

Hamstring Autograft versus Patellar Tendon Autograft for ACL Reconstruction: Is There a Difference in Graft Failure Rate? A Meta-analysis of 47,613 Patients

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Abstract

Background Bone-patellar tendon-bone (bone-tendon-bone) and four-strand hamstring tendon grafts (hamstring) are the most commonly utilized autografts for primary anterior cruciate ligament (ACL) reconstruction. Existing clinical trials, registry studies, and meta-analyses offer conflicting opinions regarding the most favorable graft choice.

Questions/purposes Which graft type for ACL reconstruction (bone-tendon-bone or hamstring) has a higher risk of (1) graft rupture and/or (2) graft laxity?

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This work was performed at the Mayo Clinic, Rochester, Rochester, MN, USA; and the School of Allied Health, La Trobe University, Melbourne, Australia.

Methods We performed a meta-analysis of randomized controlled trials (RCTs), prospective cohort studies, and high-quality national registry studies to compare the outcomes of primary ACL reconstruction with bone-tendon-bone autograft or hamstring autograft. Studies that compared these graft types were identified through a comprehensive search of electronic databases (PubMed, MEDLINE, EMBASE, and the Cochrane Library). Two independent reviewers utilized the Jadad scale for RCT study quality and the Modified Coleman Methodology Score for prospective comparative and registry study quality. The included studies were analyzed for the primary outcome measure of graft rupture with or without revision ACL surgery. In surviving grafts, secondary outcomes of graft laxity were quantified by KT1000/2000™ testing, a positive pivot shift test, and a positive Lachman test. Meta-analysis was performed with Review Manager. A total of 47,613 ACL reconstructions (39,768 bone-tendon-bone and 7845 hamstring) from 14 RCTs, 10 prospective comparative studies, and one high-quality national registry study were included in this meta-analysis. Mean age was

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28 years in both groups. Sixty-three percent of patients in the bone-tendon-bone cohort were men versus 57% of patients in the hamstring cohort. Mean followup was 68 ± 55 months.

Results Two hundred twelve of 7560 (2.80%) bone-tendon-bone grafts ruptured compared with 1123 of 39,510 (2.84%) in the hamstring group (odds ratio = 0.83, 95% confidence interval, 0.72-0.96; $p = 0.01$). The number needed to treat analysis found that 235 patients would need to be treated with a bone-tendon-bone graft over a hamstring tendon graft to prevent one graft rupture. Instrumented laxity analysis showed that 22% (318 of 1433) of patients in the bone-tendon-bone group had laxity compared with 18% (869 of 4783) in the hamstring tendon group (odds ratio = 0.86; $p = 0.16$). Pivot shift analysis showed a positive pivot shift in 19% (291 of 1508) of the bone-tendon-bone group compared with 17% (844 of 5062) in the hamstring group (odds ratio = 0.89; $p = 0.51$). Lachman testing showed a positive Lachman in 25% (71 of 280) of patients receiving bone-tendon-bone grafts compared with 25% (73 of 288) in the hamstring group (odds ratio = 0.96; $p = 0.84$).

Conclusions In this meta-analysis of short- to mid-term followup after primary ACL reconstruction, hamstring autografts failed at a higher rate than bone-tendon-bone autografts. However, failure rates were low in each group, the difference observed was small, and we observed few differences between graft types in terms of laxity. Both graft types remain viable options for primary ACL reconstruction, and the difference in failure rate should be one part of a larger conversation with each individual patient about graft selection that should also include potential differences in donor site morbidity, complication rates, and patient-reported outcome measures. Continued prospective collection of patient data will be important going forward as we attempt to further characterize the potential differences in outcomes attributable to graft selection.

Level of Evidence Level III, therapeutic study.

Introduction

Anterior cruciate ligament (ACL) rupture is a devastating injury that can lead to recurrent instability, chronic pain, and degenerative changes in the knee [5–8, 42]. Arthroscopic reconstruction is the standard approach, but controversy remains over the most favorable graft selection. The most commonly utilized autografts for ACL reconstruction in the United States are the bone-patellar tendon-bone (bone-tendon-bone) and the four-strand hamstring tendon (hamstring) [13, 43]. Some authors suggest that bone-tendon-bone autograft is the most favorable graft

choice because of faster graft incorporation [33], a higher proportion of patients returning to preinjury activity levels [47], and potentially a lower risk of graft rupture [32]. However, others favor hamstring autografts because of lower donor site morbidity, anterior knee pain, extensor strength deficit, and osteoarthritis [11, 27, 32, 39, 42].

Although controversy remains on specific advantages and disadvantages, clearly the most significant adverse outcome after ACL reconstruction is graft rupture and subsequent revision surgery. There have been a number of prospective studies that compared bone-tendon-bone and hamstring that demonstrated similar risk of rupture between the two graft types [2, 4, 21, 30, 38, 40, 41, 46]. A 2014 meta-analysis by Xie et al. [47] effectively summarized the literature before 2013 with roughly 1000 patients in each group and found no difference in the risk of graft rupture.

In subsequent years, there have been multiple prospective studies published on this topic [3, 13, 34, 35]. The most notable has been data on greater than 40,000 patients from Scandinavian ACL registries, in which researchers identified a higher risk of rupture/revision for patients receiving hamstring than those receiving bone-tendon-bone [15]. This finding directly contradicts what was reported by Xie et al. in their 2014 meta-analysis [47] and thus raises new questions about failure rate after ACL reconstruction. It remains unclear whether there is an inherent difference in graft type that prior studies have been underpowered to detect or whether the difference found by Gifstad et al. [13] is a uniquely Scandinavian phenomenon that is not generalizable to the orthopaedic community at large.

The goal of this study was to perform an up-to-date meta-analysis, incorporating high-quality evidence from randomized controlled trials (RCTs), prospective comparative studies, and national registries in an attempt to address the aforementioned questions. Specifically, we asked which approach to ACL reconstruction (bone-tendon-bone or hamstring) has a higher risk of (1) graft rupture and/or (2) graft laxity?

Materials and Methods

This study considered for inclusion RCTs, prospective comparative studies, and large national registries with prospective data collection comparing bone-tendon-bone autograft and hamstring autograft in primary ACL reconstruction (Table 1).

Inclusion criteria were minimum 2-year followup, documentation of graft failure rate (graft rupture or revision ACL reconstruction), and/or documentation of measures of graft laxity in the form of instrumented laxity (KT1000/2000™; MEDmetric Corp, San Diego, CA, USA), pivot

Table 1. Summary of included studies

Study	Year of publication	Study design	Number of patients	BPTB male	BPTB female	4SHT male	4SHT female	BPTB age (years)	4SHT age (years)	Followup (months)	Lost to followup	Mean MCMS	Median Jadad
Marder et al. [30]	1991	PCS	80	24	13	26	9	22	24	29	8	73	
Aglietti et al. [1]	1994	PCS	60	N/A	N/A	N/A	N/A	N/A	N/A	28	3	73	
Shaieb et al. [38]	2002	RCT	82	26	7	21	16	32	30	33	12	78	3
Aglietti et al. [2]	2004	RCT	120	46	14	46	14	25	25	24	0	78	3
Ibrahim et al. [22]	2005	PCS	110	40	0	45	0	22	22	81	25	76	
Laxdal et al. [25]	2005	RCT	79	29	11	28	11	28	26	26	0	84	3
Wagner et al. [44]	2005	PCS	110	40	15	40	15	34	31	24	0	82	
Harilainen et al. [16]	2006	RCT	99	N/A	N/A	N/A	N/A	N/A	N/A	60	16	78	3
Zaffagnini et al. [48]	2006	RCT	50	16	9	15	10	31	31	60	0	78	3
Svensson et al. [40]	2006	PCS	61	0	28	0	31	28	25	26	2	79	
Maletis et al. [28]	2007	RCT	99	31	15	44	7	27	28	24	2	78	3
Taylor et al. [41]	2009	RCT	64	N/A	N/A	N/A	N/A	22	22	34	11	77	3
Barenius et al. [4]	2010	RCT	164	40	38	51	24	33	35	100	11	80	4
Holm et al. [21]	2010	RCT	72	18	10	15	14	25	27	120	15	85	3
Sadoghi et al. [36]	2011	PCS	92	N/A	N/A	N/A	N/A	30	29	24	0	83	
Wipfler et al. [46]	2011	RCT	62	18	11	15	10	40	34	105	8	77	3
Sajovic et al. [37]	2011	RCT	64	N/A	N/A	N/A	N/A	27	25	132	2	84	3.5
Gifstad et al. [14]	2013	RCT	114	N/A	N/A	N/A	N/A	27	27	84	12	76	3
Rahr-Wagner et al. [35]	2014	PCS										70	
Gifstad et al. [13]	2014	PCS	45,402	4239	2497	22,132	16,534	N/A	N/A	36	0	68	
Leitgeb et al. [26]	2014	PCS	96	45	11	23	17	28	29		0	82	
Mohtadi et al. [31]	2015	RCT	220	N/A	N/A	N/A	N/A	29	29	39	14	79	5
Hejine et al. [19]	2015	PCS	68	22	12	14	20	29	30	62	0	81	
Webster et al. [45]	2016	RCT	65	16	6	20	5	27	26	180	18	84	5
Thompson et al. [42]	2016	PCS	180	N/A	N/A	N/A	N/A	25	24	240	28	87	
Totals			47,613	4650	2697	22,535	16,737	28	28	68		79	3

BPTB = bone-patellar tendon-bone; 4SHT = four-strand hamstring tendon; MCMS = Modified Coleman Methodology Score; PCS = prospective cohort study; RCT = randomized controlled trial; N/A = not available.

shift test, or Lachman test among surviving grafts. Exclusion criteria for studies included case reports, single-center retrospective comparative studies, narrative reviews, or image reviews. Studies were not excluded based on patient demographics or surgical technique. When articles that reported on the same patient group were identified, the most recent data were utilized.

Search Strategy

Search engines utilized were PubMed, Cochrane Library, MEDLINE, and EMBASE. All articles that were not in English were excluded. Further studies were found utilizing the reference lists of the studies initially identified. Search terms included “ACL” or “anterior cruciate ligament” in combination with “hamstring autograft” or “semitendinosus” and “bone tendon bone autograft” or “patellar tendon”.

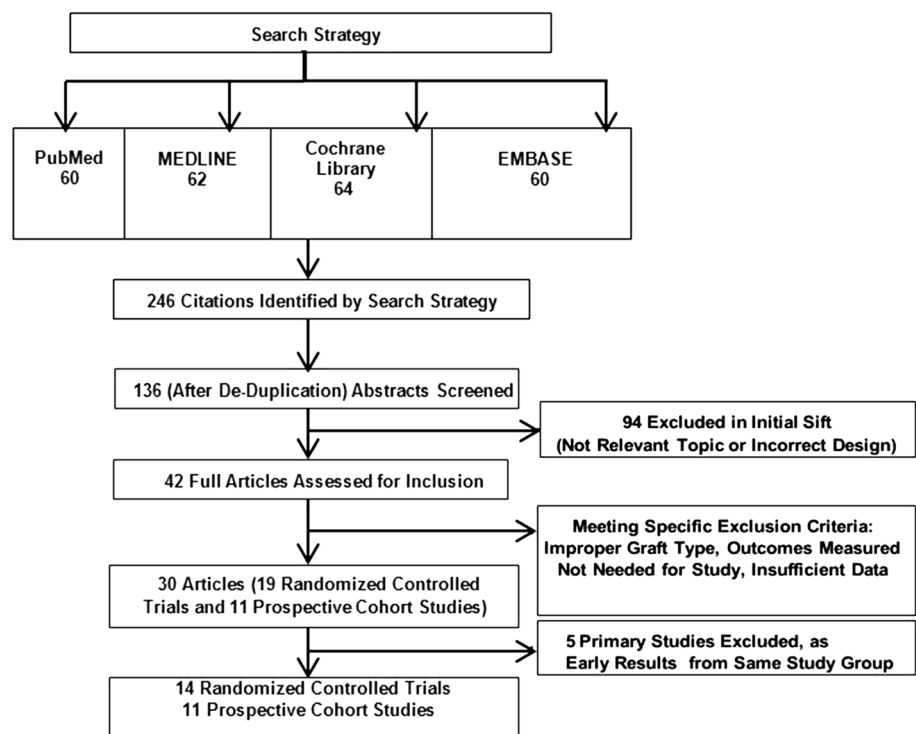
After duplicates were removed, 136 abstracts were screened. The titles and abstracts of all records retrieved by the search were assessed independently by two authors (BTS, NRJ). Any disagreements were resolved by discussion and arbitration by the three senior authors (KEW, TEH, AJK). After initial screening of these abstracts, two authors (BTS, NRJ) assessed the remaining full-text articles for inclusion in the study (Fig. 1).

Studies meeting inclusion criteria were assessed for quality by one of two methods. RCTs were assessed using

the Jadad scale [23], whereas prospective comparative studies and registries were assessed using the Modified Coleman Methodology Scores (MCMS) (range, 0–90) [9]. Interrater reliability was assessed with the Pearson correlation coefficient. Values of correlation range from +1 (perfect positive correlation) to -1 (perfect negative correlation) with a value greater than +0.7 considered a strong positive correlation. This method has been utilized in the past to assess the validity of interrater reliability when using the MCMS in assessing the quality of articles reviewed [18]. The mean MCMS score of the included studies was 79 ± 5 and the median Jadad for the RCTs included was 3 (range, 3–5) (Table 1). Blinded review of the selected articles was conducted to ensure interrater reliability, and a correlation coefficient of 0.79 was found for MCMS scores and 0.89 for Jadad scores. The majority of studies lost points from their MCMS scores as a result of incomplete followup and the study investigators being the surgeons who performed the operations.

Two authors (BTS, NRJ) independently extracted data from each included study. Any discrepancies were resolved by a third author (KEW). Patient demographics were extracted from each study as well as the number of patients in each study group (bone-tendon-bone versus hamstring). Specific outcomes measured were failure rates (defined as graft rupture or revision ACL reconstruction) in addition to instrumented laxity (positive defined as ≥ 3 mm), pivot shift (positive defined as 1+ or greater), and Lachman test (positive defined as 1+ or greater) in surviving grafts.

Fig. 1 PRISMA diagram shows how the final studies included were obtained. Overall, there were 14 RCTs, 10 prospective cohort studies, and one national registry study.



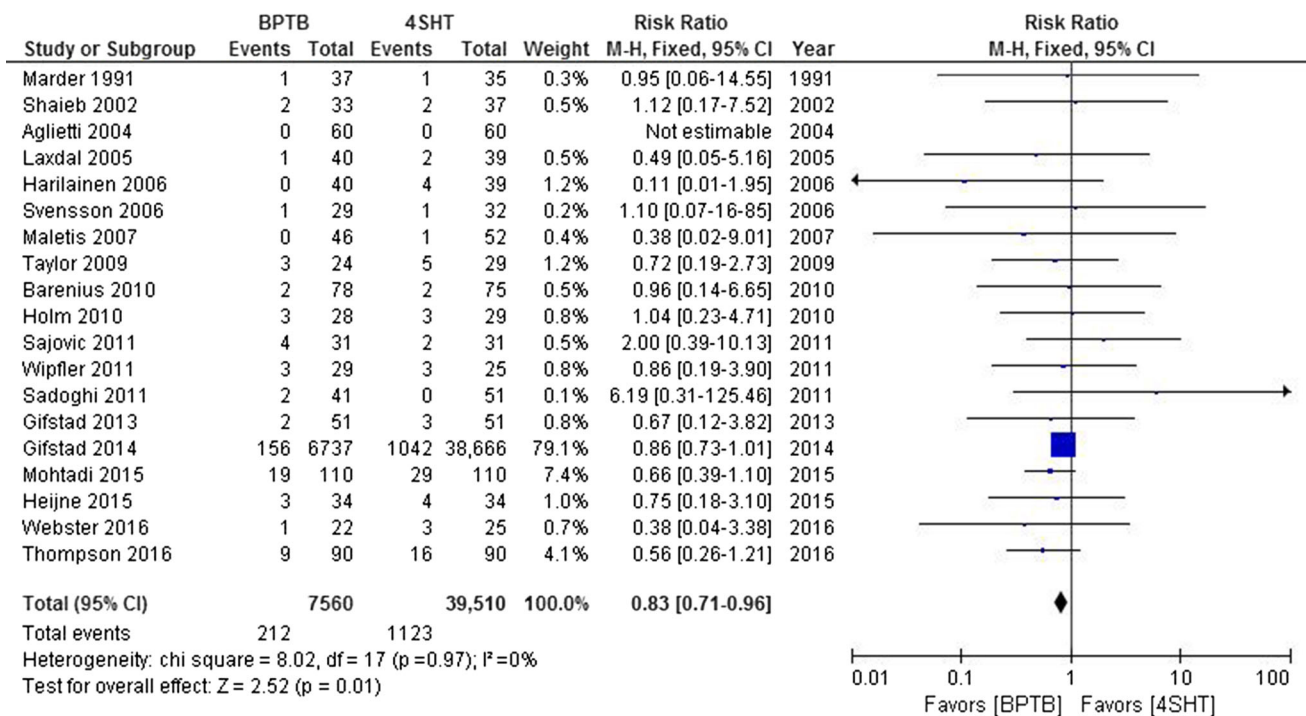


Fig. 2 Analysis of failure rate between the studies is demonstrated. OR for graft failure was 0.83 favoring bone-tendon-bone (95% CI, 0.72-0.96; $p = 0.01$). BPTB = bone-patellar-tendon bone; 4SHT = four-stranded hamstring tendon; M-H = Mantel-Haenszel.

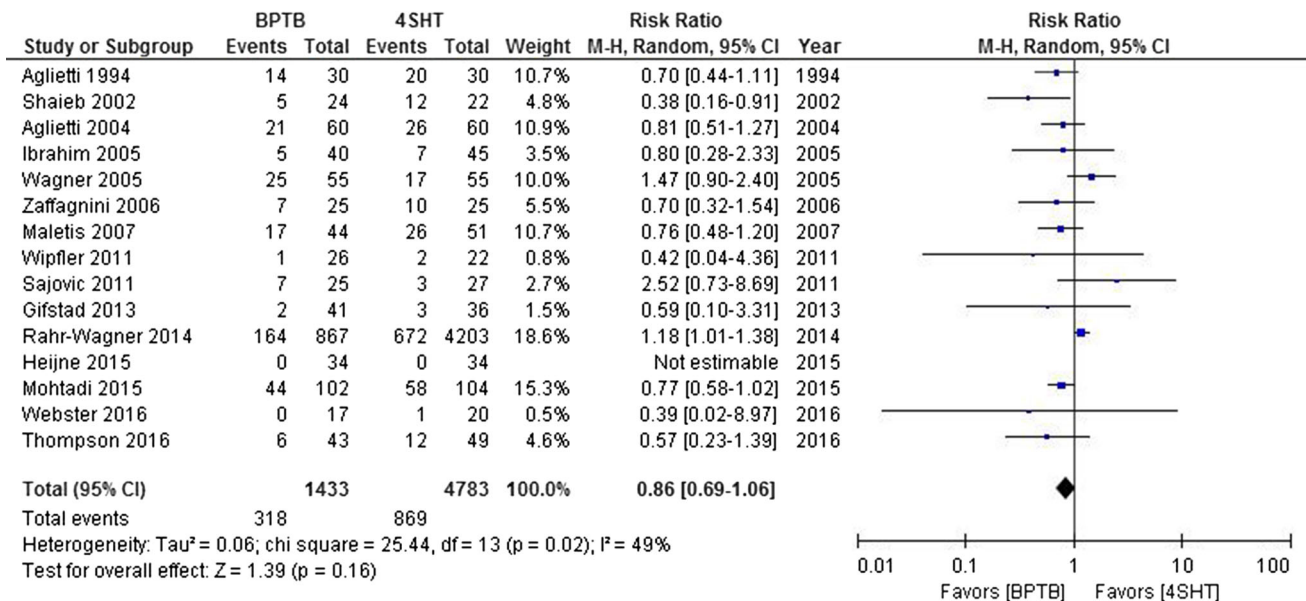


Fig. 3 Instrumented laxity was measured by KT1000/2000TM. Positive test equals ≥ 3 -mm side-to-side difference. No major difference was observed between either group in the study.

Outcomes Measured

There were 47,613 patients from 14 RCTs, 10 prospective comparative studies, and one national registry included in

the meta-analysis (Table 1). Mean age for patients who underwent ACL reconstruction with bone-tendon-bone was 28 ± 3 years versus 28 ± 4 years for those who received hamstring autografts. Sixty-three percent of patients in the

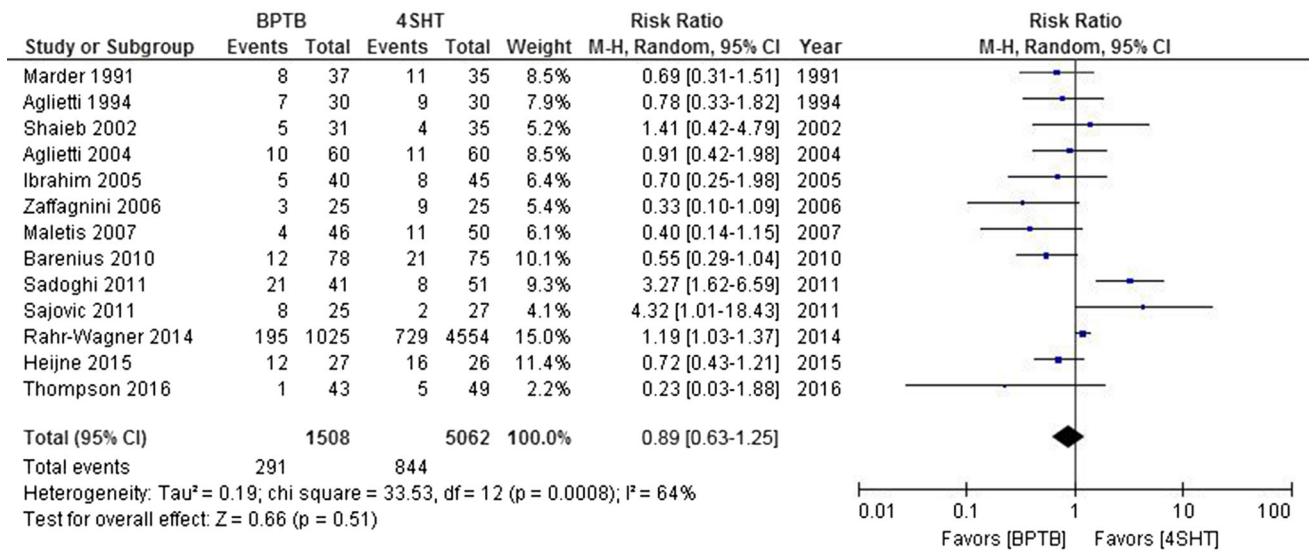


Fig. 4 Pivot shift analysis between the studies is shown. No major difference was observed between either group in terms of the study.

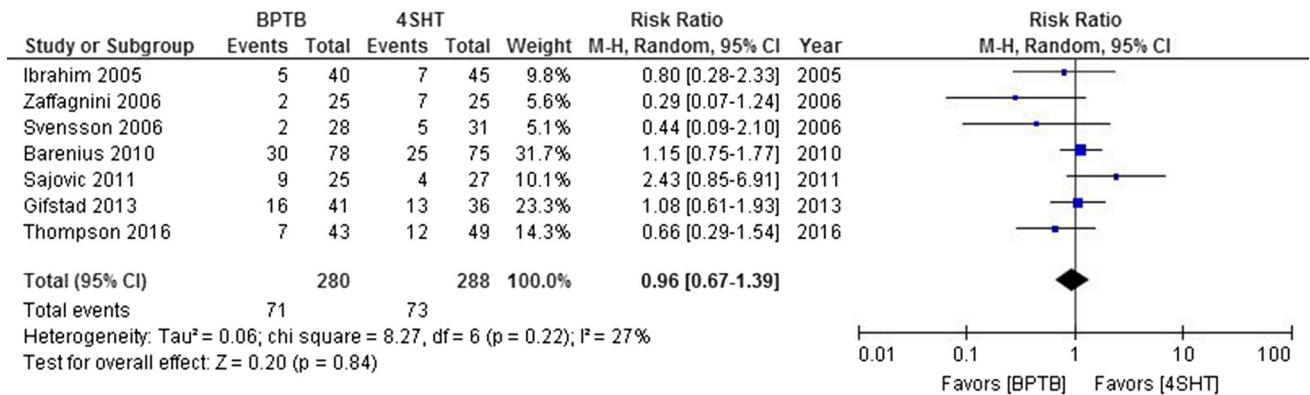


Fig. 5 Lachman testing analysis between the studies is shown. No major difference was observed between either group in terms in the study.

Table 2. Subgroup analysis

Outcome measure	Type of study	Number of studies	Number of patients	Test for heterogeneity (p value)	Statistical model	Risk ratio (95% CI)	p value
Failure rate	RCT	13	1194	0.91	Fixed	0.72 (0.51–1.02)	0.06
	PCS	6	45,876	0.72	Fixed	0.85 (0.73–1.0)	0.05
Instrumented laxity	RCT	9	731	0.58	Fixed	0.76 (0.62–0.92)	0.006
	PCS	6	5485	0.08	Random	1.00 (0.73–1.36)	0.98
Pivot shift	RCT	6	537	0.05	Random	0.77 (0.42–1.41)	0.40
	PCS	7	6033	0.008	Random	0.99 (0.66–1.51)	0.98
Lachman testing	RCT	4	332	0.14	Random	1.12 (0.68–1.84)	0.67
	PCS	3	236	0.83	Fixed	0.66 (0.36–1.21)	0.18

Value < 1 favors bone-patellar tendon-bone; CI = confidence interval; RCT = randomized controlled trial; PCS = prospective cohort study.

bone-tendon-bone cohort were men versus 57% of patients in the hamstring cohort. Average followup was 68 ± 55 months for the included studies.

Nineteen studies that included a total of 47,070 (7560 bone-tendon-bone, 39,510 hamstring) patients reported on graft rupture and/or revision ACL reconstruction. Seven

studies, including 568 patients (280 bone-tendon-bone, 288 hamstring), reported Lachman test data. Fifteen studies reported data on instrumented laxity as defined by patients with a side-to-side difference of ≥ 3 mm at manual maximum testing with KT1000/2000TM. This included 6216 patients (1433 bone-tendon-bone, 4783 hamstring). Overall, 13 studies reported on pivot shift testing and 6570 patients were included (1508 bone-tendon-bone, 5062 hamstring). Pivot shift was denoted as positive if patients had a grade greater than 1+ on physical examination.

Statistical Analysis

Data analysis was performed with Review Manager (Version 5.3; The Cochrane Collaboration, London, UK). Odds ratio was used as summary statistics for dichotomous variables. Odds ratios (ORs) were reported with 95% confidence intervals, and statistical significance was set to a *p* value of < 0.05 . Statistical heterogeneity between included studies was evaluated by the I^2 and chi square tests with significance set at $p < 0.10$. The number needed to treat (NNT) was calculated utilizing observed relative risks and the patient's expected event rate [12].

Random-effects or fixed-effects models were used depending on heterogeneity of the study. Random-effects modeling was utilized for I^2 values of $> 25\%$ [20]. A sensitivity analysis was performed by excluding one study in each round and evaluating the influence of any single study on the primary meta-analysis estimate. Subgroup analysis was also performed based on type of study design (RCT versus prospective cohort studies [PCS]) to identify potential differences between bone-tendon-bone and hamstring grafts across trials.

Publication Bias

A funnel plot was created for each outcome measure to determine if there was bias in the studies. These plots showed no evidence of positive outcome bias in any of the outcomes measured and were relatively symmetric (Appendix 1 [Supplemental materials are available with the online version of *CORR*[®]]).

Results

The meta-analysis found that patients undergoing primary ACL reconstruction with bone-tendon-bone autograft were less likely to experience graft rupture and/or revision ACL reconstruction than patients treated with hamstring autograft (OR, 0.83; 95% confidence interval [CI], 0.72–0.96; *p*

= 0.01) (Fig. 2). A NNT analysis showed that 235 patients would need to be treated with a bone-tendon-bone graft over a hamstring graft to prevent one graft rupture.

Among patients who did not experience graft rupture or revision, there were no differences observed between the two graft types in any of our secondary analyses of graft laxity. No difference was found based on KT1000/2000TM testing between bone-tendon-bone and hamstring (OR, 0.86; 95% CI, 0.69–1.06; *p* = 0.16) (Fig. 3), pivot shift testing (OR, 0.89; 95% CI, 0.63–1.25; *p* = 0.51) (Fig. 4), or Lachman testing (OR, 0.96; 95% CI, 0.67–1.39; *p* = 0.84) (Fig. 5).

A subgroup analysis of the outcomes included in the study was performed according to the type of study design (PCS or RCT). The sole finding of difference was an OR of 0.76 favoring bone-tendon-bone over hamstring when instrumented laxity in RCTs alone was analyzed (95% CI, 0.62–0.92; *p* = 0.006); there were no differences in terms of Lachman or pivot shift testing (Table 2).

Discussion

Graft rupture is a feared complication after ACL reconstruction, because revision surgery often results in inferior patient-reported outcome measures, increased laxity with pivot shift testing, and increased rates of tibiofemoral arthritis [15]. Although bone-tendon-bone and hamstring autograft are common graft choices, the available evidence is mixed on which graft type is associated with a higher risk of graft rupture and revision ACL reconstruction. A recent large Scandinavian registry study [13] reported a higher risk of graft rupture with hamstring than bone-tendon-bone, but a prior meta-analysis [47] found no difference between graft types. The goals of this study were to utilize the statistical power of a meta-analysis to compare the risk of graft rupture/revision and metrics of graft laxity between graft types. We found a small increased risk of graft rupture/revision in the hamstring group when compared with the bone-tendon-bone group. The NNT was calculated at 235, meaning that 235 patients would need to be treated with bone-tendon-bone rather than hamstring to prevent one rupture. We observed few differences between graft types in terms of graft laxity reported by the primary source studies.

We interpret this study in light of several limitations. First, most of the patients included in this study came from the Scandinavian registry studies and those results factor heavily into the results of the current study. Although the methodology for a registry study is not as rigorous as that of an RCT, the data were collected longitudinally, and the authors have published on the validity of their registry [15]. The inclusion of these data was critical to this study as we

attempted to determine whether the results of the registry studies would hold up in the setting of a larger meta-analysis. Second, this study was designed to investigate differences in the risk of graft rupture between the two graft types without considering clinical outcome scores and knee function. This fact keeps the study clear and focused but precludes its use in isolation when a clinician debates the merits of bone-tendon-bone versus hamstring autograft. We believe that the small increased risk of graft rupture observed in this meta-analysis should be only one aspect of a larger discussion with patients regarding optimal graft choice. Another limitation is that the nature of a meta-analysis is such that the authors can only analyze and interpret the data available in light of heterogeneous reporting of data across studies. This fact limits the number of patients available for analysis within the individual outcomes studied but does not alter the validity of the results. Lastly, the relatively short-term minimum followup in some of the included studies prevents us from evaluation of the long-term outcomes between graft types.

In this study, patients who received bone-tendon-bone autograft had a reduced risk of graft failure compared with those receiving hamstring autograft at a minimum 2-year followup with a NNT of 235 patients. These data support the recent findings from the Scandinavian ACL registries [3, 13, 34, 35] and by Maletis et al. in their retrospective registry review [29]. However, the observed difference in this study was small and clinicians must weigh the clinical importance of this finding while also considering differences in donor site morbidity, patient-reported outcome metrics, and knee function scores. All of these areas represent opportunities for continued research.

Secondary outcome measures of graft laxity included KT1000/2000™ instrumented laxity testing, pivot shift test, and the Lachman test. Instrumented laxity testing favored bone-tendon-bone when including RCTs in isolation; however, on examination of the entire cohort, none of these measures was found to be different between groups in the current study. This is in contrast to the meta-analysis by Xie et al. [47] that reported that pivot shift testing favored bone-tendon-bone and the Cochrane review by Mohtadi et al. [32] in which they found all three of these factors favored bone-tendon-bone. The absence of a difference in graft laxity between groups in this study indicates that previously observed differences might have been the result of sampling bias or recent improvements in surgical technique. Newer generation fixation devices for hamstring ACL reconstruction are designed to allow for more anatomic tunnel placement without compromising load to failure [10, 17]. The routine pretensioning of hamstring grafts also may contribute to less graft laxity regardless of graft type [24].

In this meta-analysis of short- to mid-term followup after primary ACL reconstruction, hamstring autografts failed at a higher rate than bone-tendon-bone autografts. However, failure rates were low in each group, the difference observed was small, and the grafts performed similarly in metrics of graft laxity. Both graft types remain viable options for primary ACL reconstruction, and the difference in failure rate should be one part of a larger conversation with each individual patient about graft selection that should also include potential differences in donor site morbidity, complication rates, and patient-reported outcome measures. Continued prospective collection of patient data will be important going forward as we attempt to further characterize the potential differences in outcomes attributable to graft selection.

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