

## Systematic Review

# Hamstring Autograft Versus Soft-Tissue Allograft in Anterior Cruciate Ligament Reconstruction: A Systematic Review and Meta-analysis of Randomized Controlled Trials

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**Purpose:** To compare outcomes of anterior cruciate ligament (ACL) reconstruction with hamstring autograft versus soft-tissue allograft by systematic review and meta-analysis. **Methods:** A systematic review of randomized controlled studies comparing hamstring autograft with soft-tissue allograft in ACL reconstruction was performed. Studies were identified by strict inclusion and exclusion criteria. Descriptive statistics were reported. Where possible, the data were pooled and a meta-analysis was performed using RevMan software (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark). Dichotomous data were reported as risk ratios, whereas continuous data were reported as standardized mean differences and 95% confidence intervals. Heterogeneity was assessed by use of  $I^2$  for each meta-analysis. Study methodologic quality was analyzed with the Modified Coleman Methodology Score and Jadad scale. **Results:** Five studies with 504 combined patients (251 autograft and 253 allograft; 374 male and 130 female patients) with a mean age of  $29.9 \pm 2.2$  years were included. The allografts used were fresh-frozen hamstring, irradiated hamstring, mixture of fresh-frozen and cryopreserved hamstring, fresh-frozen tibialis anterior, and fresh-frozen Achilles tendon grafts without bone blocks. The mean follow-up period was  $47.4 \pm 26.9$  months, with a mean follow-up rate of  $83.3\% \pm 8.6\%$ . Two studies found a longer operative time with autograft than with allograft ( $77.1 \pm 2.0$  minutes v  $59.9 \pm 0.9$  minutes,  $P = .008$ ). Meta-analysis showed no statistically significant differences between autografts and allografts for any outcome measures ( $P > .05$  for all tests). One study found significantly greater laxity for irradiated allograft than for autograft. The methodologic quality of the 5 studies was poor, with a mean Modified Coleman Methodology Score of  $54.4 \pm 6.9$  and mean Jadad score of  $1.6 \pm 1.5$ . **Conclusions:** On the basis of this systematic review and meta-analysis of 5 randomized controlled trials, there is no statistically significant difference in outcome between patients undergoing ACL reconstruction with hamstring autograft and those undergoing ACL reconstruction with soft-tissue allograft. These results may not extrapolate to younger patient populations. The methodology of the available randomized controlled trials comparing hamstring autograft and soft-tissue allograft is poor. **Level of Evidence:** Level II, systematic review of Level I and II studies.

Anterior cruciate ligament (ACL) tears are a common injury, with approximately 250,000 ACL tears occurring in the United States each year.<sup>1,2</sup> Surgical reconstruction of the ACL is considered the gold standard of treatment for active patients with ACL injury, with the goals of surgery being restoration of knee stability and prevention of further intra-articular

damage.<sup>3,4</sup> Graft options for ACL reconstruction include bone-patellar tendon-bone autograft, hamstring autograft, quadriceps autograft, and various allografts.<sup>5</sup> Hamstring autografts and bone-tendon-bone autografts generally have similar outcomes in the literature.<sup>6,7</sup> Some available evidence suggests that hamstring autografts may cause less donor-site

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morbidity and faster quadriceps recovery post-operatively compared with bone-tendon-bone autografts.<sup>6,7</sup> Some studies suggest that bone-tendon-bone grafts may have improved stability compared with hamstring grafts.<sup>6,7</sup>

Hamstring autograft harvest may still result in significant donor-site morbidity, including saphenous nerve damage and postoperative knee flexion weakness.<sup>8-11</sup> The use of allografts for ACL reconstruction is appealing in that allograft use avoids donor-site morbidity and may reduce operative time.<sup>5-7</sup> Because of these advantages, the use of allografts in ACL reconstruction has increased in recent years.<sup>12</sup> Possible disadvantages of allograft use are disease transmission, delayed graft incorporation, and graft laxity and failure with prolonged use.<sup>13</sup> Two systematic reviews recently found no significant difference between allograft and autograft for ACL reconstruction; however, the majority of articles reviewed addressed bone-tendon-bone grafts.<sup>14,15</sup> Only a few studies with a high level of evidence have compared hamstring autograft with soft-tissue allograft, and no systematic review on the topic has been published to date.<sup>16-19</sup>

The purpose of this systematic review and meta-analysis was to review the published literature to compare outcomes of ACL reconstruction with hamstring autograft versus soft-tissue allograft. The hypothesis was that there would be no statistically significant differences in clinical outcomes between patients undergoing ACL reconstruction with hamstring autograft and those undergoing ACL reconstruction soft-tissue allograft.

## Methods

### Search Strategy and Study Selection

A systematic review was conducted according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines using a PRISMA checklist.<sup>21</sup> Systematic review registration was performed using the PROSPERO international prospective register of systematic reviews.<sup>22</sup> Two reviewers (G.L.C., R.M.) independently conducted the search using the following databases: PubMed, Cochrane Central Register of Controlled Trials, and Embase. The electronic search citation algorithm used was as follows: (((((anterior cruciate ligament [Title/Abstract]) AND hamstring [Title/Abstract]) AND allograft [Title/Abstract]) AND autograft [Title/Abstract]) AND randomized [Title/Abstract]) AND (English[lang])).

Randomized controlled trials comparing hamstring autograft with soft-tissue allograft in ACL reconstruction with a minimum of 6 months' follow-up were included (Fig 1). Studies including bone-tendon-bone grafts were excluded. After the search results were obtained, studies were scrutinized for relevance by

use of strict inclusion and exclusion criteria. Medical conference abstracts were ineligible for inclusion. All references within included studies were cross-referenced for inclusion if missed by the initial search. Duplicate subject publications within separate unique studies were not reported twice. The study with the longer duration of follow-up, greater number of subjects, or more explicit reporting of rehabilitation was retained for inclusion. Case reports, retrospective studies, review articles, letters to the editor, basic science studies, biomechanical studies, imaging studies, surgical technique reports, and classification studies were excluded.

### Data Extraction and Analysis

Data were extracted from the included studies by 2 reviewers (G.L.C., R.M.) using data abstraction forms. All study, subject, and surgery parameters were collected. Study and subject demographic parameters analyzed included year of publication, years of subject enrollment, presence of study financial conflict of interest, number of subjects and knees, gender, age, diagnoses treated, operative time, graft type used, number of patients and knees available for follow-up, and surgical procedures performed. Clinical outcomes recorded included range of motion, loss of terminal extension, Lysholm score, anterior drawer test, Lachman test, pivot-shift test, KT arthrometer (MEDmetric, San Diego, CA) examination, and reoperation rate.

Study methodologic quality was analyzed with the Modified Coleman Methodology Score (MCMS) and Jadad scale.<sup>23,24</sup> The Jadad scale is a 3-question test evaluating study randomization, blinding, and withdrawals/dropouts, with scores ranging from a minimum of 0 to a maximum of 5. Jadad scores below 3 are generally considered to indicate studies of poor quality. The MCMS is a score based on 15 questions evaluating study methodology, with scores ranging from a minimum of 0 to a maximum of 100. The MCMSs of excellent studies range from 85 to 100; good studies, from 70 to 84; fair studies, from 55 to 69; and poor studies, under 55.

### Statistical Analysis

Study descriptive statistics were calculated. Continuous variable data were reported as mean  $\pm$  standard deviation from the mean. Categorical variable data were reported as frequency with the percentage. Significance was set at  $P < .05$ . When possible, the data were pooled and a meta-analysis was performed with RevMan software.<sup>25</sup> Dichotomous data were reported as risk ratio (RRs) using a random-effects model, whereas continuous data were reported as standardized mean differences and 95% confidence intervals (CIs). When possible, the outcomes were dichotomized into good and poor results. Heterogeneity was assessed using  $I^2$  for each meta-analysis.

An  $I^2$  of less than 60% was the cutoff for homogeneity of the data, justifying pooling.

## Results

### Characteristics of Included Studies

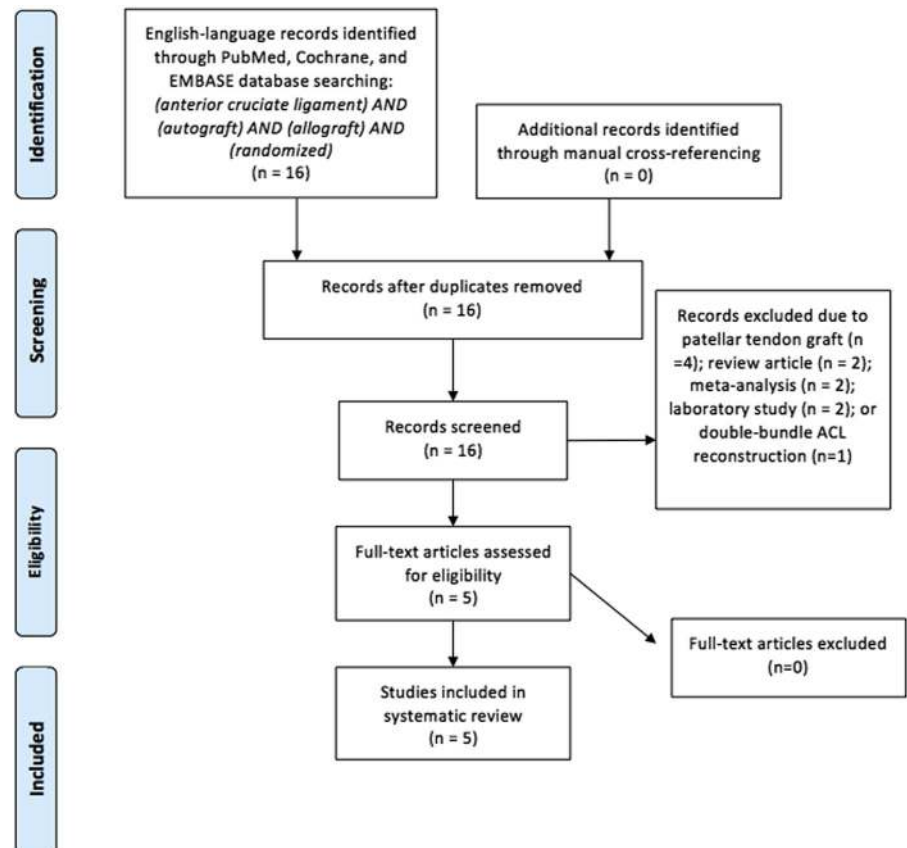
Five studies with 504 combined patients (251 autograft and 253 allograft; 374 male and 130 female patients) with a mean age of  $29.9 \pm 2.2$  years were included in the analysis. Figure 1 shows the search strategy and results. All studies randomized patients to ACL reconstruction using hamstring autograft or soft-tissue allograft and had at least 2 years' follow-up. The allografts for the studies were fresh-frozen hamstring, irradiated hamstring, mixture of fresh-frozen and cryopreserved hamstring, fresh-frozen tibialis anterior, and fresh-frozen Achilles tendon grafts without bone blocks. Each of the 5 included studies used the same fixation method for both the autograft and allograft groups, although the fixation methods differed among studies. Femoral fixation was obtained with an EndoButton (Smith & Nephew Endoscopy, Andover, MA) in 3 studies, an EndoButton with a bioabsorbable interference screw in 1 study, and a cross-pin in 1 study. Tibial fixation was achieved with a bioabsorbable interference screw with a screw and

spiked washer in 2 studies, a bioabsorbable interference screw with a staple in 2 studies, and an Intrafix device (DePuy Mitek, Raynham, MA) in 1 study. The variety of fixation methods used made meta-analysis of this variable not possible. The mean follow-up period was  $47.4 \pm 26.9$  months, with a mean follow-up rate of  $83.3\% \pm 8.6\%$ . Table 1 shows the characteristics of the included studies.

### Meta-analysis of Clinical Outcomes

Two studies found a significantly longer operative time for autograft than for allograft (mean,  $77.1 \pm 2.0$  minutes *v*  $59.9 \pm 0.9$  minutes;  $P = .008$ ). Meta-analysis showed that there were no statistically significant differences between autografts and allografts for any of the selected outcome measures including Lysholm score (RR,  $-0.07$ ; 95% CI, 0.28 to 0.15;  $P = .53$ ), Tegner score (RR, 0.11; 95% CI,  $-0.15$  to 0.36;  $P = .40$ ), and International Knee Documentation Committee grade (RR, 1.01; 95% CI, 0.96 to 1.05;  $P = .8$ ) (Fig 2). There were 7 reoperations in the autograft group versus 6 in the allograft group, which was not a significant difference (RR, 1.14; 95% CI, 0.40 to 3.25;  $P = .81$ ). Subsequent revision ACL reconstruction was required due to failure of the graft in 3 cases in the autograft group and 2 cases in the allograft group. There were 2 cases of

**Fig 1.** Search strategy and search results.



**Table 1.** Characteristics of Included Studies

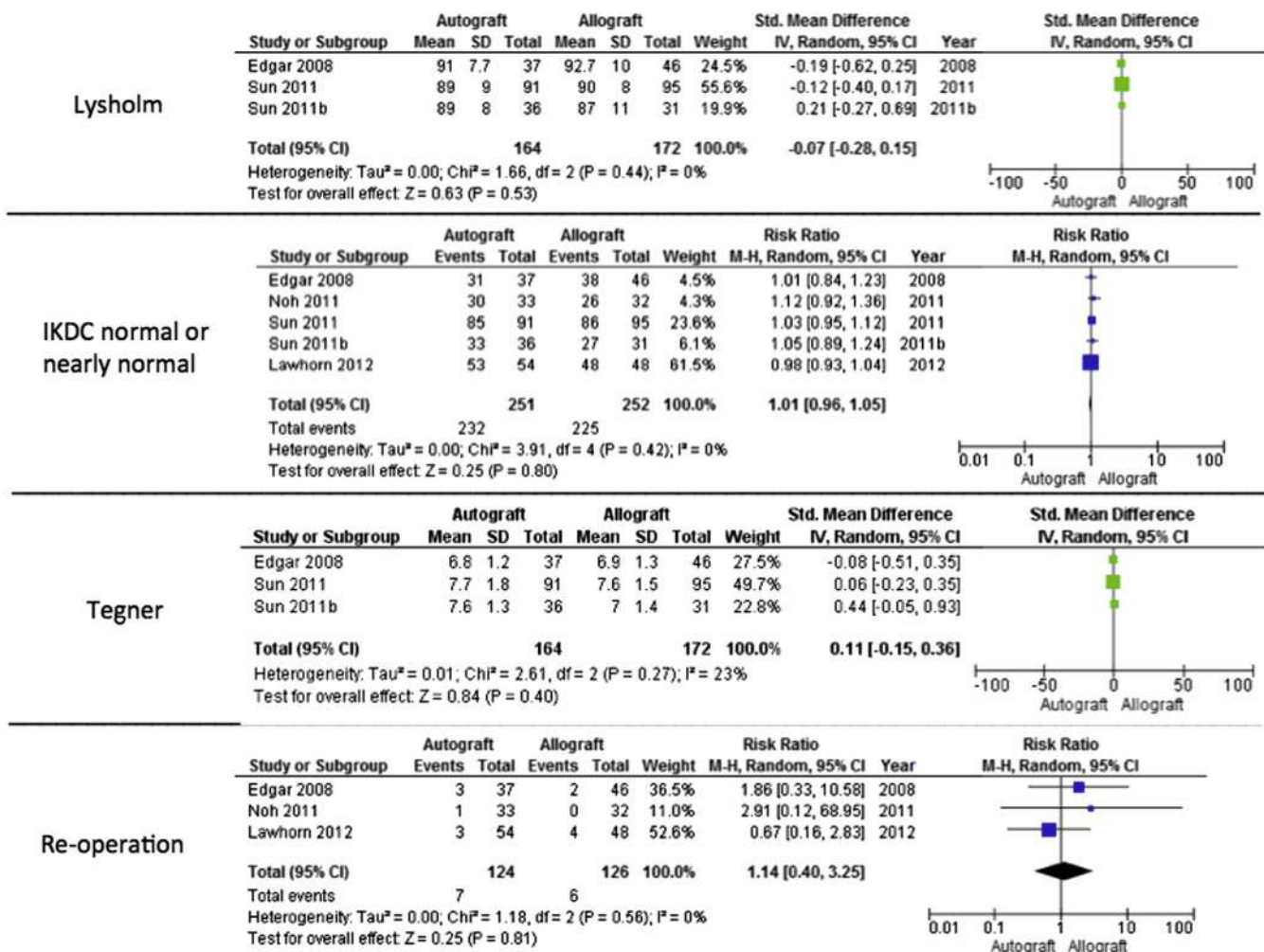
Study	Study Design	Inclusion/Exclusion Criteria*	Allograft Used <sup>†</sup>	Sample Size (% Male)	Mean Age (yr)	Follow-up		Outcome Measures	Statistically Significant Difference for Autograft v Allograft
						%	Length (mo)		
Edgar et al., <sup>16</sup> 2008	Level II, partially randomized	Meniscal tear requiring repair or debridement included; cartilage surgery excluded	Hamstring: 20 cryopreserved, 27 fresh frozen	84 (54.8)	29.0	80.8	50.0	KT-1000, Lysholm, IKDC, Tegner	None
Lawhorn et al., <sup>17</sup> 2012	Level II, randomized	Meniscal tear included; cartilage injury requiring surgery excluded	Tibialis anterior, fresh frozen	102 (68.6)	32.7	69.4	24.0	KT-1000, IKDC, pivot shift	None
Noh et al., <sup>18</sup> 2011	Level I, randomized	Only meniscal tear requiring partial meniscectomy included; cartilage damage requiring surgical management and meniscal tear requiring repair excluded	Achilles, fresh frozen	65 (86.2)	23	87.8	29.9	KT-1000, Lysholm, IKDC, Tegner, pivot shift, Lachman	None
Sun et al., <sup>19</sup> 2011	Level II, randomized	Meniscal tear requiring repair or debridement included; cartilage damage treated with debridement included	Hamstring, fresh frozen	186 (80.1)	30.4	89.4	93.0	Operative time, KT-1000, Lysholm, IKDC, Tegner, pivot shift, Lachman, anterior drawer	Autograft operative time longer than allograft
Sun et al., <sup>20</sup> 2011	Level II, randomized	Meniscal tear requiring repair or debridement included; cartilage damage treated with debridement included	Hamstring, irradiated	67 (77.6%)	30.6	89.3	42.3	Operative time, KT-1000, Lysholm, IKDC, Tegner, pivot shift, Lachman, anterior drawer	Greater laxity on clinical examination and KT-1000 testing for irradiated allograft; autograft operative time longer than allograft

IKDC, International Knee Documentation Committee.

\*All studies included only primary ACL tear without other ligament injury requiring surgery, with injured knee not having prior surgery and contralateral knee not requiring ACL reconstruction.

<sup>†</sup>All studies used hamstring autografts.





**Fig 2.** Results of meta-analysis of outcomes between hamstring autograft and soft-tissue allograft for Lysholm score, Tegner score, normal or nearly normal International Knee Documentation Committee (IKDC) grade, and reoperations. No significant difference was identified. (IV, inverse variance; M-H, Mantel-Haenszel.)

arthrofibrosis in the autograft group compared with 1 in the allograft group. There was 1 case of symptomatic hardware leading to hardware removal in the autograft group versus 2 in the allograft group. There was 1 reoperation for meniscectomy in each group. None of the included studies reported any cases of deep infection, nerve injury, deep venous thrombosis, or failure of fixation.

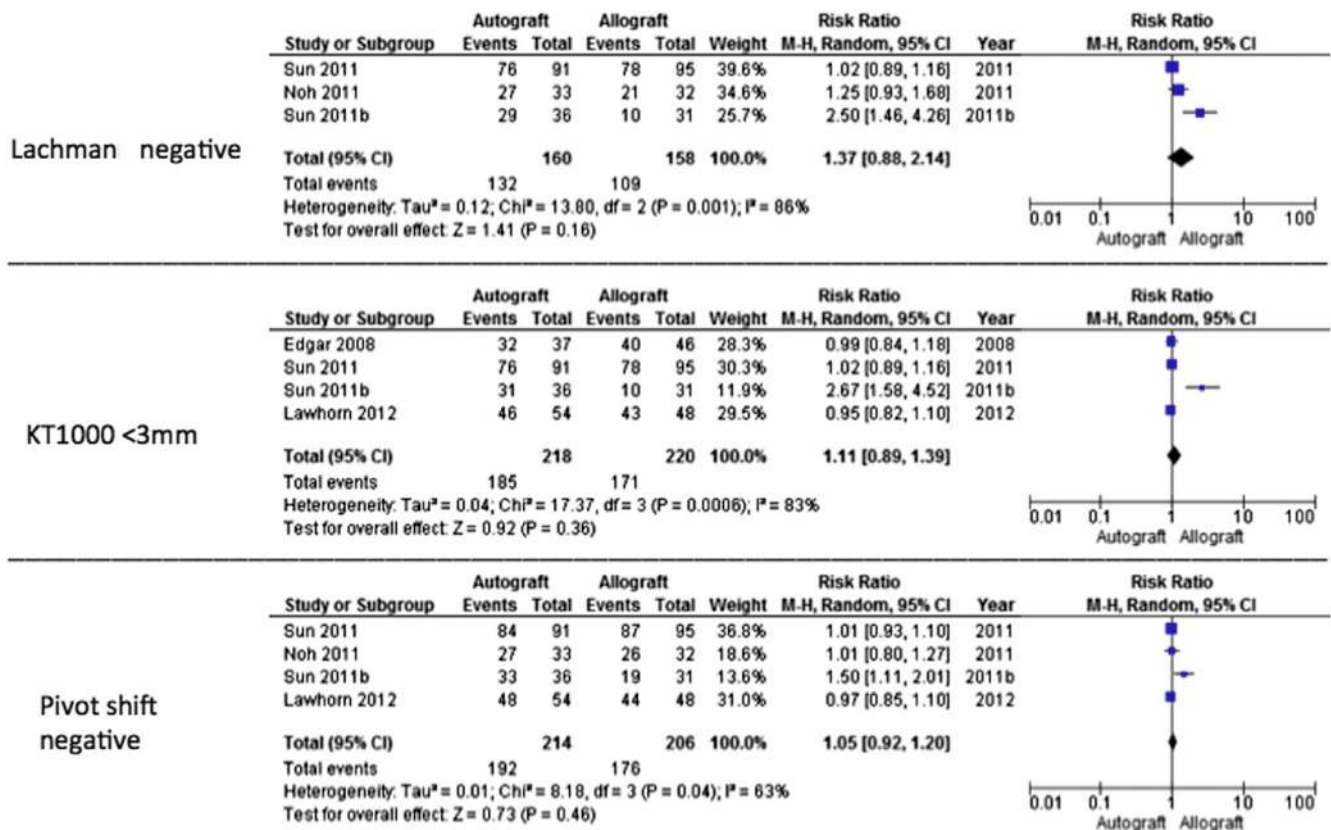
### Meta-analysis of ACL Laxity

Meta-analysis showed no significant differences between hamstring allograft and soft-tissue autograft for the Lachman test (RR, 1.37; 95% CI, 0.88 to 2.14;  $P = .16$ ), pivot-shift test (RR, 1.05; 95% CI, 0.92 to 1.20;  $P = .46$ ), and KT arthrometer testing (RR, 1.11; 95% CI, 0.89 to 1.39;  $P = .36$ ). Meta-analysis of these parameters showed high or substantial heterogeneity (Fig 3). After a retrospective assessment of heterogeneity, the study by Sun et al.<sup>20</sup> was identified as different from the other

studies; this study was the only study to use irradiated allograft and individually showed greater laxity for the irradiated soft-tissue allograft compared with hamstring autograft. Exclusion of this study removed the statistical heterogeneity but did not affect the results of meta-analysis, which again showed no significant difference between autograft and allograft ( $P > .05$  for all tests).

### Study Quality

The methodologic quality of the 5 studies was poor, with a mean MCMS of  $54.4 \pm 6.9$  and mean Jadad score of  $1.6 \pm 1.5$ . One study did not report whether a conflict of interest was present, 3 studies indicated that there was no conflict of interest to disclose, and 1 study disclosed a conflict of interest. One study was Level I, and 4 studies were Level II. Four studies were single-center studies, and one study was a multicenter study. Patients were not blinded in any of the studies, and outcome observers were blinded in 1 study.



**Fig 3.** Results of meta-analysis of ACL laxity between hamstring autograft and soft-tissue allograft for Lachman test, pivot-shift test, and KT-1000 assessment (<3 mm difference in laxity compared with contralateral [normal] knee). No significant difference was identified, although the study of irradiated allograft showed increased laxity by all metrics. (M-H, Mantel-Haenszel.)

## Discussion

This review and meta-analysis showed no statistically significant differences in clinical outcome measures, measures of ACL laxity, and reoperations in patients undergoing ACL reconstruction with hamstring autograft versus soft-tissue allograft.

Surgeons must work in an individualized fashion with patients to determine the optimal graft selection for ACL reconstruction, considering factors including patient age and activity level, patient goals and preference, surgeon experience, and prior surgery.<sup>5</sup> Hamstring autografts offer the advantage of less donor-site morbidity and faster quadriceps recovery after surgery compared with bone-tendon-bone autografts but may result in donor-site morbidity such as knee flexion weakness and saphenous nerve damage.<sup>6-11</sup> Soft-tissue allografts offer the advantage of a lack of donor-site morbidity and may also reduce operative time.<sup>5-7</sup> Potential disadvantages of allografts are rare risk of disease transmission, higher rates of graft laxity and failure, and delay in graft incorporation.<sup>5-7,13</sup>

Quoted rates for failure and reoperation after ACL reconstruction from the literature vary, with many studies reporting higher rates of failure for allograft than autograft. For instance, Prodromos et al.<sup>26</sup>

performed a meta-analysis and reported a 5% failure rate for autografts compared with 14% for allografts. Kaeding et al.<sup>27</sup> reported a 3.5% failure rate for autograft versus 8.9% for allograft in their cohort. Recent studies have shown that younger patients undergoing ACL allograft reconstruction have increased rates of graft failure.<sup>27,28</sup> The mean patient ages for the studies comprising this meta-analysis approached 30 years, with a mean age for the meta-analysis of  $29.9 \pm 2.2$  years. Thus the currently available Level I and II studies comparing ACL reconstruction with hamstring autograft versus soft-tissue allograft have been performed in an older and presumably less active patient population than the nonrandomized studies. The low rates of complications and graft failure in our meta-analysis may result from the fact that randomized studies to date have not evaluated this younger patient population at the highest risk of graft failure. Indeed, similar to our low rates of graft failure, a meta-analysis of all non-irradiated allografts versus all autografts (including bone-tendon-bone and soft tissue) found rates of failure of 3% to 6% in the autograft group and 2.4% to 5.5% in the allograft group.<sup>15</sup> Furthermore, the follow-up time for the included studies in our meta-analysis was an average of 47.4 months, which may underestimate

the long-term rates of graft failure and repeat surgery. Further high-level studies would be needed to determine the outcomes of ACL reconstruction with hamstring autograft compared with soft-tissue allograft in patients in their late teens and early 20s.

To our knowledge, the topic of hamstring autograft versus soft-tissue allograft has not been addressed in any prior review and meta-analysis. Carey et al.<sup>14</sup> conducted a systematic review comparing autograft versus allograft for ACL reconstruction and similarly found no difference in clinical outcomes. Carey et al. included 9 studies: 8 comparing bone-tendon-bone grafts and 1 comparing hamstring autograft with hamstring allograft.<sup>16</sup> In another recent systematic review, Mariscalco et al.<sup>15</sup> compared autograft versus allograft for ACL reconstruction and found no difference in clinical outcomes. Mariscalco et al. included 9 studies, 6 of which compared bone-tendon-bone grafts, and excluded irradiated allografts from the analysis. The strength of these prior systematic reviews lies in their inclusion of all autografts and allografts and their resultant larger patient numbers. However, the combination of soft-tissue grafts and bone-tendon-bone grafts in these studies could introduce heterogeneity and conceal a difference between autograft and allograft that might only be present between specific graft sources. Our review, by comparison, seeks to address differences specifically in hamstring autograft versus soft-tissue allograft. These have not been previously addressed by a systematic review.

Of the studies included in our systematic review, 2 found an increased operative time for autograft versus allograft.<sup>19,20</sup> The increased operative time for these 2 studies was statistically significant (mean of 77.1 minutes *v* 59.9 minutes). Theoretically, a shorter operative time could lead to a decreased rate of perioperative complications after ACL reconstruction, but this was not observed in these studies. Therefore the clinical significance of this finding is unclear and must be weighed along with the other advantages and disadvantages of allografts and autografts. There is an increased operating room cost with autograft because of the harvest time, whereas allograft also incurs extra costs because of the price of tissue.

Sun et al.<sup>20</sup> found significantly increased post-operative laxity for irradiated hamstring allograft compared with hamstring autograft, as determined by Lachman, pivot-shift, and KT-1000 testing. Of note, they also observed no significant difference in post-operative clinical outcome scores despite the differences in laxity. The proposed advantage of using irradiated allograft is a decrease in disease transmission risk, but both basic science research and biomechanical research show that allograft irradiation decreases the biomechanical properties of the graft in a dose-dependent fashion.<sup>29,30</sup> By contrast, a recent study of low-dose

(1.0- to 1.2-Mrad) gamma irradiation of bone-tendon-bone grafts showed decreased graft stiffness by 20% without any change in biomechanical properties.<sup>31</sup> Clinical studies have yielded mixed results regarding whether irradiation of allografts leads to higher rates of graft failure. Rappe et al.<sup>32</sup> found a 33% failure rate for irradiated allografts versus 2.4% for non-irradiated allografts. Conversely, Rihn et al.<sup>33</sup> found no adverse effect of irradiation on clinical outcome in ACL reconstruction with allograft.

## Limitations

The nature of our study design resulted in analysis of relatively few studies (5 studies) with relatively few patients (504 patients) and of low quality as evidenced by low MCMSs and Jadad scores. As a result, the lack of significant outcome score differences between soft-tissue autograft and allograft could represent a  $\beta$  error due to the small sample size. Larger studies would be required to further define more subtle differences in these outcomes. However, these limitations reflect the underlying limitations of the available literature and the inherent limitations of conducting randomized trials on a surgical topic because all included studies were Levels I and II, making the level of analyzed data the highest available on the subject. Another limitation lies in the fact that the allograft type differed in each study, such that our meta-analysis would be unable to detect a difference between autograft and allograft if such a difference depended on the type of allograft used. The patients in the included studies had a mean age of 29.9 years, rendering us unable to extrapolate the results to a younger, more active patient population at the highest risk of graft failure. There were also differences in the inclusion and exclusion criteria among the studies, particularly regarding the allowance of patients with coexistent meniscal and/or cartilage surgery to address injuries sustained concomitantly at the time of ACL injury. This could potentially lead to different outcomes among studies, although no significant differences were observed. In addition, there were differences in the gender characteristics of the studies, with some studies treating more male patients and others having a more even gender ratio. Finally, the duration of final follow-up was substantially different among the studies, ranging from 24 to 93 months, which could obscure the reporting of differences between hamstring autografts and soft-tissue allografts.

## Conclusions

On the basis of this systematic review and meta-analysis of 5 randomized controlled trials, there is no statistically significant difference in outcome between patients undergoing ACL reconstruction with hamstring autograft and those undergoing ACL reconstruction with soft-tissue allograft. These results may



not extrapolate to younger patient populations. The methodology of the available randomized controlled trials comparing hamstring autograft and soft-tissue allograft is poor.

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