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Graft failure rates in bone-patellar tendon-bone, hamstring, and quadriceps tendon autografts in patients younger than 25 years-old: A systematic review and meta-analysis

TITLE: Graft failure rates in bone-patellar tendon-bone, hamstring, and quadriceps tendon autografts in patients younger than 25 years-old: A systematic review and meta-analysis

ABSTRACT

Background: Anterior cruciate ligament reconstruction (ACLR) is being increasingly performed due in part to higher injury rates among young athletes (≤ 25 years old). High allograft failure rates support the use of autograft for ACLR in young patients. However, reported data examining the failure rates of the different autografts used in this population are lacking.

Purpose: The purpose of this study was to compare graft failure rates among bone-patellar tendon-bone (BPTB), hamstring tendon (HT), and quadriceps tendon (QT) autografts in patients ≤ 25 years old. The secondary aim was to stratify graft failure by potential modifiers, including sex, mean follow-up (FU), time to graft rupture, and concomitant meniscus surgery.

Study Design: Systematic review and Meta-analysis

Methods: Studies that reported ACL graft (BPTB, HT, QT) reinjury rates in patients ≤ 25 years old with a minimum 24 months of follow-up were included. Studies examining revision ACLR, allograft ACLR, allograft augmentation ACLR, concomitant lateral extraarticular tenodesis, and studies without graft reinjury rates reported by both graft type and young age (≤ 25) were excluded.

Results: 46 studies comprising 10,624 patients (HT: n = 6,090, 47.0% female, 54.5-month mean FU; BPTB: n = 3,990, 63.0% female, 63.6-month mean FU; QT: n = 544, 40.3% female, 41.6-month mean FU) were included. HT exhibited the highest failure rate at 11.1% (95% CI, 8.8%-13.9%). Failure rates for BPTB and QT were 5.1% (95% CI, 3.5%-7.2%) and 2.5% (95% CI, 0.5%-11.2%), respectively. HT had a significantly higher failure rate than BPTB ($Q = 13.1$; $p < 0.001$). There were no significant differences in failure rate between HT and QT ($Q = 3.7$; $p =$

0.06) or between BPTB and QT (Q = 0.8, p = 0.4). Males and females had similar risk of graft failure regardless of graft type.

Conclusion: The results of this meta-analysis suggest that HT grafts are not the optimal choice for young patients undergoing ACLR. Instead, these patients should consider BPTB to reduce the risk of graft failure. Further research including RCTs with larger sample sizes are required to determine how QT grafts compare with BPTB grafts in this population.

Clinical Relevance: These findings can guide autograft selection in patients ≤25 years undergoing ACLR who wish to minimize the risk of graft failure.

Key Terms: ACL, autograft, young, athlete, graft failure

What is known about the subject: Patients 25 years and younger have an increased risk of ACL graft failure. Autografts are used more frequently in young patients due to higher failure rates of allografts. Autograft type, age, and sex are known risk factors for ACL graft failure.

What this study adds to existing knowledge: This study provides a meta-analysis of graft failure rates in young patients aged 25 years and younger who underwent HT, BPTB, or QT ACLR. This study reports graft-specific pooled failure rates for this high-risk young age group. Despite increasing popularity, there is a lack of sufficient data regarding QT ACLR failure rates in young patients.

Level of evidence: 4

Conflicts of interest: The authors report no conflicts of interest relevant to the study of interest.

Funding: The authors report no funding was used to complete the study of interest.

INTRODUCTION

Anterior cruciate ligament (ACL) ruptures continue to occur in high numbers in patients under the age of 25.[21,41] Although there has been a modest decrease in the incidence of ACL tears from 90.11 tears per 100,000 person-years in 2010 to 53.32 tears per 100,000 person-years in 2020, the relative use of ACLR has increased in incidence over the last decade.[9] Following ACL injury, young patients are at risk of knee instability, meniscal injuries, osteochondral defects, and early degenerative joint disease.[1,12,39] ACL reconstruction (ACLR) is the standard of care for ACL ruptures and has shown long-lasting, favorable subjective outcomes and objective stability.[81] Despite this, graft failure remains a challenging problem in young athletic populations due to high levels of physical activity resulting in increased stress on the graft over longer periods of time,[88] with greatest risk of failure within the first two years following return to sport.[55,88]

While there is debate as to which graft type minimizes the risk of graft failure, [18,36] ACLR with autograft has been consistently reported as superior to allograft in patients ≤ 25 years of age due to lower graft failure rates.[4,6,20,22,38] The most commonly used autografts include ipsilateral bone-patellar tendon-bone (BPTB), hamstring tendon (HT), and quadriceps tendon (QT) with or without a patellar bone block and have all demonstrated positive patient outcomes.[23,81] Previously, BPTB was the most frequent primary ACLR choice, but in recent years HT and QT grafts have increased in popularity as an alternative to avoid the anterior knee pain and kneeling discomfort of BPTB.[3,87] However, observed differences in graft strength and stiffnesses, donor site morbidity, graft incorporation, and healing properties result in unequal failure rates.[27,50,90,94] Hamstring tendon has demonstrated high failure rates,[29] which has lead to increased interest in the quadriceps tendon for patients wishing to avoid anterior knee pain and reduce failure rates.

Previous studies examining autograft reinjury rates often fail to stratify between older adults and younger patients despite higher rates of failure in younger cohorts.[2,93] Furthermore, many studies fail to separate adolescents (≤18 yrs) and young adults (19-25 yrs), notwithstanding a higher risk of graft failure in adolescents.[77,82] The higher risk observed may be due in part to the mixed demographic of skeletally immature (open physes) and mature (closed physes) patients within the adolescent population.[82]

Aggregated failure rates and the effects of risk factors across studies in young patients have not been well described; therefore, surgical guidelines are unclear. The purpose of this study was to compare graft failure rates between BPTB, HT, and QT autografts in patients younger than 25 years old at a minimum follow-up of 24 months. The secondary aim of this review was to stratify graft failure by potential modifiers, including sex, mean follow-up, mean time to graft rupture, and concomitant meniscus surgery. The hypothesis was that HT would have a significantly higher failure rate compared to BPTB and QT.

METHODS

Search strategy

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement was used to guide this review. An information specialist/librarian (MSW) searched PubMed/MEDLINE (National Library of Medicine: 1946-), Embase (Elsevier: 1966-), Cochrane CENTRAL (Cochrane Library 1996-)*, and Web of Science Core Collection (Clarivate: 1900-) from origin of database to March 3, 2022. A combination of controlled vocabulary and text words related to autografts were combined with the Boolean operator "AND" with controlled vocabulary and text words associated with ligaments, tendons, and bone grafts related to the patella (**Appendix**

1). Language was limited to English, and we excluded case reports, comments, commentaries, editorials, reviews, or letters. Age filters were not added to the searches to avoid inadvertent exclusion of relevant studies.

On January 16, 2024, the original searches were rerun from the previous date of search: March 2022 to January 2024, and 3480 new studies were retrieved. Precise date searching is not available in some of the databases. The 3480 studies were compared to the original search results from January 16, 2024, and overlapping duplicates were removed using EndNote 20©. Next, 1501 new studies were uploaded to Covidence© and an additional 104 duplicates were removed by Covidence©. Following this, 1397 studies remained to be reviewed in the title/abstract screening. On August 28, 2024, 318 studies were retrieved. Using EndNote 21© and via visual screening, 105 duplicate studies were removed. The 213 studies were compared to the results from January 16th and overlapping duplicate studies were removed. Subsequently, 201 studies were uploaded to Covidence© where one additional duplicate study was removed, leaving 200 studies to be screened.

Data Extraction

A total of 6,220 studies were retrieved and imported into the citation manager EndNote 20©. Using EndNote's "Find duplicates" feature, 2,110 duplicates were removed, and 5,812 studies were uploaded to Covidence©, a Systematic Review platform. A total of 737 duplicates were removed, and 5,075 studies were advanced for the initial title/abstract screening. Of the 5,075 studies reviewed, 4,726 studies were deemed irrelevant or out of scope for this study. Team members (CBP, ZBH) reviewed the studies and additional team members (JDL, AM, GDM) served as the conflict resolvers of studies. Three-hundred forty-nine (349) studies were determined

to be eligible for full text review, and ultimately 46 papers were included for this study. The PRISMA figure summarizing the data extraction can be seen in **Figure 1.**

Selection Criteria

Studies on autograft ACLR using hamstring tendon [HT], quadriceps tendon [QT] (comprising a combination of quadriceps tendon–bone [QTB] and all–soft tissue quadriceps tendon [ASTQT]),or bone-patellar tendon-bone [BPTB] autograft in patients ≤ 25 years old with a minimum follow-up of 24 months years were included. Studies had to report ACL graft reinjury rates in patients ≤ 25 years to be included in the review. Those on revision, allograft, and/or allograft augmentation ACLR, ACLR with concomitant lateral extraarticular tenodesis, and studies without graft reinjury rates reported by both graft type and young age (≤ 25) were excluded. If more than one study reported outcomes on the same patient population, only the most appropriate study (complete outcomes dataset) was included in the meta-analysis. The inclusion and exclusion criteria are also detailed in **Table 1**.

Table 1: Inclusion/Exclusion Criteria

Inclusion	Exclusion
Proportions of graft used and graft failures by graft type and age	No proportion of grafts and graft failures for younger population (≤ 25 years)
All ages permitted in study, but study must include the proportion of grafts and graft failures for younger population (≤ 25 years)	Revision ACLR
Patient underwent ACL reconstruction (ACLR) using autograft (hamstring, quadriceps tendon-bone [QTB], all-soft tissue quadriceps tendon [ASTQT], or bone-patellar tendon-bone [BPTB])	ACLR using allograft
Rates of clinical failure (grade 2+ or worse Lachman, grade 2+ or worse pivot shift, overall IKDC grade C or D, instrumented laxity with side-to-side difference of greater than 5 mm)	ACLR with concomitant lateral extraarticular tenodesis
Observational study	Multiligament knee injury (MCL, LCL, PLC, and/or PCL repaired or reconstructed)
Therapeutic intervention	Concomitant cartilage repair or restoration surgery

Human study	Minimum follow-up < 24 months
Peer-reviewed literature, articles published in scientific journals	Laboratory or animal study
Origin of database – date search is performed	Reviews without original data
English	Non-peer reviewed study
	General/systematic reviews, meta-analyses, case reports, editorials, conference abstracts, book chapters
	Non-English
	Data already reported in a separate, included manuscript

Methodological Quality Assessment

The Risk of Bias in Non-Randomized Studies of Interventions (ROBINS-I) tool was utilized.[79] The 7 criteria of the ROBINS-I tool were assessed by two independent reviewers (CBP, ZBH): (1) bias due to confounding, (2) bias in selection of participants into the study, (3) bias in classification of interventions, (4) bias due to deviations from intended interventions, (5) bias due to missing data, (6) bias in measurement of outcomes, and (7) bias in selection of the reported result. Each criterion was rated as low risk, moderate risk, serious risk, critical risk, or no information in accordance with the ROBINS-I tool.[79]

Statistical Analysis

A meta-analysis of proportions was conducted using the metaprop function from the meta R package[71], applying a generalized linear mixed-effects model (GLMM) with a logit transformation (PLOGIT) to account for sparse binary outcome data and study-level variability. Subgroup analyses were performed by graft type, with pooled estimates back-transformed for interpretability, and differences evaluated using the standard Wald-type Q test for categorical moderators. A pairwise meta-analysis of binary outcomes was also performed using the metabin function in the meta package[71], comparing re-rupture rates between BTB and HT grafts using the

inverse variance method to estimate pooled odds ratios (ORs) with corresponding confidence intervals. Due to the limited number of studies, QT was not included in the odds ratio comparison/estimation. Moderator analysis was conducted using the metareg function from the meta R package[71] with between-study variance estimated using restricted maximum likelihood. Sensitivity analysis was conducted to assess if the rate estimates were similar utilizing only two-arm studies. Statistical significance was set at $p<.05$.

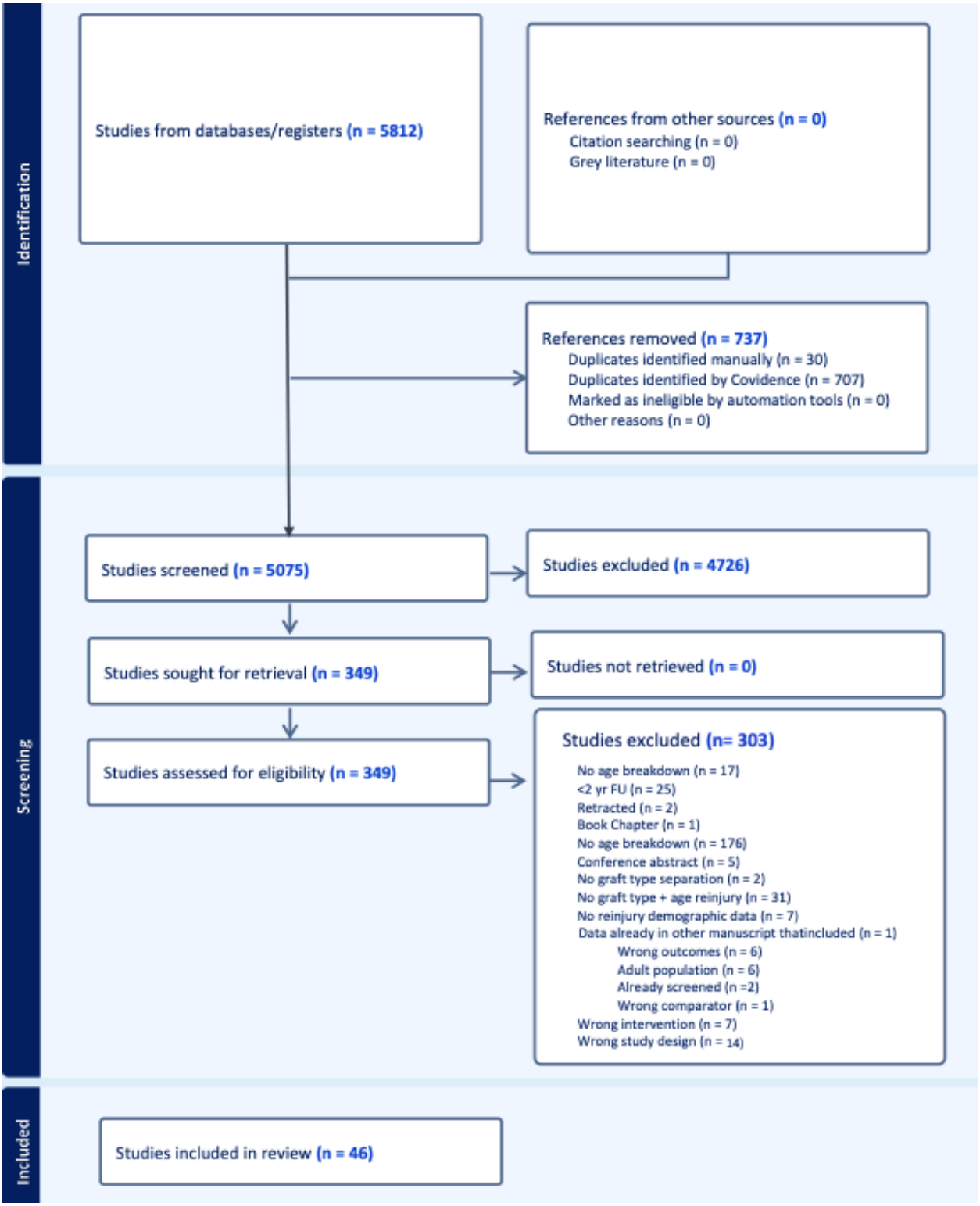


Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart for inclusion and exclusion of articles.

RESULTS

Demographic Characteristics

Across all 46 included studies, there were 6,090 HT (33 studies), 3,990 bone-patellar tendon-bone (19 studies), and 544 quadriceps tendon (6 studies total; 109 QTB [3 studies][23,65,86], 435 ASTQT [3 studies]) patients included. The mean age of patients who underwent hamstring tendon, bone-patellar tendon-bone, and quadriceps tendon autograft ACLR was 15.5 yrs (SD, 11.0-25.0), 16.8 yrs (SD, 11.5-25.0), and 15.3 yrs (SD, 10.0-22.9), respectively. The mean follow-up duration was 54.5 months (SD, 24.0-246.0) for patients who underwent hamstring tendon autograft ACLR, 63.6 months (SD, 24.0-246.0) for bone-patellar tendon-bone autograft ACLR, and 41.6 months (SD, 24.0-139.0) for quadriceps tendon autograft ACLR. On average, the follow-up completion was 86.6% for patients who underwent hamstring tendon autograft ACLR, 77.3% for patients who underwent bone-patellar tendon-bone autograft ACLR, and 84.1% for patients who underwent quadriceps tendon autograft ACLR. There were 47% females who underwent hamstring tendon autograft ACLR, 63% females who underwent bone-patellar tendon-bone autograft ACLR, and 40.3% females who underwent quadriceps tendon autograft ACLR **(Table 2)**. Forty-three studies included follow up range data, 34 included sex data, 9 included mean time to graft rupture, and 12 included concomitant injury data.

Table 2: Study Demographics

Author	Patients, n	Mean age, yrs (range)	Sex (% female)	Mean follow-up (FU), months (range)	FU completion (%)
Bone-Patellar Tendon-Bone Autograft					
Barber et al 2014[4]	53	18.6 (13-25)	51	31 (24-132)	100.0
Britt et al 2020[10]	41	15.4 (NR-18)	100	37.4 (24-NR)	78.9
Cordasco et al 2019[16]	209	16.2 (12-20)	NR	38.9 (24-84)	97.6
Ellis et al 2012[21]	59	16 (14-18)	NR	50.4 (24-135.6)	84.3

Hurt et al 2017[32]	377	17.62 (NR-25)	46.7	24 (24-NR)	41.0
Kane et al 2016[38]	101	19.8 (NR-25)	48.5	24 (24-NR)	59.4
McCarroll et al 1994[45]	60	14.2 (13-17)	51.7	50.4 (24-84)	NR
Morgan et al 2016[49]	48	16 (13-18)	NR	198 (180-246)	84.0
Nelson et al 2016[52]	55	15.2 (11.5-16.9)	54.5	34.8 (24-NR)	NR
Rauck et al 2021[63]	53	16.6 (14.2-18.7)	71.7	45.36 (31.2-59.3)	37.0
Salem et al 2019[66]	175	18.56 (15-25)	100	45.12 (31.2-63.6)	71.4
Salmon et al 2006[67]	13	NR (NR-21)	NR	156 (156-NR)	NR
Sanada et al 2021[69]	27	16.3 (13-20)	100	34.2 (24-60)	100.0
Schilaty et al 2017[70]	310	NR (NR-25)	NR	163.2 (24-NR)	66.0
Shelbourne et al 2009[74]	878	NR (14-25)	47.1	60 (60-NR)	78.0
Smith et al 2020[75]	32	17.8 (13-24)	53	24 (24-NR)	92.0
Spindler et al 2020[78]	492	17 (14-22)	47	72 (72-NR)	92.0
Persson et al 2014[59]	936	NR (15-19)	33	48 (24-NR)	86.0
Tomihara et al 2024[83]	71	16.9 (NR-NR)	4	33.6 (24-NR)	NR
Hamstring Tendon Autograft					
Berdis et al 2019[8]	143	16 (8-21)	55.2	52 (25-94)	73.7
Britt et al 2020[10]	30	15.4 (NR-18)	100	46.1 (24-NR)	78.9
Calvo et al 2015[11]	27	13 (12-16)	40.7	127.2 (120-156)	100.0
Cohen et al 2009[14]	26	13.3 (11-15)	57.7	45 (24-84)	NR
Cordasco et al 2019 B[16]	66	14.3 (12-17)	NR	36.6 (24-84)	97.6
Cordasco et al 2019 C[16]	49	12 (8-16)	NR	41.4 (24-84)	97.6
Courvoisier et al 2011[17]	37	14 (11-15)	54.1	36 (24-48)	100.0
Engelman et al 2014[22]	35	15.6 (12.7-18.6)	34.3	50.9 (24-NR)	65.0
Getgood et al 2020[24]	298	18.8 (14-25)	52	24 (24-NR)	95.0
Jacobs et al 2017[33]	46	14.6 (NR-18)	56.5	46.7 (24-NR)	NR
Jeffers et al 2022[34]	34	NR (17-23)	0	102 (24-NR)	NR
Kamien et al 2013[37]	48	16.99 (12-25)	NR	24 (24-NR)	NR
Larson et al 2016[42]	22	14.4 (12.3-16)	59.1	48 (24-84)	NR
Mariscalco et al 2013[43]	85	NR (13-18)	NR	24 (24-NR)	82.2
Matava et al 1997[44]	8	14.4 (11.8-15.6)	25	32 (27-44)	100.0
McIntosh et al 2006[46]	16	13.6 (11.2-14.9)	31	41.1 (24-112)	NR
Monaco et al 2022[48]	40	16.3 (13.9-17.6)	6	43.8 (24-89)	81.4
Morgan et al 2016[49]	194	16 (13-18)	NR	198 (180-246)	84.0
Nelson et al 2016[52]	388	14.8 (11.5-16.9)	31.7	34.8 (24-NR)	NR
Nikolaou et al 2011[53]	94	13.7 (11.6-15.9)	40	38 (24-60)	NR
Pennock et al 2019[57]	56	14.8 (NR-18)	31	34.8 (24-NR)	92.0

Persson et al 2014[59]	2783	NR (15-19)	264	48 (24-NR)	86.0
Rao et al 2021[62]	42	NR (NR-24)	NR	50.64 (24-NR)	NR
Redler et al 2012[64]	18	14.2 (NR-18)	33.3	43.4 (24-86.6)	94.7
Runer et al 2020[65]	51	NR (NR-15)	NR	24 (24-NR)	NR
Salem et al 2019[66]	81	18.46 (15-25)	100	45.12 (32.4-64.8)	60.5
Sanada et al 2021[69]	29	16.5 (12-20)	100	33.8 (24-60)	100.0
Schilaty et al 2017[70]	56	NR (NR-25)	NR	163.2 (24-NR)	66.0
Smith et al 2020[76]	27	17.6 (13-24)	59	24 (24-NR)	92.0
Spindler et al 2020[78]	278	17 (14-22)	50	72 (72-NR)	91.8
Takazawa et al 2017[80]	58	17 (14-19)	0	56.5 (24-175)	78.0
Thorolfsson et al 2021[82]	569	17.1 (9-19)	17	NR (24-NR)	NR
Tomihara et al 2024[83]	86	17.2 (NR-NR)	19	44.5 (24-NR)	NR
Webster et al 2016[87]	316	17.2 (11-19)	37	60 (36-120)	89.0
Quadriceps tendon autograft					
Gagliardi et al 2020[23]	81	15.9 (10-18)	48.1	37.2 (24-36)	84.0
Kohl et al 2014[40]	13	12.8 (6.2-15.8)	20	49.2 (22.8-116.4)	NR
Pennock et al 2019[58]	27	14.8 (NR-18)	32	28.8 (24-NR)	92.0
Petit et al 2024[60]	395	17.8 (14.0-22.9)	44	73 (24-139)	60.2
Runer et al 2020[65]	6	NR (NR-15)	NR	24 (24-NR)	NR
Vaughn et al 2021[86]	22	15 (12-17)	50	33.6 (24-60)	100.0

Key: NR, not reported

Methodological Quality Assessment

Using the ROBINS-I tool[79], 37 (80.5%) studies were rated with an overall "serious" risk of bias. Six (13%) studies were rated with an overall "moderate" risk of bias and three (6.5%) studies were rated with an overall "low" risk of bias (**Figure 2**).[25]

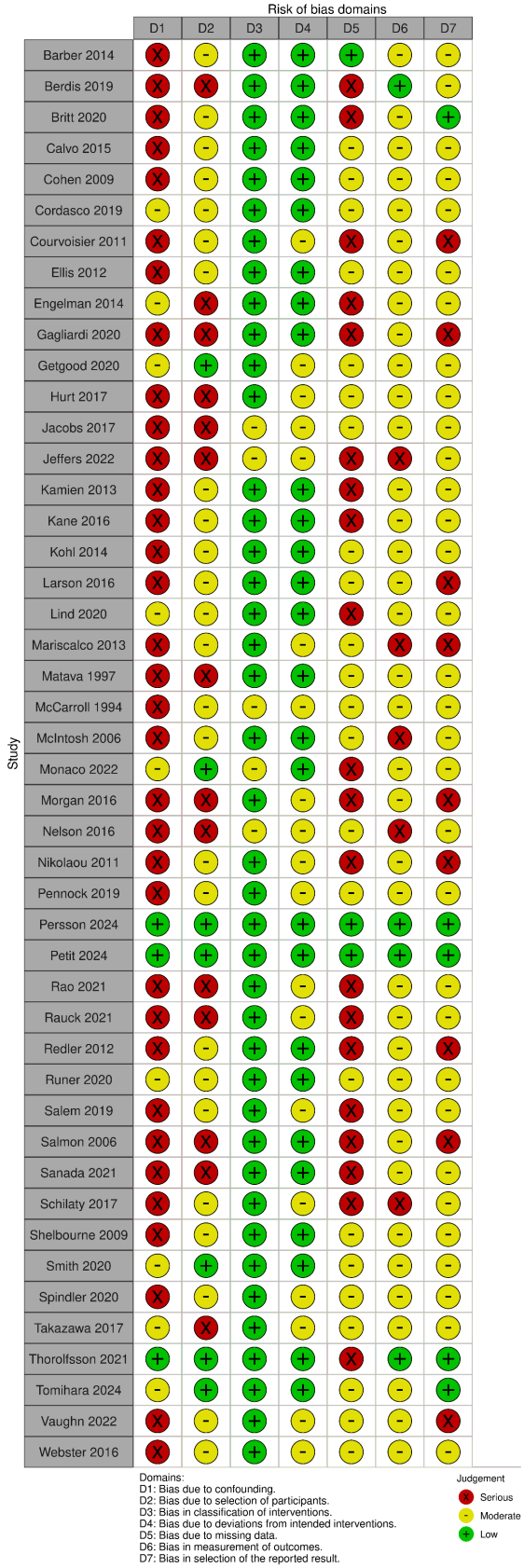

Risk of bias domains
D1
D2
D3
D4
D5
D6
D7
Study
Barber 2014
Berdis 2019
Britt 2020
Calvo 2015
Cohen 2009
Cordasco 2019
Courvoisier 2011
Ellis 2012
Engelman 2014
Gagliardi 2020
Getgood 2020
Hurt 2017
Jacobs 2017
Jeffers 2022
Kamien 2013
Kane 2016
Kohl 2014
Larson 2016
Lind 2020
Mariscalco 2013
Matava 1997
McCarroll 1994
McIntosh 2006
Monaco 2022
Morgan 2016
Nelson 2016
Nikolaou 2011
Pennock 2019
Persson 2024
Petit 2024
Rao 2021
Rauck 2021
Redler 2012
Runer 2020
Salem 2019
Salmon 2006
Sanada 2021
Schilaty 2017
Shelbourne 2009
Smith 2020
Spindler 2020
Takazawa 2017
Thorolfsson 2021
Tomihara 2024
Vaughn 2022
Webster 2016
Domains:
D1: Bias due to confounding.
D2: Bias due to selection of participants.
D3: Bias in classification of interventions.
D4: Bias due to deviations from intended interventions.
D5: Bias due to missing data.
D6: Bias in measurement of outcomes.
D7: Bias in selection of the reported result.
Judgement
Serious
Moderate
Low

Figure 2. Risk-of-bias assessments for included studies using the Risk of Bias in Non-Randomized Studies of Interventions tool.

Meta-analysis

Overall graft failure rates

The pooled autograft graft failure rate was 11.1% (95% CI 8.8-13.9) for hamstring tendon, 5.1% (95% CI 3.5-7.2) for bone-patellar tendon-bone, and 2.5% (95% CI 0.5-11.2) for quadriceps tendon. There was a significant difference among failure rates by ACLR graft type ($\chi 2$= 15.7, $p<0.01$) (**Figure 3**). Hamstring tendon had significantly higher failure rates compared to bone-patellar tendon-bone (Q=13.1, $p<0.001$). There were no differences in failure rate between hamstring tendon and quadriceps tendon (Q=3.7, p=0.06) or bone-patellar tendon-bone and quadriceps tendon (Q=0.8, p=0.4).

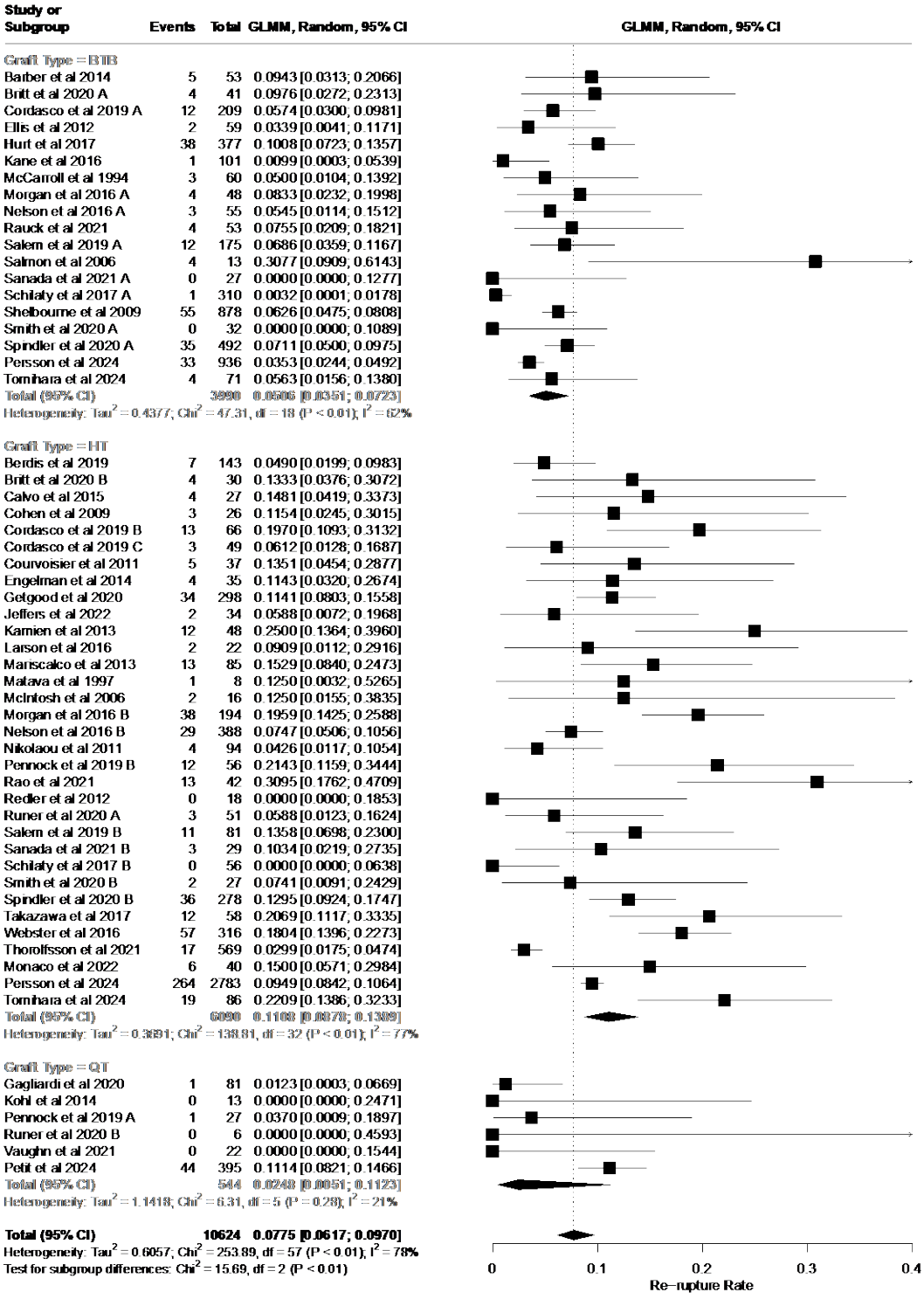

Study or Subgroup
Events
Total
GLMM, Random, 95% CI
GLMM, Random, 95% CI
Graft Type = BTB
Barber et al 2014 5 53 0.0943 [0.0313; 0.2066]
Britt et al 2020 A 4 41 0.0976 [0.0272; 0.2313]
Cordasco et al 2019 A 12 209 0.0574 [0.0300; 0.0981]
Ellis et al 2012 2 59 0.0339 [0.0041; 0.1171]
Hurt et al 2017 38 377 0.1008 [0.0723; 0.1357]
Kane et al 2016 1 101 0.0099 [0.0003; 0.0539]
McCarroll et al 1994 3 60 0.0500 [0.0104; 0.1392]
Morgan et al 2016 A 4 48 0.0833 [0.0232; 0.1998]
Nelson et al 2016 A 3 55 0.0545 [0.0114; 0.1512]
Rauck et al 2021 4 53 0.0755 [0.0209; 0.1821]
Salem et al 2019 A 12 175 0.0686 [0.0359; 0.1167]
Salmon et al 2006 4 13 0.3077 [0.0909; 0.6143]
Sanada et al 2021 A 0 27 0.0000 [0.0000; 0.1277]
Schlafy et al 2017 A 1 310 0.0032 [0.0001; 0.0178]
Shelbourne et al 2009 55 878 0.0626 [0.0475; 0.0808]
Smith et al 2020 A 0 32 0.0000 [0.0000; 0.1089]
Spindler et al 2020 A 35 492 0.0711 [0.0500; 0.0975]
Persson et al 2024 33 936 0.0353 [0.0244; 0.0492]
Tomihara et al 2024 4 71 0.0563 [0.0156; 0.1380]
Total (95% CI) 3990 0.0606 [0.0351; 0.0923]
Heterogeneity: Tau² = 0.4377; Chi² = 47.31, df = 18 (P < 0.01); I² = 62%
Graft Type = HT
Berdis et al 2019 7 143 0.0490 [0.0199; 0.0983]
Britt et al 2020 B 4 30 0.1333 [0.0376; 0.3072]
Calvo et al 2015 4 27 0.1481 [0.0419; 0.3373]
Cohen et al 2009 3 26 0.1154 [0.0245; 0.3015]
Cordasco et al 2019 B 13 66 0.1970 [0.1093; 0.3132]
Cordasco et al 2019 C 3 49 0.0612 [0.0128; 0.1687]
Courvoisier et al 2011 5 37 0.1351 [0.0454; 0.2877]
Engelman et al 2014 4 35 0.1143 [0.0320; 0.2674]
Getgood et al 2020 34 298 0.1141 [0.0803; 0.1558]
Jeffers et al 2022 2 34 0.0588 [0.0072; 0.1968]
Kamien et al 2013 12 48 0.2500 [0.1364; 0.3960]
Larson et al 2016 2 22 0.0909 [0.0112; 0.2916]
Marinscalco et al 2013 13 85 0.1529 [0.0840; 0.2473]
Matava et al 1997 1 8 0.1250 [0.0032; 0.5265]
McIntosh et al 2006 2 16 0.1250 [0.0155; 0.3835]
Morgan et al 2016 B 38 194 0.1959 [0.1425; 0.2588]
Nelson et al 2016 B 29 388 0.0747 [0.0506; 0.1056]
Nikolaou et al 2011 4 94 0.0426 [0.0117; 0.1054]
Pennock et al 2019 B 12 56 0.2143 [0.1159; 0.3444]
Rao et al 2021 13 42 0.3095 [0.1762; 0.4709]
Redler et al 2012 0 18 0.0000 [0.0000; 0.1853]
Runer et al 2020 A 3 51 0.0588 [0.0123; 0.1624]
Salem et al 2019 B 11 81 0.1358 [0.0698; 0.2300]
Sanada et al 2021 B 3 29 0.1034 [0.0219; 0.2735]
Schlafy et al 2017 B 0 56 0.0000 [0.0000; 0.0638]
Smith et al 2020 B 2 27 0.0741 [0.0091; 0.2429]
Spindler et al 2020 B 36 278 0.1295 [0.0924; 0.1747]
Takazawa et al 2017 12 58 0.2069 [0.1117; 0.3335]
Webster et al 2016 57 316 0.1804 [0.1396; 0.2273]
Thorolfsson et al 2021 17 569 0.0299 [0.0175; 0.0474]
Monaco et al 2022 6 40 0.1500 [0.0571; 0.2984]
Persson et al 2024 264 2783 0.0949 [0.0842; 0.1064]
Tomihara et al 2024 19 86 0.2209 [0.1386; 0.3233]
Total (95% CI) 6090 0.1108 [0.0878; 0.1389]
Heterogeneity: Tau² = 0.3891; Chi² = 138.81, df = 32 (P < 0.01); I² = 77%
Graft Type = QT
Gagliardi et al 2020 1 81 0.0123 [0.0003; 0.0669]
Kohl et al 2014 0 13 0.0000 [0.0000; 0.2471]
Pennock et al 2019 A 1 27 0.0370 [0.0009; 0.1897]
Runer et al 2020 B 0 6 0.0000 [0.0000; 0.4593]
Vaughn et al 2021 0 22 0.0000 [0.0000; 0.1544]
Petit et al 2024 44 395 0.1114 [0.0821; 0.1466]
Total (95% CI) 544 0.0240 [0.0051; 0.1123]
Heterogeneity: Tau² = 1.1418; Chi² = 6.31, df = 5 (P = 0.28); I² = 21%
Total (95% CI) 10624 0.0775 [0.0617; 0.0970]
Heterogeneity: Tau² = 0.6057; Chi² = 253.89, df = 57 (P < 0.01); I² = 78%
Test for subgroup differences: Chi² = 15.69, df = 2 (P < 0.01)
0
0.1
0.2
0.3
0.4
Re-rupture Rate

Figure 3. Forest plot for graft failure rates by graft type. A/B/C designations were added to author groups that included more than one autograft type in their study in order to distinguish between graft type groups when performing statistical analysis

Sensitivity Analyses

There were 13 two-arm studies included in the analysis. The pooled autograft failure rate was 11.4% (95% CI 8.4-15.3) for hamstring tendon, 4.2% (95% CI 2.9-6.1) for bone-patellar tendon-bone, and 3.0% (95% CI 0.4-18.6) for quadriceps tendon (**Figure 4**). There was a significant difference among graft failure rates ($\chi 2 = 17.7$, $p<0.01$). The odds of failure were significantly lower for bone-patellar tendon-bone ACLR compared to hamstring tendon (OR=0.4, 95% CI 0.3-0.5; **Figure 5**). There were too few two-arm studies directly comparing QT with hamstring tendon (HT) or bone–patellar tendon–bone (BTB) grafts to permit a pooled comparison.

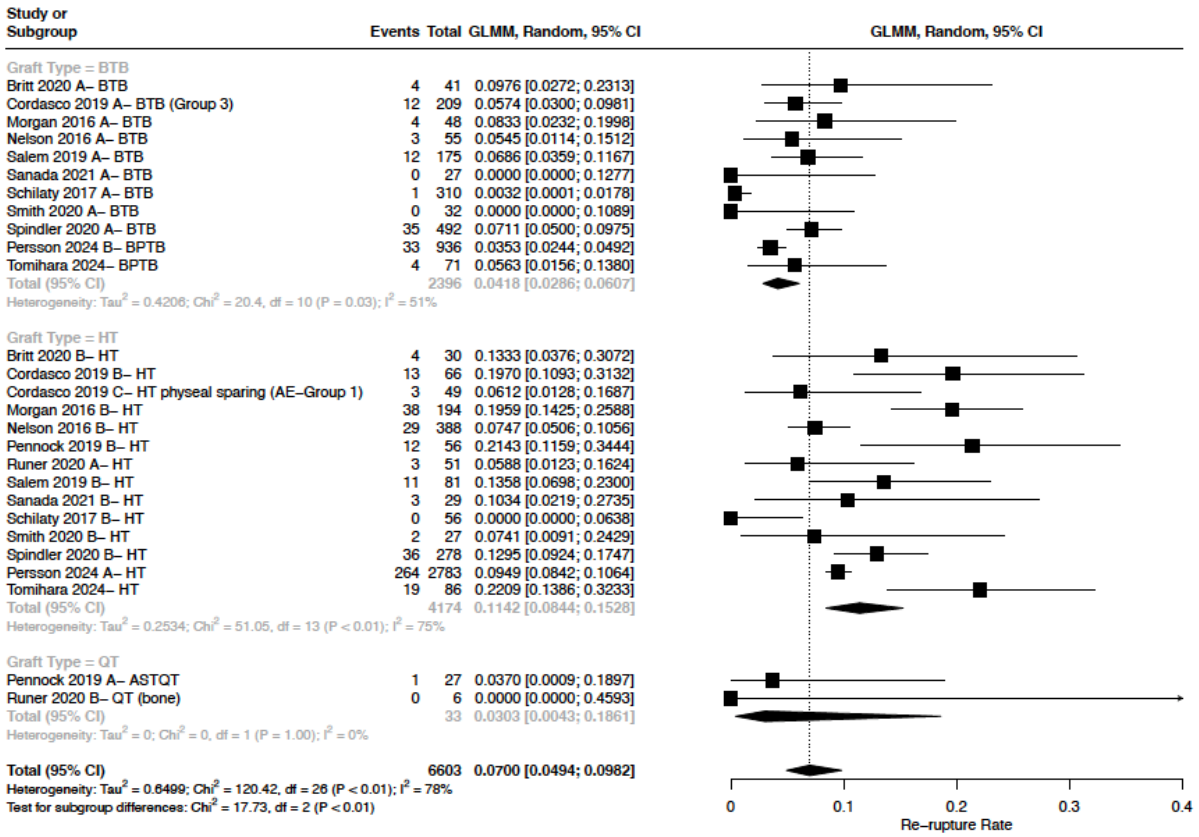


Figure 4. Risk of graft rupture among studies that included comparisons by graft type. A/B/C designations were added to author groups that included more than one autograft type in their study in order to distinguish between graft type groups when performing statistical analysis

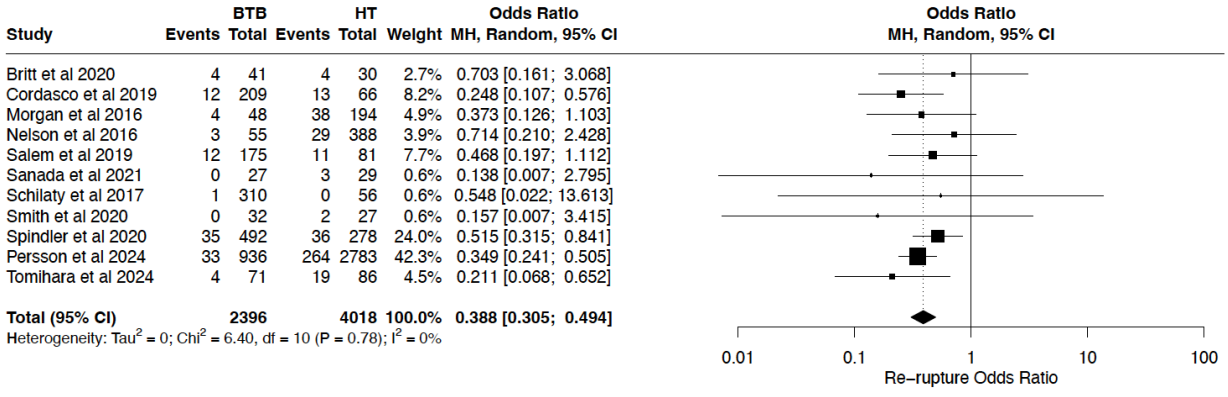


Figure 5. Odds of graft failure in two-arm studies for hamstring tendon ACLR relative to bone-patellar tendon-bone ACLR. Odds Ratio < 1 indicates lower re-rupture rate in BPTB

Follow-up, time to graft rupture, concomitant meniscus surgery, age and sex

There were no differences between graft types regarding mean follow up (Q=0.03, p=0.9), time to graft failure (Q=1.0, p=0.3), overall concomitant meniscus surgery (Q=0.8, p=0.4)**,** age (Q=0.02, p=0.9) or proportion of females (Q=0.6, p=0.5). Odds of failure by sex among graft types indicated no differences (OR=1.0, 95% CI 0.7-1.5, $\chi 2$= 0.8, p=0.7; **Figure 6**). Males and females had similar risk of graft failure regardless of graft type.

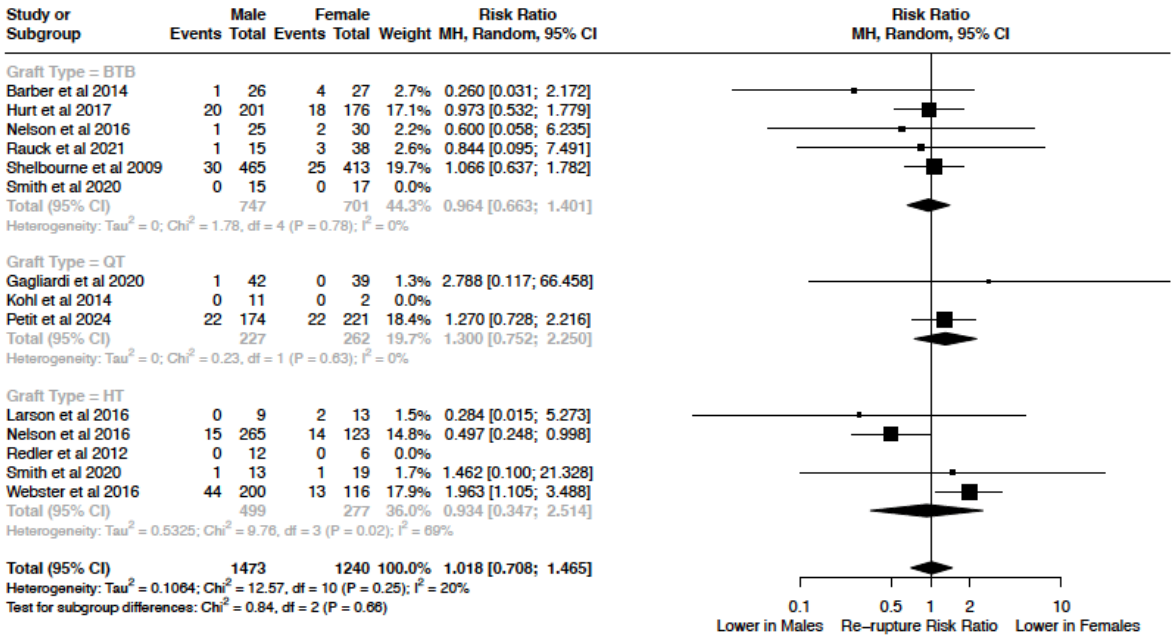


Figure 6. Odds of graft failure in females relative to males by graft type.

DISCUSSION

The purpose of this study was to compare graft failure rates among bone-patellar tendon-bone (BPTB), hamstring tendon (HT), and quadriceps tendon (QT) autografts in patients ≤ 25 years old. The secondary aim was to stratify graft failure by potential modifiers, including sex, mean follow-up (FU), time to graft rupture, and concomitant meniscus surgery. We found that BPTB autografts resulted in significantly lower rates of rupture than HT autograft. There were no differences between BPTB and QT. In aggregate, sensitivity and moderator analyses did not demonstrate differences, indicating that the main finding that lower BPTB and QT graft failure rates holds true regardless of sex, age, length of follow-up, time to graft failure, concomitant meniscal surgery, or study type.

The main finding of our meta-analysis indicates that ACL reconstruction using BPTB autografts resulted in significantly lower rates of graft rupture than HT autograft in patients ≤ 25 years. This is consistent with previous research suggesting BPTB graft has a lower failure rate[29,89]; whereas the outcomes from other related studies in the literature are less clear.[19,47,50,68,92] However, the data from previous meta-analyses included mainly adults and there was no separation based on chronological age or skeletal maturity. Barrett et al.[6] reported significantly lower rates of re-rupture in allograft and BPTB grafts vs. HT in patients < 25 years. Dai et al.[19] also reported similar graft failure rates between QT and BPTB in accordance with previous research[5,30] and the findings of the current study. Cumulatively, these data suggest QT autograft is a viable option, especially in younger patients and further research is encouraged.

Mechanical differences may in part explain divergence in graft failure rates. For instance, the HT graft has reportedly greater variability in harvested graft diameter than BPTB and QT

grafts.[54,84] Additionally, HT ACLR can lead to long lasting hamstring weakness resulting in an increased quadriceps/hamstring ratio that can increase the risk of graft failure.[35,61] The BPTB displays biomechanical similarity to a native ACL. In younger patients, the maximum load to failure of a BPTB autograft has been shown to exceed that of a native ACL by ~800 N.[15] However, it should be considered that the load to failure rate reduces with age.[73,91] QT autografts also have comparable, and potentially superior, load to failure rates, and elastic modulus to the BPTB graft and a native ACL.[73] For the QT graft, the mean ultimate load to failure was 2,185.9 ± 758.8 N compared with 1,580.6 ± 479.4 N for the BPTB graft (P = 0.045), although this biomechanical work does not take into account fixation options in patient surgery, as well as healing of different graft tissues. Moreover, the QT graft mean stiffness was 466.2 ± 133 N/mm while the BPTB mean stiffness was 278.0 ± 75 N/mm (P = 0.005).[73] Previous studies have shown that autografts such as a QT with similar characteristics to the native ACL are beneficial for graft integration, reducing failure rates and allowing the knee to function optimally.[73,85,91] More recent research has investigated the biomechanics of HT, BPTB and QT grafts in cadaveric specimens.[28] The QT displayed greater cross-sectional area than the other graft types, and increased stiffness than the HT. Cumulatively, it appears the biomechanical properties of the QT graft display characteristics which may be favorable including greater cross-sectional area and an elastic modulus that closely approximates a native ACL.[13]

The subgroup tests (Q) on our data indicated no statistically significant difference in rupture rates between BPTB and QT autografts following ACLR. However, it should be noted the QT sample size was substantially lower, with a wide confidence interval that overlapped with BPTB. Despite no statistically significant difference, we believe including the QT data is important due to the increased interest in the graft utilization for ACLR and therefore the increased need for

279 data outlining its outcomes. In a recent systematic review by Hurley et al.[31] comparing QT, BPTB
280 and HT autografts, there were no differences in autograft rupture rates. Nonetheless, the authors
281 observed that QT displayed a lower prevalence of anterior knee pain than with BPTB, and
282 improved stability compared to HT, further supporting the use of QT as an optimal choice for
283 ACLR. A potential disadvantage of the BPTB autograft is the presence of donor site morbidity
284 including anterior knee pain, kneeling discomfort, and short-term reductions in extensor torque.[87]
285 However, recent data[72] indicate no differences in quadriceps peak torque at 6- and 9 months post-
286 surgery. It should also be considered that ACLR autograft donor site morbidity following ACLR
287 with BPTB has been shown to reduce over time.[87]

288 When interpreting the findings from the current study, several factors which have the
289 potential to affect graft rupture rates should be considered. Firstly, the number of studies and
290 respective patients included was lower for the QT graft. The rehabilitation protocols were also not
291 typically well described which makes standardization across studies difficult. Similarly, physical
292 performance metrics at the time of return to sports were not measured. Deficits in quadriceps
293 strength[26] and landing biomechanics[56] have been associated with an increased risk of re-injury
294 after ACLR. Reporting these functional characteristics in athletes with different graft types would
295 appear to be an important factor in understanding the risk of graft failure. Similarly, the time of
296 return to sport can affect graft rupture rates.[7] There is not a universal agreement on when an athlete
297 is safe to return to sport, with some surgeons employing functional tests to determine readiness to
298 RTS while others determine RTS based on length of time since surgery. Younger athletes with less
299 donor site morbidity and increased quadricep strength may pass RTS tests and begin competitive
300 sport activities earlier, potentially increasing their risk of graft failure. The mean age of HT patients
301 was also higher (17 vs. 15.4, and 14.6 years on BTP and QT respectively), and the follow up for

QT was shorter. Finally, there was also a large range across studies in follow up completion rate and, in several studies, this was not reported. Cumulatively, while the data from our literature synthesis indicate that BTP and QT are preferable choices in patients ≤ 25 years, further research is warranted, including RCTs, with longer follow up, and controls in place for the range of confounding factors stated above.

Limitations

There are several limitations to this study. Between the update on January 16, 2024, and August 28, 2024, the original search strategy for Cochrane CENTRAL could not be located. In addition, CINAHL was inadvertently searched instead of Cochrane Central for the update from January 16, 2024 to August 28, 2024. When the error was recognized, the Cochrane Central search strategy was recreated as close to the original search as possible to run the search update on August 28, 2024. We believe that with the overlap of coverage among the databases, the key articles related to this meta-analysis were retrieved and included in this project. Additionally, there was not enough data on type of quadriceps tendon graft used (ASTQT vs QTB) to stratify the data for this analysis which could be a confounding factor. Furthermore, graft failure rate is multifactorial and could be dependent on other factors not reviewed in this analysis, such as sport played, return to sport, and rehabilitation protocol. There were insufficient studies that stratified meniscus surgery types or that outlined rehabilitation protocols to stratify in data analysis. Moreover, due to the nature of non-randomized studies, there is a significant risk of bias attached to many of the the studies included in this analysis.

Conclusion

The results of this meta-analysis suggest that HT grafts are not the optimal choice for young patients undergoing ACLR. Instead, these patients should consider BPTB to reduce the risk of graft failure.

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Appendix:

Appendix 1: PubMed Search Query

PubMed (NLM):

Dates searched: January 1, 1946-March 3, 2022; March 3, 2022-January 16, 2024; January 16, 2024-August 28, 2024

Filters: English

Filters: Use of Boolean "NOT" to exclude case reports, comments, reviews, letters, and editorials

1. ("hamstring tendons/transplantation"[MeSH] OR ("hamstring tendons"[MeSH] AND ("transplantation"[MeSH:noexp] OR transplant*[TW])) OR "hamstring tendons transplant*"[TW] OR "Semitendinosus Tendon"[TW] OR "semitendinosus gracilis"[TW]) AND ("autografts"[MeSH Terms:noexp] OR "Transplantation, Autologous"[Mesh] OR "Autologous Transplant*"[TW] OR "autograft*"[TW] OR "autologous repair"[TW] OR autotransplant*[TW])
2. ("Patellar Ligament/transplantation"[MESH] OR ("patellar ligament"[TW] AND ("transplantation"[MESH:noexp] OR transplant*[TW] OR graft*[TW])) OR ("patella"[MESH] AND "ligaments"[MESH] AND ("transplantation"[MESH:noexp] OR transplant*[TW]))) AND ("autografts"[MESH:noexp] OR "Transplantation, Autologous"[Mesh] OR "Autologous Transplant*"[TW] OR autograft*[TW] OR "autologous repair"[TW] OR autotransplant*[TW])
3. ("Bone-Patellar Tendon-Bone Grafts"[Mesh] OR (("BPTB"[TW] OR "Bone patellar tendon bone"[TW] OR "bone patellar bone"[TW] OR "bone tendon bone"[TW] OR "Tendon Bone Graft*"[TW] OR ("patella"[MESH] AND "tendons"[MESH:noexp]) OR "patellar tendon"[TW]) AND ("transplantation"[MESH:noexp] OR transplant*[TW] OR graft*[TW]))) AND ("autografts"[MESH:noexp] OR "Transplantation, Autologous"[Mesh] OR "Autologous Transplant*"[TW] OR autograft*[TW] OR "autologous repair"[TW] OR autotransplant*[TW])
4. ((("Quadriceps Muscle"[MeSH Terms] AND "Tendons"[MeSH Terms:noexp]) OR "bone quadriceps tendon"[TW]) AND ("autografts"[MeSH Terms:noexp] OR "Transplantation, Autologous"[Mesh] OR "Autologous Transplant*"[TW] OR "autograft*"[Text Word] OR "autologous repair"[TW] OR autotransplant*[TW])) OR "soft tissue quadriceps tendon autograft"[TW] OR "Quadriceps tendon autograft"[TW] OR "quad tendon autograft"[TW] OR "quad autograft"[TW] OR "quadriceps autograft"[TW] OR "Quadriceps tendon autograft"[TW] OR "quadriceps autograft"[TW]
5. "Anterior Cruciate Ligament Injuries/surgery"[MESH] OR "Anterior Cruciate Ligament/surgery"[MESH] OR "Anterior Cruciate Ligament Reconstruction"[Mesh] OR "anterior cruciate ligament*"[TW] OR ACLR[TW] OR ACL[TW] OR "Knee Joint/surgery"[MESH] OR "knee injuries/surgery"[MESH] OR ("knee joint"[TW] OR "knee injur*"[TW] AND (surg*[TW] OR repair[TW] OR reconstruct*[TW]))
6. (#1 OR #2 OR #3 OR #4) AND #5
7. (#6 AND English[LA]) NOT ("review"[PT] OR "systematic review"[PT] OR "systematic review"[TI] OR "meta-analysis"[PT] OR "meta analysis"[TI] OR "case reports"[PT] OR case report*[TI] OR "literature review"[TI] OR "narrative review"[TI] OR "scoping review"[TI] OR letter[PT] OR letter[TI] OR editorial[PT] OR editorial[TI] OR comment[PT] OR comment*[TI] OR booksdocs[Filter] OR preprint[PT])