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CME

A Systematic Review, Meta-analysis, and Meta-regression

Jonathan C. Riboh,*† MD, Vic Hasselblad,‡ PhD,
Jonathan A. Godin,† MD, and Richard C. Mather III,† MD
Investigation performed at Duke University, Durham, North Carolina

Background: While numerous cadaveric, in vivo, and clinical studies have compared transtibial and independent drilling of femoral tunnels during anterior cruciate ligament reconstruction, there is no evidence-based consensus on which technique affords the best outcome.

Hypothesis: There is no difference in clinical outcome between transtibial and independent drilling of femoral tunnels.

Study Design: Systematic review with meta-analysis and meta-regression.

Methods: Cadaveric, in vivo, and clinical studies comparing transtibial and independent drilling techniques were systematically identified. A qualitative synthesis of nonrandomized studies and meta-analysis of randomized controlled trials (RCTs) were performed. In addition, a meta-regression analysis of RCTs that did not directly compare drilling techniques was performed.

Results: A total of 49 studies were included in the qualitative review, and 15 were included in the meta-analysis; 22 studies were included in the meta-regression. In biomechanical studies, independent drilling placed the center of the femoral tunnel closer to the center of the femoral footprint (mean difference, 2.69 mm; 95% CI, 0.46-4.92; $P < .00001$). Independent drilling reduced anterior tibial translation with the Lachman examination (mean difference, 2.2 mm; 95% CI, 0.34-4.07; $P = .02$), 134 N of anterior load (mean difference, 1 mm; 95% CI, 0.29-1.71; $P = .006$), and simulated pivot shift (mean difference, 3.36 mm; 95% CI, 1.88-4.85; $P < .00001$). The meta-analysis showed improved Lysholm scores with independent drilling (mean difference, –0.62 points; 95% CI, –1.09 to –0.55; $P = .009$), although the clinical relevance of this small difference is questionable. There were no significant differences in International Knee Documentation Committee (IKDC) objective scores or Tegner scores between groups. With the meta-regression, there were no significant differences in failure rates or IKDC objective scores.

Conclusion: While there are biomechanical data suggesting improved knee stability and more anatomic graft placement with independent drilling, no significant clinical differences were found between the 2 techniques.

Clinical Relevance: The current evidence shows that transtibial and independent drilling techniques have equivalent clinical outcomes at short-term to midterm follow-up. The long-term effects of subtle differences in tunnel position and postoperative knee kinematics should be further studied in dedicated, prospective cohort and randomized studies.

Keywords: transtibial; outside-in; anteromedial portal; systematic review; meta-analysis; meta-regression

Anterior cruciate ligament (ACL) reconstruction is the sixth most common procedure performed in orthopaedics.[28] Approximately 100,000 ACL reconstructions are performed annually in the United States.[64] As a result, ACL reconstruction is subject to extensive research. A search in the National Center for Biotechnology Information/US National Library of Medicine's PubMed database for "anterior cruciate ligament" returns 984 studies from 2012 alone. In spite of these efforts, there is still controversy about the best technique for reconstruction.

There has been a shift in the past decade from transtibial (TT) preparation of the femoral tunnel toward independent drilling of this tunnel, either through an

*Address correspondence to Jonathan C. Riboh, MD, Division of Sports Medicine and Shoulder Surgery, Department of Orthopaedic Surgery, Duke University, 6002 Tahoe Drive, Durham, NC 27713 (e-mail: jonathan.riboh@duke.edu).

†Division of Sports Medicine and Shoulder Surgery, Department of Orthopaedic Surgery, Duke University, Durham, North Carolina.

‡Duke Clinical Research Institute, Duke University, Durham, North Carolina.

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anteromedial portal (AMP) or an outside-in (OI) technique. In a 2006 survey of the American Orthopaedic Society for Sports Medicine, 90% of the surgeons were using a TT method.[23] A more recent survey of the Canadian Orthopaedic Association, published in 2011, showed that 70% of the surgeons still preferred the TT technique.[45] The most recent survey, published in 2013, found that 68% of surgeons are using an independent drilling technique, and only 31% are still using a TT guide.[17] This trend has been driven by the goal of obtaining the most "anatomic" reconstruction possible.[57] Much has been written about this topic, but there has been no comprehensive review of the high-quality biomechanical and clinical literature to support this change in practice patterns.

In this systematic review, we address 3 principal questions: (1) Does independent drilling better re-create the anatomy of the femoral footprint? (2) Does independent drilling better re-create knee biomechanics? (3) Does independent drilling result in superior clinical outcomes?

MATERIALS AND METHODS

Review Protocol

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (www.prisma-statement.org) were used to design our systematic review and meta-analysis.

Information Sources

The online databases PubMed (www.ncbi.nlm.nih.gov/pubmed), EMBASE (www.elsevier.com/online-tools/embase), and Cochrane (www.cochrane.org) were reviewed for all English-language studies published before April 1, 2013.

Search

Four separate searches of each database were performed using the following key phrases: (1) "anterior cruciate ligament transtibial," (2) "anterior cruciate ligament anteromedial portal," (3) "anterior cruciate ligament outside-in," and (4) "anterior cruciate ligament independent tunnel." No limits were applied to the searches.

Eligibility Criteria

Eligibility criteria for inclusion in the "cadaveric study" section of the review were as follows:

1. a controlled laboratory experiment using human or animal cadaveric knees;
2. a direct comparison of TT or independent (AMP or OI) techniques;
3. randomization of specimens into different study groups;
4. full reporting of outcomes including means, standard deviations, and sample numbers; and
5. the use of appropriate statistical methods.

Eligibility criteria for inclusion in the "in vivo" section were as follows:

1. an analysis of human patients undergoing ACL reconstruction;
2. a direct comparison of TT or independent (AMP or OI) techniques;
3. an analysis of biomechanical or radiographic outcomes;
4. full reporting of outcomes including means, standard deviations, and sample numbers; and
5. the use of appropriate statistical methods.

Eligibility criteria for inclusion in the "clinical studies" section were as follows:

1. a clinical trial of human patients undergoing ACL reconstruction;
2. a direct comparison of TT or independent (AMP or OI) techniques;
3. an analysis of validated clinical outcomes;
4. full reporting of outcomes including means, standard deviations, and sample numbers; and
5. the use of appropriate statistical methods.

Eligibility criteria for inclusion in the "meta-regression" section were as follows:

1. a randomized controlled trial comparing different ACL grafts or comparing single- versus double-bundle reconstruction,
2. an overall low risk of bias based on the standardized Cochrane questionnaire,
3. a clear indication in the methods section of the use of TT or independent drilling, and
4. a single drilling technique used for all patients in a given study.

Study Selection

All abstracts were reviewed in duplicate by 2 of the authors (J.C.R. and J.A.G.) and assessed based on the above criteria. The full text of eligible studies was then reviewed by the same authors before final inclusion in the systematic review. If $\geq$2 studies assessed the same outcome, they were considered candidates for meta-analysis.

Data Collection Process

Data were then extracted in duplicate from all studies using a standardized form created by the authors at the onset of the review. Any inconsistencies between reviewers were resolved by joint review of the involved studies.

Data Items

All outcome variables reported in the literature were included in our data extraction sheet.

Summary Measures

For continuous outcomes, the summary measure was the difference of the means. For dichotomous outcomes, the summary measure was an odds ratio.

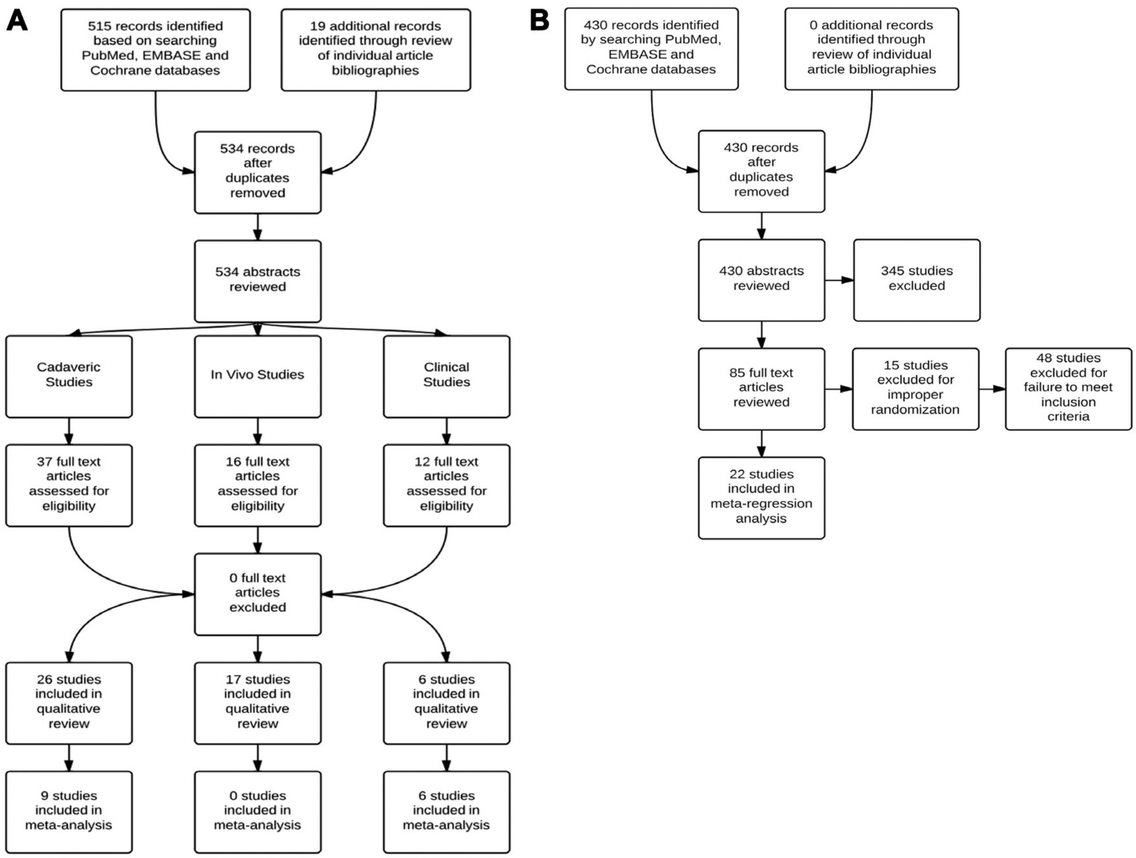

Figure 1. Study design flowchart. (A) Characteristics of the systematic review and meta-analysis. (B) Characteristics of the meta-regression.

Synthesis of Results

All studies included in the meta-analysis were reviewed in duplicate for study quality using the standardized Cochrane database questionnaire (www.cochrane.org). Heterogeneity was assessed by comparing study designs, interventions, and outcomes. In addition, statistical tests of heterogeneity (τ^2, χ^2, and I^2) were used. Given the observed heterogeneity, random-effects DerSimonian and Laird models were used for continuous and dichotomous variables included in the meta-analysis. All statistical analyses were performed using Review Manager (RevMan, Version 5.1, The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark). Statistical significance was defined as a P value <.05.

Sensitivity Analysis

The most important assumption in this study was that the AMP and OI drilling techniques are equivalent. This hypothesis was tested by running separate meta-analyses for the OI versus TT comparison, the AMP versus TT comparison, and the OI/AMP versus TT comparison. We also tested the importance of the meta-analysis model by computing fixed-effects and random-effects models for each of the clinical trial outcomes. Fixed-effects inverse variance models were used for continuous variables, and fixed-effects Mantel-Haenszel models were used for dichotomous variables.

Meta-regression Analysis of Randomized ACL Studies

Based on the recommendation of the Agency for Healthcare Research and Quality,[46] outcomes that were reported in ≥10 studies were included in the meta-regression. The analysis was based on the log odds of these events. We used a random-effects model that was a generalization of the standard random-effects models used in meta-analyses. We assumed that the log odds for each arm, $log\text{-}odds_{ij}$, could be described by the following model:

$$Log - oddsij = \alpha_i + \sum_{j=1}^{3} x_{ij}\beta_{ij},$$

where i denotes the study, and j denotes the specific treatment within a study. α_i represents the mean for usual care and is assumed to be random and normal with variance $({SE_{ij}}^2 + \sigma^2)$; SE_{ij} is the standard error of the jth log odds from the ith study, and σ^2 is the extra variation from the random-effects model. x_{ij} is "1" if the jth treatment is present and "0" if otherwise. β_j (j = 1, 2, 3) are the log odds ratios to be estimated for each treatment. This model was fitted using SAS PROC NLMIXED (Version 2009,

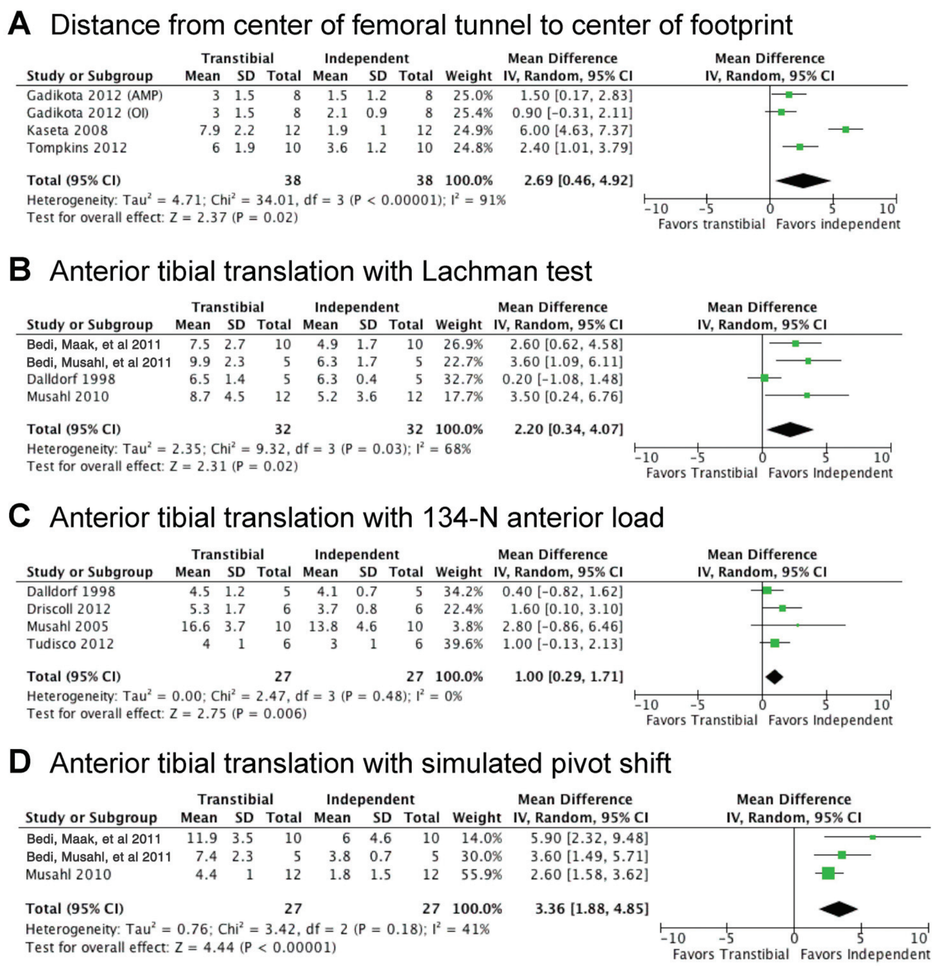

Figure 2. Outcomes of cadaveric studies. (A) Distance between the center of the native femoral footprint of the anterior cruciate ligament and the center of the femoral tunnel. (B) Anterior tibial translation with a manual Lachman test. (C) Anterior tibial translation with the application of a 134-N load. (D) Anterior tibial translation with a simulated pivot-shift maneuver. All distances are reported in millimeters.

SAS Institute Inc, Cary, North Carolina) with "subject" set to the particular study, *i*.

RESULTS

Cadaveric Studies

Tunnel Characteristics. Our literature search yielded 21 studies that compared, in vitro, the characteristics of tunnels drilled with the TT and independent techniques. A summary of the study selection process can be seen in Figure 1A.

Drilling independently placed the femoral tunnel 2.69 mm closer to the center of the anatomic femoral footprint than drilling through the tibial tunnel (95% confidence interval [CI], 0.46-4.92; P = .02) (Figure 2A).[27,36,66,72] Specifically, TT femoral tunnels were anterior and proximal to the ideal location.[8,27,36] In addition, a TT tunnel covers only 60% of the native femoral footprint as compared with 97.7% for a tunnel drilled through an AMP.[56,72] Specifically, a TT femoral tunnel catches a smaller portion of the posterolateral bundle footprint.[27]

Two studies provide counterevidence that an anatomic femoral tunnel position can be achieved with TT drilling.[32,52] A series of technical modifications were required.[52] First, a modified starting point, proximal and medial to the standard technique,[32,52] was used. The posterolateral rim of the tibial tunnel was then beveled with a cannulated reamer. This allowed the femoral guide pin to be placed within 0.3 mm of the center of the native femoral footprint.[52] These modifications did come at a price, resulting in a shorter bone bridge between the tibial tunnel and the medial plateau as well as shorter tibial tunnels.

It is widely believed in the clinical setting that the length of the graft within bone tunnels influences the graft's healing potential, even though basic science support for this claim is sparse.[25] Direct comparison of mean femoral tunnel lengths between the TT, OI, and AMP techniques failed to show a statistically significant difference in 2 studies.[9,39] However, a third study showed that TT femoral tunnels were longer than those drilled through an AMP.[16]

Several biomechanical studies have shown that increasing obliquity of the femoral tunnel in the coronal plane correlates with better restoration of knee kinematics and better tibial rotational control.[33,42,59,78] In the 3 cadaveric studies reporting this outcome, independent drilling consistently resulted in greater femoral tunnel obliquity than TT drilling.[4,9,39]

Posterior wall blowout is a well-known contributor to ACL reconstruction failure, particularly when intraosseous fixation is used.[55] While 1 study found no significant difference in the posterior femoral tunnel wall thickness between the TT and AMP drilling techniques, all other studies demonstrated thinner posterior walls and a higher incidence of posterior blowout with the independent drilling technique.[9,27,39]

Biomechanical Implications. Knee stability with respect to the ACL can be measured by the amount of anterior tibial translation with the Lachman examination. On average, an additional 2.2 mm of translation occurs after TT reconstruction as compared with independent reconstruction (95% CI, 0.34-4.07; P = .02) (Figure 2B).[7,8,19,48] Another strategy is to measure the amount of anterior translation with the application of 134 N of anterior load and the knee in 30° of flexion. Using this method, an additional 1 mm of anterior tibial translation occurs after TT reconstruction as compared with independent reconstruction (95% CI, 0.29-1.71; P = .006) (Figure 2C).[19,21,47,73]

Several groups have performed a rigorous assessment of rotational stability after ACL reconstruction. Three studies from a single institution used a custom continuous passive motion device to re-create the pivot shift.[7,8,48] The consistency of their methods allowed a quantitative meta-analysis, which showed that there was significantly more anterior tibial subluxation in knees undergoing TT reconstruction as compared with independent reconstruction (mean difference, 3.36 mm; 95% CI, 1.88-4.85; $P < 10^{-5}$) (Figure 2D).[7,8,48]

The other approach to a standardized pivot shift was to apply simultaneous valgus and internal rotation moments using a robotic arm in various angles of knee flexion. Four of these studies reported increased anterior tibial translation after TT reconstruction as compared with independent reconstruction.[38,47,61,65] A single study, in a porcine cadaveric model, failed to show a difference between the 2 techniques.[37]

Another important outcome is the stress seen by the reconstructed ACL and the resultant strain patterns within the graft. Ideally, the stress and strain characteristics of a graft should match those of the native ACL.[14] Two of 3 studies showed that in response to an anterior-directed load, graft forces and elongation were lower after TT reconstruction as compared with independent reconstruction.[37,38] No difference was seen between the groups in the third study.[61] However, neither independent nor TT reconstruction was able to re-create the stress-strain patterns of the native ACL.[61] Similarly, all 3 studies agreed

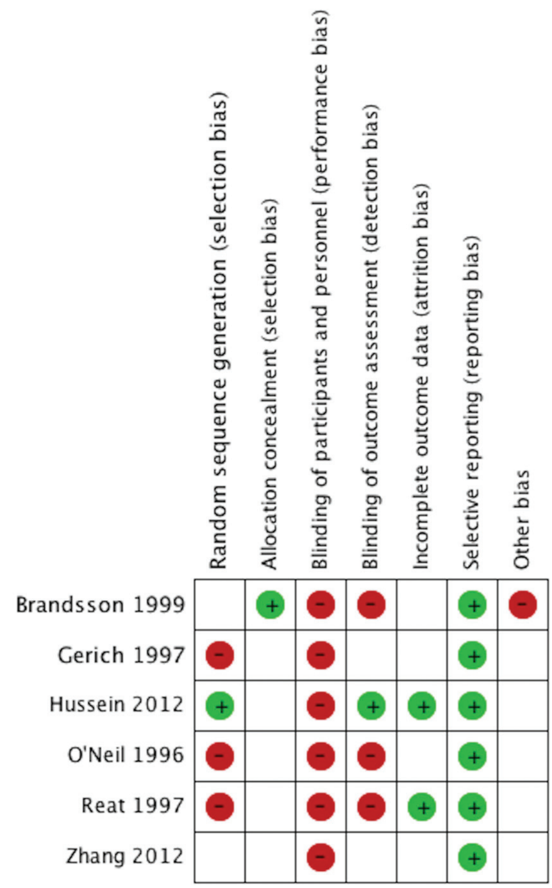

Figure 3. Methodological characteristics of the randomized clinical trials included in the meta-analysis. +, low risk of bias; –, high risk of bias.

that in response to a rotational load, there was no significant difference between drilling techniques in the graft stress-strain patterns, and neither technique could re-create the native ACL properties.[37,38,61]

Resting graft tension has also been of great interest. Excessive tension can lead to graft wear at the femoral tunnel, poor graft vascularity, myxoid degeneration, inferior mechanical properties, posterior subluxation of the tibia, and limited knee extension.[62] In our review, a single cadaveric study assessed resting graft tension.[62] The authors demonstrated that increasing tunnel obliquity in the coronal plane, as is done with independent drilling, led to decreased graft tension in flexion.

In Vivo Studies

A smaller number of studies are available comparing tunnel properties and knee kinematics in vivo. Radiographic analysis was the most commonly used method.[15,20,51,59,77] On both anteroposterior and notch views, femoral tunnels drilled independently were more horizontal and oblique when compared with tunnels drilled through the tibia.[15,20,51] Femoral tunnels drilled independently were

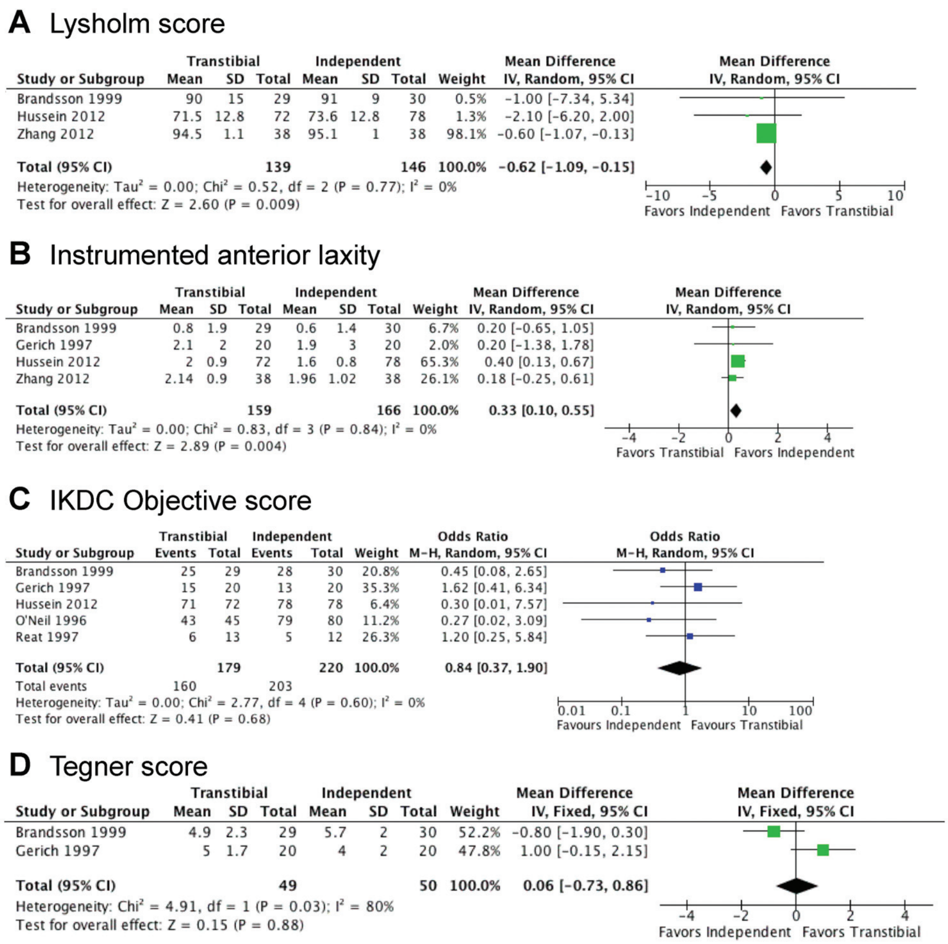

Figure 4. Meta-analysis of randomized clinical trials. (A) Lysholm scores. Scores are reported on a standard 100-point scale. (B) Instrumented anterior laxity. All values are reported in millimeters of anterior tibial translation. (C) International Knee Documentation Committee (IKDC) objective scores. An event was defined as an IKDC score of normal (A) or nearly normal (B). (D) Tegner scores. Scores are reported on a standard 10-point scale.

also more horizontal in the sagittal plane.[20,51] Additionally, TT reconstruction resulted in greater tibial and femoral tunnel enlargement on radiographs obtained 1 year after surgery.[77]

Postoperative cross-sectional imaging was also frequently used to compare tunnel characteristics after ACL reconstruction.[11,18,31,60] Three magnetic resonance imaging (MRI) studies demonstrated that femoral tunnels drilled independently were more oblique in the coronal and sagittal planes as compared with TT femoral tunnels.[11,18,31] There was also evidence that the aperture of the femoral tunnel was closer to the center of the anatomic footprint when independent drilling was used.[1,11,18,60]

Studies in a motion analysis laboratory have also been performed. One group found that reconstruction through an AMP restored the normal tibial translation profile but led to more tibial rotation than in the normal knee.[54] In a larger study of 84 patients, tibial rotation was measured during level walking.[75] Using a TT technique, the greater the coronal graft obliquity, the more stable the knee was to tibial rotation.[75]

The most sophisticated in vivo biomechanical data come from the combination of MRI and biplanar fluoroscopy, creating a 3-dimensional model of the knee during a functional movement. After TT reconstruction, there was significantly more anterior tibial translation, medial tibial translation, and tibial internal rotation during a single-leg lunge.[2]

Clinical Studies

Six randomized studies met inclusion criteria for our analysis. Four of the studies compared OI and TT drilling,[12,30,50,53] while 2 compared AMP and TT drilling.[34,80] An assessment of study quality was performed, and the results are summarized in Figure 3.

The meta-analysis results are shown in Figure 4. The results of the sensitivity analysis are shown in Table 1. This analysis confirmed the validity of grouping OI and AMP drilling into a single category. It also showed that the results of fixed-effects and random-effects models were essentially identical.

TABLE 1
Results of the Sensitivity Analysis[a]

	Lysholm Score			Instrumented Anterior Laxity			IKDC Objective Score			Tegner Score		
	Mean Difference	95% CI	*P*	Mean Difference	95% CI	*P*	Odds Ratio	95% CI	*P*	Mean Difference	95% CI	*P*
Technique												
OI	–1	–7.34 to 5.34	.76	0.2	–0.55 to 0.95	.6	0.9	0.39 to 2.09	.81	0.09	–1.67 to 1.86	.92
AMP	–0.62	–1.09 to 0.15	.01	0.34	0.11 to 0.57	.004	0.3	0.01 to 7.57	.47	NA	NA	NA
OI + AMP	–0.62	–1.09 to –0.15	.009	0.33	0.1 to 0.55	.004	0.84	0.37 to 1.9	.68	0.09	–1.67 to 1.86	.92
Meta-analysis model												
Random effects	–0.62	–1.09 to –0.15	.009	0.33	0.1 to 0.55	.004	0.84	0.37 to 1.9	.68	0.09	–1.67 to 1.86	.92
Fixed effects	–0.62	–1.09 to –0.15	.009	0.33	0.1 to 0.55	.004	0.82	0.38 to 1.8	.63	0.06	–0.73 to 0.86	.88

[a]The effect of combining the outside-in (OI) and anteromedial portal (AMP) drilling techniques on results of the meta-analysis was evaluated as well as the influence of using a random- or fixed-effects model for the meta-analysis. Mean differences are reported for continuous variables and odds ratios for categorical variables. IKDC, International Knee Documentation Committee; NA, not applicable.

TABLE 2
Results of the Meta-regression Analysis[a]

	Failure Rate			
Technique	Mean ± SD, %	OR	95% CI	*P*
Transtibial	2.9 ± 3.4	0.74	0.25-2.219	.56
Independent	2.8 ± 5.1	—	—	—
	IKDC Objective Score, % A/B			
Technique	Mean ± SD, %	OR	95% CI	*P*
Transtibial	85.3 ± 17.0	1.48	0.49-4.49	.46
Independent	92.9 ± 6.7	—	—	—

[a]No significant differences were seen in failure rates at final clinical follow-up or in the incidence of International Knee Documentation Committee (IKDC) objective scores of A (normal) and B (nearly normal). OR, odds ratio.

Meta-regression Analysis of High-Quality Randomized ACL Studies. Given the lack of conclusive evidence in this meta-analysis, we used the highest quality randomized studies in the ACL literature for a meta-regression analysis in which the effect of the drilling technique was assessed as part of a global multivariate model that also included the graft type and number of bundles. Twenty-two studies were included (Figure 1B).[§] The independent drilling technique was used in 9 studies[3,10,34,58,68-70,76,79] and the TT technique in the remaining 13 studies.[‖] The results are summarized in Table 2. There was no significant difference between failure rates with the independent (2.8% ± 5.1%) and TT techniques (2.9% ± 3.4%) (odds ratio [OR], 0.74; 95% CI, 0.25-2.219; *P* = .56). There was also no significant difference in the likelihood of achieving an IKDC objective score of A and B between the independent (92.9% ± 6.7%) and TT techniques (85.3% ± 17.0%) (OR, 1.48; 95% CI, 0.49-4.49; *P* = .46).

DISCUSSION

The key findings of the present study indicate that while biomechanical differences are seen in cadaveric models and in vivo, the clinical outcomes of ACL reconstruction using TT and independent drilling of the femoral tunnel are not significantly different. In biomechanical studies, improved translational and rotational stability were observed with independent tunnels.[7,8,19,21,47,48,73] Furthermore, independent femoral tunnels were more oblique in the sagittal and coronal planes, resulting in decreased resting graft tension, a closer approximation of natural graft forces during motion, shorter tunnel lengths, and a greater risk of posterior wall blowout.

In clinical outcome studies, there were no differences in failure rates, IKDC objective scores, or Tegner scores.[12,30,34,50,53,80] While a statistically significant difference in a Lysholm score of 0.62 points favored independent

[§]References 3, 6, 10, 22, 24, 26, 34, 35, 40, 41, 43, 44, 49, 58, 67-71, 74, 76, 79.

[‖]References 6, 22, 26, 34, 35, 40, 41, 43, 44, 49, 67, 71, 74.

drilling, this is well below the clinically important difference of 8.9 points for the Lysholm score after ACL injury.[13]

With respect to internal validity, there are several limitations to this study. First, variations in technique exist within each group. This is particularly true within the TT group, where multiple surgical modifications have been described in the studies that we compared. For the purpose of our analysis, an assumption was made that OI and AMP reconstructions are equivalent. This was based on cadaveric data showing that an equal footprint coverage is achieved with these techniques.[27] In addition, a sensitivity analysis showed that analyzing the OI and AMP techniques separately or as a single group did not change the results of the meta-analysis. All of the randomized clinical trials suffered from performance bias because surgeons could not be blinded to the procedure that they were performing. Also, our systematic review included only published data, leaving a potential for reporting bias, because negative results are less likely to be reported. Finally, the sensitivity of the outcome measures used in this study (IKDC objective score, Lysholm score, and Tegner score) may be too low to detect small but meaningful differences in patient outcomes. The Knee Injury and Osteoarthritis Outcome Score (KOOS) is the most detailed score available and is used as the major outcome score in the Multicenter Orthopaedic Outcomes Network (MOON).[63] However, it was not included in a sufficient number of randomized trials to be assessed in our meta-analysis.

With respect to external validity, no characteristics of the study patients were identified that would prevent generalization of these results to the typical population undergoing ACL reconstruction. Exceptions to this would be the skeletally immature or very elderly patient and revision ACL reconstructions.

There is a single prior systematic review on this topic.[29] This included only a comparison of the OI and TT techniques. In addition, no quantitative meta-analysis was performed. However, their conclusions were similar to ours: that validated clinical outcome scores were no different between groups. Another study tried to perform an indirect comparison of the TT and AMP techniques by analyzing randomized trials comparing patellar tendon and hamstring grafts.[5] This is not unlike the idea behind our meta-regression analysis. However, they used inappropriate statistical methods that overestimated the significance of their results.

The ideal study design to compare the clinical outcomes of TT and independent drilling is a large multicenter randomized trial. In particular, it would be of great interest to directly compare modern modified TT reconstructions with independent techniques. Many surgeons, based on the available basic science data reviewed here, believe that independent drilling is superior and would be unwilling to participate in randomization. The results of this meta-analysis suggest that the clinical differences are not dramatic and will hopefully prompt the execution of more prospective studies. In addition, several key outcomes were not consistently reported in the reviewed studies. These include the development of arthritis, return to sport, and revision rates.

In summary, a meta-analysis of cadaveric and human biomechanical data finds statistically significant improvements in knee stability and more anatomic graft placement with independent drilling, but no significant differences in clinical outcome measures can be seen between the 2 groups based on the current evidence. As many surgeons are still in the learning curve with independent techniques, a critical analysis of outcome measures is important going forward. Further randomized studies and the analysis of large prospective databases like the MOON ACL registry will help guide future practice patterns.

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