The Reverse Fragility Index Of Graft Failure Rates Between Hamstring and Bone-Patellar Tendon-Bone Autografts for ACL Reconstruction: A Systematic Review and Meta-Analysis of RCTs Reporting a Non-Significant Result

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INTRODUCTION:

While arthroscopic anterior cruciate ligament (ACL) reconstruction is one of the most frequently performed procedures in orthopaedics, much controversy exists regarding the optimal graft type. In a recent survey study of members of the American Orthopaedic Society for Sports Medicine (AOSSM) and Arthroscopy Association of North America (AANA), the second most important factor for graft selection was graft failure rates reported in the literature. However, the current evidence on failure rates between two of the most frequently used grafts, HT autografts and BTB autografts, is conflicting. For example, Samuelsen et al. performed a meta-analysis which demonstrated a significantly lower re-rupture rate among BTB autografts (P = 0.01) whereas a meta-analysis from Mouarbes et al. showed no significant difference in re-rupture rates between these two graft types (P = 0.46). This contradictory evidence underscores the difficulty in interpreting the current evidence regarding graft superiority.

The reverse fragility index (RFI) is a novel tool that may be used to appraise the results of studies reporting statistically non-significant results. The purpose of this study was to determine the statistical robustness of randomized controlled trials (RCTs) reporting non-significant differences in anterior cruciate ligament reconstruction (ACLR) graft failure rates between hamstring tendon (HT) and bone-patellar-tendon-bone (BTB) autografts by calculating RFIs.

METHODS: A systematic review and meta-analysis was performed to identify RCTs that compared HT to BTB grafts for ACLR through January 2022. Studies reporting non-significant differences in graft failures ($P \geq 0.05$) were included. The RFI, defined as the fewest number of event reversals needed to change the non-significant graft failure outcome to statistically significant ($P < 0.05$), was recorded for each study. In addition, the number of studies in which the loss to follow-up exceeded the RFI was recorded.

RESULTS:

Among the 16 included RCTs, the median (IQR) sample size was 71 (64-114), and the median (IQR) total number of graft failure events was 4 (4-6). The median (IQR) graft failure rate was 4.28% (2.95-6.43) overall, 4.11% (2.60-6.69) in the BTB group, and 5.41% (2.97-6.25) in the HT group. The median (IQR) RFI was 3 (3-4**).** Thus, 3 changes from “no graft failure” to “graft failure” in either the BTB group or the HT group were needed to change the results to significant from non-significant. Thirteen (81.3%) studies had a loss to follow-up that was greater than the RFI. Among these 13 trials, the median (IQR) loss to follow-up was 11 (8-15) and the median (IQR) RFI was 3 (3-4). The median (IQR) RFQ was 0.038 (0.028-0.050), meaning that 4% of participants had to have a different outcome to flip the results for graft failure from non-significant to significant (Table 2). RFI was not significantly correlated with the total number of observed events (P value = 0.952), sample size (P value = 0.320), or with the number of participants lost to follow-up (P value = 0.210). These trends remained true when analyzing correlation based on autograft group.

DISCUSSION AND CONCLUSION:

The main finding of our meta-analysis is that among the 16 RCTs reporting a non-significant difference in graft failure rates between BTB and HT autografts, the median RFI was 3. This signifies that in each trial, a reversal of the graft failure outcome in only 3 patients would have flipped the result from statistically non-significant to significant ($P < 0.05$). In addition, the median number of patients lost to follow-up was 11 (3-13), and 13 (81.3%) of the studies had a loss to follow-up rate that exceeded the study RFI. Further, the median RFQ was 3.8% meaning that event reversals in 3.8% of the study population would have flipped the trial results. Since P values are often misunderstood, are not always reliable, and the value of their use is debated, consistent reporting of an RFI and RFQ in addition to P values is recommended to provide a more complete understanding of the stability of neutral study results.

Among the 1498 subjects included in our analysis, 69 graft failures occurred (4.28%). Samuelsen et al. found a comparable rate of graft failure of 2.84% in a meta-analysis of 47,613 patients. They also identified a significantly higher failure rate among HT autografts compared to BTB autografts (2.84% vs. 2.8%, P = 0.01). Our systematic review also identified 1 RCT (which was excluded from our analysis) that similarly reported significantly different failure rates between these graft types. Additionally, a notable retrospective study of 45,000 patients from the Scandinavian ACL registries also found a significant difference in graft failure rates, in favor of BTB autografts. These studies’ results are direct contradictions to the 16 studies we included in this review and multiple prior meta-analyses, which found no significant difference in failure rates between HT and BTB autografts. The results of our study provide insight that may reconcile this conflicting body of evidence by suggesting that the results of the studies showing non-significant differences in failure rates are fragile.

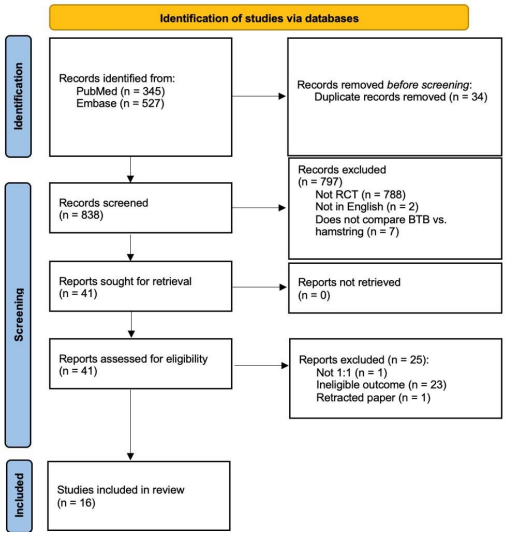

Table 1. Characteristics of Included Randomized Controlled Trials

Characteristic	No. of Studies (%)
Total No.	16
Sample size, median (IQR)	
Total	72 (64-115)
BTB	34 (32-58)
Hamstring	37 (32-57)
Year of publication	
2001-2005	3 (18.8)
2006-2010	5 (31.3)
2011-2015	3 (18.8)
2016-2020	4 (25.0)
2021	1 (6.3)
Industry funding	
Yes	0
No/unclear	16 (100.0)
Journal	
American Journal of Sports Medicine	9 (56.3)
Knee Surgery, Sports Traumatology, Arthroscopy	2 (12.5)
Other	5 (31.3)

Other includes *Arthroscopy (n=1), International Orthopaedics* (n=1), *Journal of Clinical Orthopaedics and Trauma* (n=1), *Orthopaedic Journal of Sports Med* (n=1), *Scandinavian Journal of Medicine & Science in*