear between autografts and allografts.

With this definition of failure and without enough numbers to further subdivide the allograft types and processing, the analysis of the pooled characteristics results in the following model:

$$P = 1 / (1 + e^{-[-1.37 + [-0.09 (\text{age}) + [1.38 (\text{allograft})]])})$$

The following are 2 clinical examples of the above equation: A 14-year-old with an allograft ACLR has a 22.0% chance of retearing the ACL; the same 14-year-old with an autograft ACLR has a 6.6% chance of retear. A 40-year-old with an autograft ACLR has a 0.6% chance of retear; the same 40-year-old with an allograft ACLR has a 2.6% chance of retear.

## DISCUSSION

The aim of this study was to evaluate the influence of graft choice (autograft vs allograft) on the risk of tearing an ACLR graft and to identify other patient or surgical variables associated with subsequent failure of ACL grafts. A logistic regression model was developed using a single surgeon's data that included a similar amount of autografts and allografts for primary ACLRs. Within the single-surgeon cohort, the

same operative technique, graft fixation, postoperative rehabilitation, and return-to-play guidelines were used regardless of graft source, thus eliminating the potential that these surgical and rehabilitation variables could influence the primary outcome of ACL graft rupture. According to multivariable regression for the single-surgeon data, age and graft type (allograft) were both associated with an increased risk of ACL graft rupture. Patient characteristics (sex, body mass index) and surgical characteristics (revision ACL surgery and meniscal pathology) were not associated with ACL graft rupture.

Data for the entire group of surgeons were analyzed using the logistic regression model created from the single surgeon's data. Age and graft type remained significant risk factors or predictors of ACL graft rupture. Marx activity score at index injury was found to be a significant predictor of ACL graft rupture but was also found to be closely related to age and therefore not included in the model. Unlike the single-surgeon cohort, the multicenter cohort used varied graft types and fixation techniques, but the single-surgeon model was found to be generalizable to the larger group.

The consortium chose the Marx activity scale<sup>20</sup> because it was designed to measure patient activity level instead of health status or knee function. The Marx score has been shown to positively correlate with patient activity and returning to pivoting sports and inversely with age.<sup>12,20</sup> Even though the Marx score is a validated measure of activity, it was not chosen to be included in the model. Marx score can change over time. The Marx score chosen for this study was that at the time of index injury. We do not know if the patients who tore their ACL graft returned to the same level of activity at a different rate compared to those who did not tear their ACL graft, but an analysis of the MOON data by Dunn et al<sup>8</sup> showed that the strongest predictor of return to activity after ACLR was the Marx score at time of index injury.

A statistically significant increase in ACL graft ruptures was found in younger patients. The highest percentage (37.5%) of ACLR graft failures in the consortium cohort was in the 10- to 19-year age group. The risk of ACL graft tear for this youngest age group was 2.33 times higher than their peers who were 10 years older, controlling for graft type. Our analysis showed that the risk of graft retear fell approximately in half for each 10-year increase in age. Shelbourne et al showed a similar relationship between age and risk of graft retear.<sup>33,34</sup> Patient age

is likely a proxy for activity level in patients with ACL injuries and graft failures. The inverse relationship between the Marx activity score and age has been demonstrated<sup>20</sup> after ACLR.

Female patients have been shown to have a higher likelihood of sustaining a primary ACL injury.<sup>2,3,13</sup> Salmon et al<sup>31</sup> reported no sex difference in the risk of ACL graft failure or contralateral ACL injury. In a prospective cohort of 1820 patients, Shelbourne showed that female patients had an increased risk of tearing the contralateral ACL but no increased risk of ACL graft failure.<sup>33</sup> Others have also found no sex differences in the risk of graft failure after ACLR with bone–patellar tendon–bone autograft.<sup>4,10,33</sup> In this study, sex was not a predictor of ACL graft failure. To the contrary, Stevenson et al, in a survey of Alpine skiers with a 40% response rate, showed increased ACL graft retears in female patients that did not reach statistical significance, and Noojin et al, in a series of 65 ACLR patients, showed female patients to have a higher re-tear rate.<sup>22,38</sup> That sex is a risk factor for native ACL tears but possibly not for ACL graft tears warrants further investigation.

Patients in this study who had an allograft reconstruction were 4 times more likely to tear their ACL graft than those who underwent autograft reconstruction. The data used in the model to generate this increased risk of failure came from all consortium surgeons and included tibialis anterior, tibialis posterior, Achilles tendon, and bone–patellar tendon–bone allografts. The choice of which allograft and fixation method to use was made by each surgeon and patient. Several individual studies have reported a similar risk of failure for bone–patellar tendon–bone autografts and allografts, but all were underpowered.<sup>7,14,16,17,19,26,39</sup> One meta-analysis found a significantly higher failure rate ( $P < .004$ ) between allograft versus autograft, but the limited number of failures within the allograft sample precluded risk factor identification.<sup>11</sup> In a retrospective case series review of primary ACLRs using tibialis anterior allograft, Singhal et al<sup>36</sup> reported a 23.1% risk of graft failure. Two groups of patients were created, younger and older than 25 years, 35% and 13% of whom required revision ACLR, respectively. Given the higher risk of ACL graft failure in the younger group, these authors did not recommend the use of tibialis anterior allograft in patients younger than 25 years. In this study, the use of allograft in younger patients increased the absolute rate difference of graft failure between autograft and allograft. Figure 3 can be used to make clinical decisions by placing a mark at the patient's age and then taking the absolute difference between the autograft and allograft as the expected difference in failures. For example, the absolute differences by age are as follows: 14 years, 15%; 18 years, 13%; 22 years, 9%; 30 years, 4%; and 40 years, 2%. If you now choose autograft ACLR rather than allograft, the expected number of ACLR graft failures prevented can be predicted by dividing 100 by the absolute rate difference from Figure 3 (also called the number needed to treat). For each age, the number of autograft ACLRs performed to prevent one failure is as follows: 14 years, 7 ACLRs; 18 years, 8 ACLRs; 22 years, 11

ACLRs; 30 years, 25 ACLRs; 40 years, 50 ACLRs. Thus, either the absolute difference or the number needed to treat can be discussed with the patient and factored into the overall risks and benefits of ACLR graft choice.

Scheffler et al<sup>32</sup> evaluated the biological incorporation and mechanical properties of allografts and autografts in a sheep model. They found that allografts incorporated more slowly than autografts at 6 and 12 weeks, with this difference decreasing at 52 weeks. That allograft ACLR patients have a quicker postoperative rehabilitation course and diminished pain compared to patients with autografts may lead the former to return to high level of activity earlier than the latter and before sufficient biological healing of the graft,<sup>27</sup> which may place allograft ACLR at a higher risk of re-tear. In this cohort, it is possible that although the return-to-play guidelines were identical, the allograft ACLRs may have achieved a higher activity level sooner than the autograft ACLRs. Shino et al<sup>35</sup> reported a 3% risk of ACL graft failure for soft tissue allografts after allowing patients to return to sports at 12 months. Singhal et al<sup>36</sup> commented that their postoperative protocol of release to sport at 4 months could have been a driver of increased risk of graft failure given the increased time needed for tendon graft incorporation.<sup>25</sup> In this study, all patients followed a similar postoperative protocol and were released to sports at 4 to 6 months postreconstruction if they had achieved the following criteria: no functional complaints; confidence when running, cutting, jumping at full speed; and at least 85% contralateral values on hop tests. Patients who underwent allograft reconstruction were 4 times more likely to tear their ACL graft, holding age constant.

Allograft type and processing may also influence risk of re-tear. Rappe et al<sup>29</sup> reported a statistically higher risk of failure for irradiated Achilles allograft (33.0%) versus nonirradiated Achilles allograft (2.4%). Krych et al<sup>18</sup> performed a meta-analysis demonstrating that irradiation and chemical processing may place allografts at increased risk of failure. The focus of this study was to evaluate the risk of graft failure between allograft and autograft tissue; thus, we did not evaluate the effect of allograft processing. Due to the large number of potential variables regarding allografts, such as type, donor characteristics, and processing techniques, a much larger number of allograft failures would be needed for a logistic regression. The allografts in this study were predominantly fresh frozen, without proprietary processing, and were nonirradiated or irradiated less than 2.5 mRad. In an ad hoc analysis, we could not identify tissue bank, allograft type, or processing (eg, irradiation status) as a significant variable for allograft re-tear. Future studies will be completed to determine the contributions of allograft tissue–processing details and age or sex of donor on the risk of failure.

The choice of graft type was driven by patient choice and not randomly assigned. This possible source of bias with respect to age, sex, and activity level is addressed by the multivariate regression analysis, which controlled for these variables. This

lack of randomization does not account for any other unknown confounders.

Graft failure in this study was defined as that which went on to a revision ACLR within 2 years of primary ACLR. This definition does not include patients who may have torn their grafts but chose to modify their activities and not undergo a revision ACLR, those who tore greater than 2 years after their primary ACLR, and those with stretching of the graft with laxity on exam but personal satisfaction with functional result. Thus, this definition underestimates the number of failures that occurred, but it does represent the most clinically meaningful failures from the patient's perspective.

The single-surgeon cohort had identical postoperative rehabilitation and return-to-activity guidelines. The activity level analyzed in this study was the Marx score at time of index injury. This measure has been shown to be the strongest preoperative predictor of the level of activity to which patients returned after ACLR.<sup>8</sup> Thus, by controlling for the Marx score at index injury, the postoperative activity as a confounder has been evaluated. The guidelines for release to full activity were the same. Unfortunately, what was not evaluated was when the patients actually returned to high activity. This study did not evaluate whether a longer time before return to activity influences failure rates, thereby warranting further investigation. Future efforts to analyze the time interval of graft rupture after ACLR, the graft rupture in relation to allograft tissue type and processing, the extent and time frame of the biological incorporation of grafts, and the activity level at the time of graft failure would provide additional insight into risk factors for ACL graft ruptures. A more complete identification and quantification of the predictors of ACLR graft tear would be beneficial in counseling patients who are contemplating ACLR; it would aid surgeons in preoperative planning; and it would facilitate efforts to minimize repeat ACL injuries.

This prospective longitudinal cohort study demonstrates that the risk of ACL graft rupture is higher for patients who undergo allograft reconstruction. The risk of graft failure is also higher for younger patients. The clinical relevance for graft choice by age between allograft versus autograft is best shown in Figure 3. The absolute rate difference between the 2 grafts at a given age can be discussed with patients, and for surgeons, the number needed to treat is relevant to avoid the graft failure experienced in their practice.

Given that further investigation into allograft type and processing, as well as the time interval to return to full activity, may influence outcomes, allograft ACLRs should be performed with caution in the younger population, with the decision being made with an understanding of the available evidence. Analysis of number needed to treat shows that in older patients, allograft use is less of a concern.

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## REFERENCES

1. Agel J, Arendt EA, Bershadsky B. Anterior cruciate ligament injury in national collegiate athletic association basketball and soccer: a 13-year review. *Am J Sports Med.* 2005;33(4):524-530.
2. Anderson AF, Dome DC, Gautam S, Awh MH, Rennitt GW. Correlation of anthropometric measurements, strength, anterior cruciate ligament size, and intercondylar notch characteristics to sex differences in anterior cruciate ligament tear rates. *Am J Sports Med.* 2001;29(1):58-66.
3. Arendt E, Dick R. Knee injury patterns among men and women in collegiate basketball and soccer: NCAA data and review of literature. *Am J Sports Med.* 1995;23(6):694-701.
4. Barber-Westin SD, Noyes FR, Andrews M. A rigorous comparison between the sexes of results and complications after anterior cruciate ligament reconstruction. *Am J Sports Med.* 1997;25(4):514-526.
5. Caraffa A, Cerulli G, Progetti M, Aisa G, Rizzo A. Prevention of anterior cruciate ligament injuries in soccer: a prospective controlled study of proprioceptive training. *Knee Surg Sports Traumatol Arthrosc.* 1996;4(1):19-21.
6. Carey JL, Dunn WR, Dahm DL, Zeger SL, Spindler KP. A systematic review of anterior cruciate ligament reconstruction with autograft compared with allograft. *J Bone Joint Surg Am.* 2009;91(9):2242-2250.
7. Chang SK, Egami DK, Shaieb MD, Kan DM, Richardson AB. Anterior cruciate ligament reconstruction: allograft versus autograft. *Arthroscopy.* 2003;19(5):453-462.
8. Dunn WR, Spindler KP, Wolf BR, Parker RD, Kaeding CC, Wright RW. Predictors of activity level two years after ACL reconstruction: a multicenter ACLR cohort study. *Am J Sports Med.* In press.
9. Ettliger CF, Johnson RJ, Shealy JE. A method to help reduce the risk of serious knee sprains incurred in alpine skiing. *Am J Sports Med.* 1995;23(5):531-537.
10. Ferrari JD, Bach BR Jr, Bush-Joseph CA, Wang T, Bojchuk J. Anterior cruciate ligament reconstruction in men and women: An outcome analysis comparing gender. *Arthroscopy.* 2001;17(6):588-596.
11. Foster TE, Wolfe BL, Ryan S, Silvestri L, Kaye EK. Does the graft source really matter in the outcome of patients undergoing anterior cruciate ligament reconstruction? An evaluation of autograft versus allograft reconstruction results: a systematic review. *Am J Sports Med.* 2010;38(1):189-199.
12. Gobbi A, Francisco R. Factors affecting return to sports after anterior cruciate ligament reconstruction with patellar tendon and hamstring graft: a prospective clinical investigation. *Knee Surg Sports Traumatol Arthrosc.* 2006;14(10):1021-1028.
13. Gwinn DE, Wilckens JH, McDevitt ER, Ross G, Kao TC. The relative incidence of anterior cruciate ligament injury in men and women at the United States Naval Academy. *Am J Sports Med.* 2000;28(1):98-102.
14. Harner CD, Olson E, Irrgang JJ, Silverstein S, Fu FH, Silbey M. Allograft versus autograft anterior cruciate ligament reconstruction: 3- to 5-year outcome. *Clin Orthop Relat Res.* 1996;324(324):134-144.
15. Hewett TE, Lindenfeld TN, Riccobene JV, Noyes FR. The effect of neuromuscular training on the incidence of knee injury in female athletes: a prospective study. *Am J Sports Med.* 1999;27(6):699-706.
16. Indelicato PA, Linton RC, Huegel M. The results of fresh-frozen patellar tendon allografts for chronic anterior cruciate ligament deficiency of the knee. *Am J Sports Med.* 1992;20(2):118-121.
17. Kleipool AE, Zijl JA, Willems WJ. Arthroscopic anterior cruciate ligament reconstruction with bone-patellar tendon-bone allograft or autograft: a prospective study with an average follow up of 4 years. *Knee Surg Sports Traumatol Arthrosc.* 1998;6(4):224-230.
18. Krych AJ, Jackson JD, Hoskin TL, Dahm DL. A meta-analysis of patellar tendon autograft versus patellar tendon allograft in anterior cruciate ligament reconstruction. *Arthroscopy.* 2008;24(3):292-298.

19. Kustos T, Balint L, Than P, Bardos T. Comparative study of autograft or allograft in primary anterior cruciate ligament reconstruction. *Int Orthop*. 2004;28(5):290-293.
20. Marx RG, Stump TJ, Jones EC, Wickiewicz TL, Warren RF. Development and evaluation of an activity rating scale for disorders of the knee. *Am J Sports Med*. 2001;29(2):213-218.
21. Mickey RM, Greenland S. The impact of confounder selection criteria on effect estimation. *Am J Epidemiol*. 1989;129(1):125-137.
22. Noojin FK, Barrett GR, Hartzog CW, Nash CR. Clinical comparison of intraarticular anterior cruciate ligament reconstruction using autogenous semitendinosus and gracilis tendons in men versus women. *Am J Sports Med*. 2000;28(6):783-789.
23. Oates KM, Van Eenenaam DP, Briggs K, Homa K, Sterett WI. Comparative injury rates of uninjured, anterior cruciate ligament-deficient, and reconstructed knees in a skiing population. *Am J Sports Med*. 1999;27(5):606-610.
24. Orchard J, Seward H, McGivern J, Hood S. Intrinsic and extrinsic risk factors for anterior cruciate ligament injury in Australian footballers. *Am J Sports Med*. 2001;29(2):196-200.
25. Papageorgiou CD, Ma CB, Abramowitch SD, Clineff TD, Woo SL. A multidisciplinary study of the healing of an intraarticular anterior cruciate ligament graft in a goat model. *Am J Sports Med*. 2001;29(5):620-626.
26. Peterson RK, Shelton WR, Bomboy AL. Allograft versus autograft patellar tendon anterior cruciate ligament reconstruction: a 5-year follow-up. *Arthroscopy*. 2001;17(1):9-13.
27. Poehling GG, Curl WW, Lee CA, et al. Analysis of outcomes of anterior cruciate ligament repair with 5-year follow-up: allograft versus autograft. *Arthroscopy*. 2005;21(7):774-785.
28. Prodromos C, Joyce B, Shi K. A meta-analysis of stability of autografts compared to allografts after anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc*. 2007;15(7):851-856.
29. Rappe M, Horodyski M, Meister K, Indelicato PA. Nonirradiated versus irradiated Achilles allograft: in vivo failure comparison. *Am J Sports Med*. 2007;35(10):1653-1658.
30. Rozzi SL, Lephart SM, Gear WS, Fu FH. Knee joint laxity and neuromuscular characteristics of male and female soccer and basketball players. *Am J Sports Med*. 1999;27(3):312-319.
31. Salmon L, Russell V, Musgrove T, Pinczewski L, Refshauge K. Incidence and risk factors for graft rupture and contralateral rupture after anterior cruciate ligament reconstruction. *Arthroscopy*. 2005;21(8):948-957.
32. Scheffler SU, Schmidt T, Gangey I, Dustmann M, Unterhauser F, Weiler A. Fresh-frozen free-tendon allografts versus autografts in anterior cruciate ligament reconstruction: delayed remodeling and inferior mechanical function during long-term healing in sheep. *Arthroscopy*. 2008;24(4):448-458.
33. Shelbourne KD, Gray T, Haro M. Incidence of subsequent injury to either knee within 5 years after anterior cruciate ligament reconstruction with patellar tendon autograft. *Am J Sports Med*. 2009;37(2):246-251.
34. Shelbourne KD, Sullivan AN, Bohard K, Gray T, Urch SE. Return to basketball and soccer after anterior cruciate ligament reconstruction in competitive school-aged athletes. *Sports Health*. 2009;1:236-241.
35. Shino K, Inoue M, Horibe S, Hamada M, Ono K. Reconstruction of the anterior cruciate ligament using allogeneic tendon: long-term followup. *Am J Sports Med*. 1990;18(5):457-465.
36. Singhal MC, Gardiner JR, Johnson DL. Failure of primary anterior cruciate ligament surgery using anterior tibialis allograft. *Arthroscopy*. 2007;23(5):469-475.
37. Spindler KP, Kuhn JE, Freedman KB, Matthews CE, Dittus RS, Harrell FE Jr. Anterior cruciate ligament reconstruction autograft choice: bone-tendon-bone versus hamstring: does it really matter? A systematic review. *Am J Sports Med*. 2004;32(8):1986-1995.
38. Stevenson H, Webster J, Johnson R, Beynon B. Gender differences in knee injury epidemiology among competitive alpine ski racers. *Iowa Orthop J*. 1998;18:64-66.
39. Stringham DR, Pelmas CJ, Burks RT, Newman AP, Marcus RL. Comparison of anterior cruciate ligament reconstructions using patellar tendon autograft or allograft. *Arthroscopy*. 1996;12(4):414-421.
40. Wright RW, Dunn WR, Amendola A, et al. Risk of tearing the intact anterior cruciate ligament in the contralateral knee and rupturing the anterior cruciate ligament graft during the first 2 years after anterior cruciate ligament reconstruction: a prospective MOON cohort study. *Am J Sports Med*. 2007;35(7):1131-1134.

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