

# Higher Rates of Residual Postoperative Instability after Anterior Cruciate Ligament Reconstruction in Female Patients: A Systematic Review of Level II Studies



Garrett R. Jackson, M.D., Jonathan Lee, B.S., Trevor Tuthill, B.S., Jimmy Chan, M.D., Joan Sugrañes, M.D., Colton C. Mowers, B.S., Anjay Batra, B.S., Zeeshan A. Khan, M.D., Enzo S. Mameri, M.D., Christopher M. Brusalis, M.D., Jorge Chahla, M.D., Ph.D., and Nikhil N. Verma, M.D.

**Purpose:** To compare revision rates and residual postoperative instability after anterior cruciate ligament (ACL) reconstruction based on biological sex. **Methods:** A systematic review was conducted according to the 2020 PRISMA guidelines. PubMed, Embase, MEDLINE, and Cochrane library databases were queried from database inception through October 2022. Level I and II prospectively-enrolling human clinical studies that compared revision rates and physical examination of postoperative stability after ACL reconstruction between male and female patients were included. Outcomes were stratified by patient sex and quantitatively compared using a  $\chi^2$  test. Study quality was assessed using the MINORS criteria. **Results:** Four studies consisting of 406 patients (50% males) with a mean age of 25 years (range, 13.9-62 years) were identified. Mean follow-up time was 34.4 months (range, 22-60 months). Hamstring tendon autografts were used in 62% of ACL reconstructions in males and in 65% of ACL reconstructions in females, whereas bone-patellar tendon-bone autografts were used in 38% and 35% of procedures in males and females, respectively. A residual positive Lachman test result was more frequently reported among females compared to males (5.8% vs 0.6%;  $P = 0.03$ ). No significant difference in revision rates or residual pivot-shift on examination was observed between males and females ( $P = 0.38$  and  $P = 0.08$ , respectively). **Conclusion:** Female patients undergoing ACL reconstruction have higher reported rates of residual anterior instability with Lachman than male patients. However, no sex-based differences were identified with residual pivot-shift on examination or rate of revision ACL surgery. **Level of Evidence:** II; Systematic Review of level II studies.

The incidence of anterior cruciate ligament (ACL) injuries has grown considerably in recent years,<sup>1,2</sup> with an estimated 250,000 ACL reconstructions performed annually in the United States.<sup>1</sup> Increased participation in high school and collegiate athletics among female athletes accounts for a significant proportion of growth in ACL injuries and subsequent ACL

reconstruction.<sup>1,3,4</sup> Consequently, there has been an abundance of research exploring the etiology, mechanisms of ACL injuries, and risk factors for ACL injury.<sup>5-7</sup> Females are 2 to 8 times more likely to sustain an ACL injury.<sup>5-7</sup> This increased relative risk among females is multifactorial and may be secondary to anatomic factors, such as a more narrow femoral intercondylar

From the Department of Orthopaedic Surgery, Rush University Medical Center (G.R.J., T.T., J.C., J.S., C.C.M., A.B., Z.A.K., E.S.M., C.M.B., J.C., N.N.V.), Chicago, Illinois; Johns Hopkins University School of Medicine (J.L.), Baltimore, Maryland, U.S.A.; the Department of Orthopaedic Surgery, Hospital de La Santa Creu I Sant Pau, Universitat Autònoma de Barcelona (J.S.), Barcelona, Spain; the Instituto Brasil de Tecnologia da Saúde (E.S.M.), Rio de Janeiro; and the Department of Orthopedics and Traumatology, Federal University of São Paulo (EPM-UNIFESP) (E.S.M.), São Paulo, Brazil.

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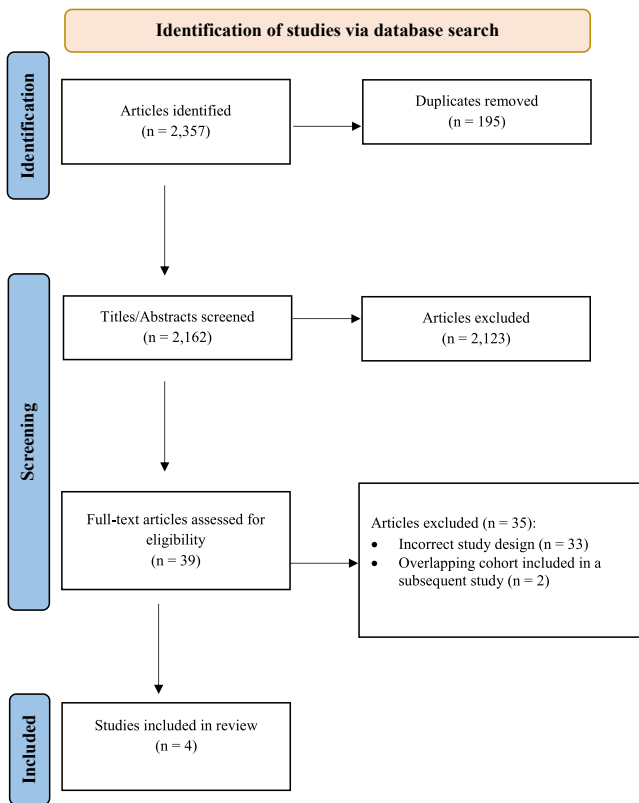
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Address correspondence to Nikhil Verma, M.D., Department of Orthopaedic Surgery, Rush University Medical Center, 1611 W Harrison St., Chicago, IL 60612, U.S.A. E-mail: [Nikhil.verma@rushortho.com](mailto:Nikhil.verma@rushortho.com)

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**Fig 1.** Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) flow diagram.

notch width<sup>8,9</sup> and increased lateral compartment convexity,<sup>10,11</sup> differential dynamic biomechanics<sup>12,13</sup> during landing, and hormonal differences on ligament elasticity.<sup>14</sup> However, despite an increased understanding of ACL injuries over the past few decades, sex-based differences in clinical outcomes after ACL reconstruction is less well defined.<sup>15</sup>

Although current literature has examined the prevalence, etiology, and management of ACL injuries and reconstruction, few studies have explored how biological sex influences ACL reconstruction failure.<sup>1,5,7,16,17</sup> To date, low-level studies (level of evidence III and IV) have established conflicting results when analyzing the effect of patient sex on ACL revision surgery.<sup>15,18,19</sup> One systematic review by Ryan et al.<sup>20</sup> reported no difference in graft failure risk, contralateral ACL rupture risk, or postoperative knee laxity on physical examination between male and female sex. A second systematic review by Mok et al.<sup>21</sup> found no difference in rates of revision; however, females had lower postoperative international knee documentation committee scores and lower rates of graft rerupture. This highlights a distinct gap in knowledge regarding postoperative outcomes. The purpose of this study was to compare revision rates and residual postoperative instability based on biological sex after ACL reconstruction. We hypothesized that no significant differences in revision

rate or physical examination findings of knee instability exist between male and female patients.

## Methods

### Search Strategy and Article Identification

A systematic review was conducted in accordance with the 2020 Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines.<sup>22</sup> A comprehensive literature search was performed on October 10, 2022, by 2 independent reviewers (J.L., T.T.) using the PubMed, Embase, MEDLINE, and Cochrane library databases for level I or II human clinical studies reporting rate of revision surgery and postoperative physical examination tests for knee stability for patients who underwent ACL reconstruction. The following Boolean search string was applied: ((Anterior Cruciate Ligament) OR (ACL) OR (Anterior Cruciate Ligament Reconstruction) OR (ACLR)) AND ((Male) OR (Female) OR (Sex) OR (Gender)) AND ((Reoperation) OR (Revision) OR (Failure)) NOT (review) NOT (Biomechanical) NOT (cadaver) NOT (cadaveric) NOT (animal).

Studies were included if they consisted of human clinical studies with level of evidence I or II, were prospectively enrolling in nature, in English or with English-language translation, and reported revision rate and postoperative knee stability examination for male and female patients after ACL reconstruction. Studies were excluded if they (1) were not written in English or with English-language translation, (2) were biomechanical or cadaveric studies, (3) included patients with open physis, (4) failed to stratify demographics and outcomes by male and female patients, or (5) were retrospective in nature. Systematic reviews, meta-analyses, commentaries, abstracts, editorials, and studies that included patients from national or international registries were also excluded.

The initial search identified 2357 articles. Sequential screening of the articles was performed using the following approach: assessment of duplicate articles, content within the article title, content of the abstract, and full-text review. Full-text review was performed during the study selection process, when appropriate, to determine if an article met eligibility criteria. After title

**Table 1.** Patient Demographics and Procedure Characteristics

	Male (n = 203)	Female (n = 203)
Mean age (y), (range)	25.1 (14-59)	24.9 (13.9-62)
Mean follow-up (mo), (range)	33.4 (22-60)	35.4 (22-60)
Mean Time from injury to surgery, mo (range)	15.8 (0.5-348)	19.2 (0.3-362)
Graft used		
Hamstring tendon	125 (61.6%)	132 (65%)
BTB	78 (38.4%)	71 (35%)
Concomitant meniscal surgery	89 (43.8%)	132 (65%)

**Table 2.** ACL Reconstruction Techniques

Author (Year)	Femoral Tunnel Drilling	Single-Bundle vs Double-Bundle	Graft Type	Graft Diameter, mm	Graft Fixation Method	MINORS Score
Tohyama et al. <sup>27</sup> (2011)	Transtibial	Double-bundle	HT Autograft	Female AM bundle: 6.7 ± 0.4 Female PL bundle: 5.8 ± 0.2 Male AM bundle: 7.2 ± 0.5 Male PL bundle: 6 ± 0.2	Tibia: Two spiked staples Femur: EndoButton (Smith & Nephew, London, UK)	19
Barber-Westin et al. <sup>28</sup> (1999)	AM or Outside-in	Single-bundle	BTB Autograft	9 to 10	Tibia: Interference screw Femur: Interference screw	19
Noojin et al. <sup>29</sup> (2000)	Transtibial	Single-bundle	HT Autograft	—	Tibia: Button or post with spike washer Femur: EndoButton (Smith & Nephew, London, UK)	21
Tsuda et al. <sup>30</sup> (2009)	Transtibial	Both	HT or BTB Autograft	BTB: 10 or 11 HT: —	Tibia: Post screw Femur: EndoButton (Smith & Nephew, London, UK)	20

HT, hamstring tendon; AM, anteromedial; PL, posterolateral; MINORS, methodological index for nonrandomized studies.

and abstract screening, a total of 39 full-text articles were evaluated for eligibility. After full-text review, 4 articles met the inclusion/exclusion criteria and were included in the final analysis (Fig 1). To ensure that all available studies were identified, references from all included studies were reviewed and reconciled to verify that no relevant articles were missing from the systematic review, during which no further studies were identified. To reduce the risk of publication bias, when multiple studies reported on the same or overlapping patient populations, the study with the longest mean duration of follow-up was preferentially included.

### Data Extraction

Data extraction from the included studies was performed using Microsoft Excel version 16.63 (Redmond, WA). Collected variables included study title, publication year, first author name, level of evidence (per Wright et al.<sup>23</sup>), patient demographics, postoperative follow-up time, ACL reconstruction technique, graft type, ACL reconstruction revision rate, and physical examination findings of knee stability (e.g., pivot shift examination, Lachman examination). Collected variables were stratified based on patients' biological sex. The proportions of patients across the total pooled sample with significant residual Lachman ( $\geq 2+$ ), and residual pivot shift ( $\geq 1+$ ) were documented. A 5 mm threshold was chosen in the KT-1000 measurements based on prior studies that determined this numerical value to be associated with an increased risk of knee instability, reduced knee function, and a higher likelihood of requiring surgical intervention to repair the damaged ligament.<sup>24,25</sup> Final follow-up time points were used during extraction and analysis.

### Risk of Bias

Two independent authors (J.L., T.T.) performed a methodological quality assessment among the included studies using the Methodological Index for Non-Randomized Studies (MINORS) criteria. Disagreements were resolved by a third investigator (G.J.), during which time no disagreements occurred. The MINORS criteria is a numerical scale comprised of 12 questions for comparative, nonrandomized studies.<sup>26</sup> The scoring for each question includes a 0 if not reported, 1 if reported, but insufficient, and 2 if reported and sufficient. The maximal score for a comparative study is 24 points.

### Statistical Analysis

The primary outcome measure was the rate of revision surgery after ACL reconstruction at final follow-up in each included study. Secondary outcomes included residual Lachman and residual pivot shift at final follow-up. Statistical comparison for revision rates, residual Lachman, and residual pivot shift between male

**Table 3.** Revision ACL Reconstructions

Author (Year)	Male Mean F/U (mo)	Female Mean F/U (mo)	Male Revision ACLR	Female Revision ACLR
Tohyama et al. <sup>27</sup> (2011)	31.8 (24-60)	36.8 (24-60)	0	0
Barber-Westin et al. <sup>28</sup> (1999)	26.9 (22-42)	25.4 (22-31)	0	0
Noojin et al. <sup>29</sup> (2000)	39.00	40.90	0	2 (5.1%)
Tsuda et al. <sup>30</sup> (2009)	37.5 (24-56)	37.7 (25-56)	1 (1.5%)	2 (2.6%)

ACLR, anterior cruciate reconstruction; F/U, follow-up.

and female patients was performed using a risk-difference analysis and were further illustrated in forest plots which were created using Review Manager 5 (The Nordic Cochrane Center, Copenhagen, Denmark). Statistical significance was set at  $P < 0.05$ . Heterogeneity was assessed using the  $I^2$  statistic.

## Results

Four prospectively-enrolling comparative studies assessing sex-based difference in ACL reconstruction outcomes<sup>27-30</sup> with a total pooled sample of 406 patients were identified. The mean MINORS score of the included studies was 19.8 (range, 19-21). All studies were of level II evidence. Male and female groups were each composed of 203 patients. A total of 65 patients (13.8%) were reported lost to follow-up. Mean patient age was 25 years (range, 13.9-62 years), and mean follow-up time was 34.4 months (range, 22-60 months). Autograft sources were used exclusively among the 4 included studies. Hamstring tendon autografts were used in 62% of ACL reconstructions in males and in 65% of ACL reconstructions in females, whereas bone-patellar tendon-bone (BTB) autografts were used in 38% and 35% of procedures in males and females, respectively (Table 1). Transtibial femoral tunnel drilling was used in 3 studies,<sup>27,29,30</sup> whereas 1 study<sup>28</sup> used either an anteromedial or an outside-in technique (Table 2). Of the 203 males, 43.8% ( $n = 89/203$ ) underwent concomitant treatment of meniscal injuries whereas 65% ( $n = 132/203$ ) of females had meniscal injuries resulting in concurrent meniscal repair or partial meniscectomy at the time of ACL reconstruction.

## Revision Rates

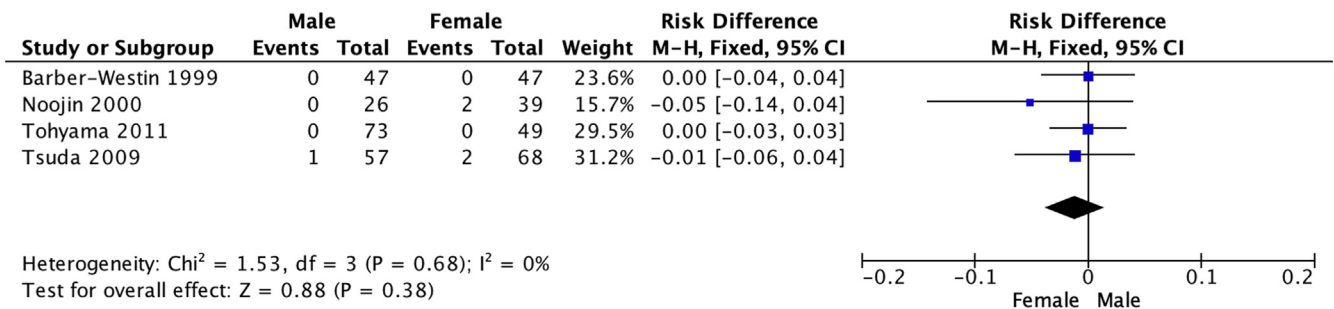
Revision ACL reconstruction occurred in four (2%; range, 0%-5.1%) female patients at final follow-up (Table 3). Graft failure in 2 of these patients occurred because of traumatic reinjury, whereas the other 2 were due to clinical failure, defined by either a 2+ Lachman test, a 1+ or greater pivot-shift, or greater than 5 mm side-to-side difference on KT-1000 arthrometer testing. Among the males, only 1 (0.5%; range, 0%-1.5%) revision ACL reconstruction was reported. This patient's graft failure was due to traumatic reinjury. Compared with revision surgery in the female group, this difference was not statistically significant ( $P = 0.38$ ) (Fig 2).

## Objective Stability Outcomes

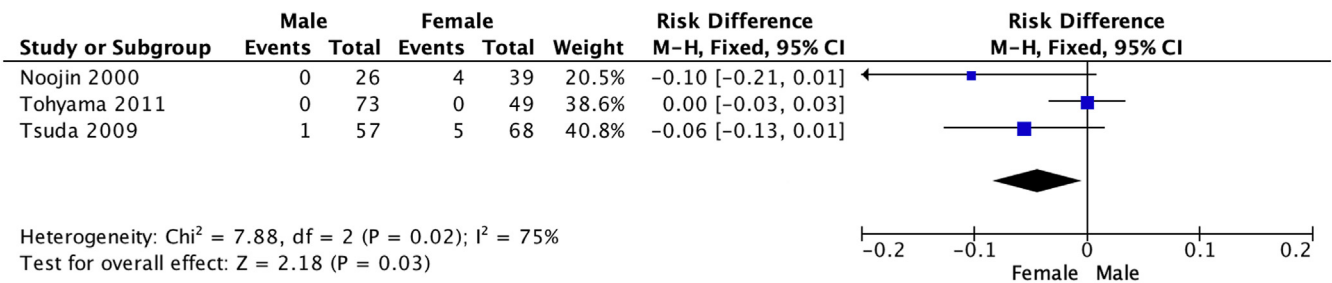
Three studies<sup>27,29,30</sup> consisting of 312 patients reported on residual Lachman. Of these patients, 5.8% ( $n = 9/156$ ; range 0%-10.3%) of females reported a Lachman of 2+ or greater at final follow-up, as compared to 0.6% ( $n = 1/156$ ; range, 0%-1.8%) of males ( $P = 0.03$ ) (Fig 3). All 4 studies reported on residual pivot shift. Additionally, there was a nonsignificant trend toward an increased proportion of female patients with postoperative 1+ or greater pivot shift examination compared to males (20.2% vs 14.3%;  $P = 0.08$ ) (Fig 4, Table 4).

## Discussion

The main finding from this investigation was that female patients undergoing ACL reconstruction have higher reported rates of residual anterior instability with Lachman than male patients, but no sex-based differences were identified in residual pivot-shift on



**Fig 2.** Forest plot illustrating the risk difference in revision rates between male and female patients. CI, confidence interval



**Fig 3.** Forest plot illustrating the risk difference in residual Lachman between male and female patients. CI, confidence interval

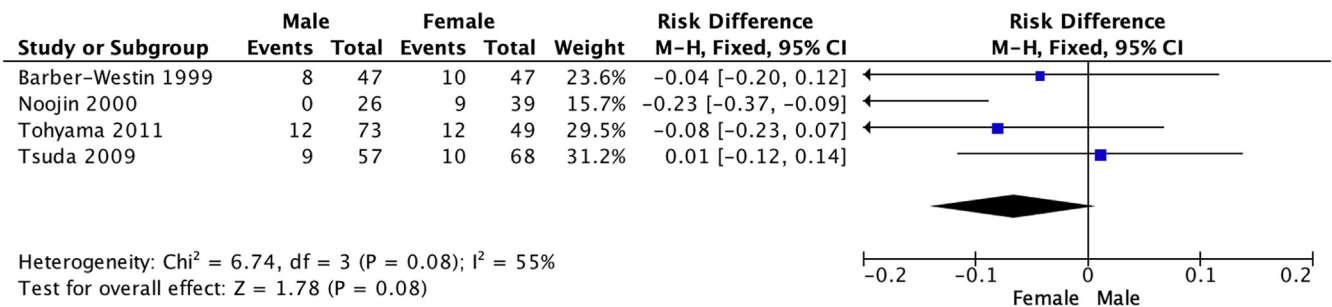
examination or rate of revision ACL surgery. The role of biological sex in ACL injury remains a key area of ongoing investigation. For index injury, female sex has clearly been identified as a risk factor. However, the risk of surgical failure related to sex is less clearly defined. This systematic review found a higher rate of residual knee instability on Lachman exam in females following ACL reconstruction. However, no significant difference based on biological sex was found in residual pivot shift exam or rate of revision surgery after ACL reconstruction.

Studies have suggested that female athletes are more prone to ACL injuries, with a 3.5 times higher incidence among female athletes in basketball and a 2.8 times higher incidence in soccer.<sup>31</sup> With a steadfast rise in female athletic participation over the past 2 decades, there has been a commensurate increase in ACL reconstructions performed among this population. Several explanations have been provided for sex-based differences in ACL injury, including anatomic difference, joint laxity, hormonal influences, and training techniques; but the cause is most likely multifactorial.<sup>31-34</sup> Given these variabilities, it is crucial to stratify outcomes of ACL reconstruction based on biological sex.

Despite a higher relative risk for ACL injury among female athletes, formal investigation and data in ACL literature have been male-focused, and few prospectively-enrolling studies have emphasized comparative assessments of postoperative outcomes based on biological sex. Corry et al.<sup>35</sup> reported that

female patients who underwent ACL reconstruction with a hamstring autograft had increased KT-1000 side-to-side difference in anterior translation compared to male patients with hamstring autograft and female patients with patellar BTB autograft reconstructions. Gobbi et al.<sup>36</sup> found greater laxity in female patients with single-bundle hamstring autograft ACL reconstructions but no difference in graft failure rate, subjective or functional outcomes between sexes. Similarly, Salmon et al.<sup>37</sup> also reported higher laxity on physical examination among females, but no difference in self-reported outcomes.

Our study found that females have a nearly 10-fold risk of experiencing residual 2+ Lachman than males; however, no difference in residual pivot shift was found. It remains unclear whether this sex-based difference in physical examination findings is related to a true biomechanical difference or simply differential sensitivities in the Lachman examination and pivot-shift examination. Historically, the Lachman examination has a higher sensitivity for ACL injuries, so it would be fair to assume that differences in this test could be more prominent than those of a pivot-shift test.<sup>38-40</sup> Alternatively, a Lachman test assesses anterior translation only, whereas a pivot-shift detects simultaneous rotational instability. A higher incidence of surgically-treated meniscal injuries among female patients may have contributed to the increased anterior laxity among females identified in this analysis, given the meniscus' function as a secondary stabilizer to anteroposterior translation.<sup>41</sup>



**Fig 4.** Forest plot illustrating the risk difference in residual pivot shift between male and female patients. CI, confidence interval.

**Table 4.** Objective Stability Outcomes

Author (Year)	Male Pivot Shift	Female Pivot Shift, n (%)	Male Lachman	Female Lachman
Tohyama et al. <sup>27</sup> (2011)	0: 61 (83.6%) 1+: 10 (13.7%) 2+: 2 (2.7%)	0: 39 (79.6%) 1+: 8 (16.3%) 2+: 2 (4.1%)	0: 71 (97.3%) 1+: 2 (2.7%)	0: 48 (98%) 1+: 1 (2%)
Barber-Westin et al. <sup>28</sup> (1999)	0: 39 (83%) 1+: 8 (17%)	0: 37 (78.7%) 1+: 8 (17%) 2+: 1 (2.1%) 3+: 1 (2.1%)	—	—
Noojin et al. <sup>29</sup> (2000)	0: 26 (100%)	0: 30 (76.9%) 1+: 8 (20.5%) 2+: 1 (2.6%)	0: 24 (92.3%) 1+: 2 (7.7%)	0+: 24 (61.5%) 1+: 11 (28.2%) 2+: 4 (10.3%)
Tsuda et al. <sup>30</sup> (2009)	0: 48 (84.2%) 1+: 8 (14%) 2+: 1 (1.8%)	0: 56 1+: 8 2+: 2 3+: 2	0: 47 (82.4%) 1+: 9 (15.8%) 2+: 1 (1.8%)	0: 54 (79.4%) 1+: 9 (13.2%) 2+: 4 (5.9%) 3+: 1 (1.5%)

Our analysis found comparable rates of revision ACL surgery between sexes. These findings are further supported by Tan et al.,<sup>15</sup> Scandinavian registries,<sup>18</sup> and Mok et al.<sup>21</sup> However, a recent study of 7402 primary isolated ACL reconstructions using the New Zealand ACL registry identified male sex as a risk factor for ipsilateral ACL revision surgery.<sup>19</sup> The discrepancy among studies may be explained by different patient demographics, activity levels, and motivation to return to sport, as well as heterogeneity of patients and surgical techniques within and across studies. The present study's findings are strengthened by its focus on Level II studies.

One potential factor that has been considered as a contributor to sex-based differences in ACL reconstruction outcomes is the differential size and quality of autograft tissue between males and females. In the present study, male and female cohorts had similar distributions of autograft sources. Tohyama et al.<sup>27</sup> used hamstring autograft with anatomic double bundle reconstruction; Noojin et al.<sup>29</sup> used hamstring autograft with single bundle reconstruction; Tsuda et al.<sup>30</sup> used patellar BTB autograft with lateralized single bundle reconstruction and hamstring autograft with double bundle reconstruction; Barber-Westin et al.<sup>28</sup> used patellar BTB autograft with single-bundle reconstruction. Tohyama et al.<sup>27</sup> demonstrated that graft diameter of each bundle was significantly smaller in female patients; however, they found no ligament laxity in the female group at 2 years after surgery. These findings support the notion that the inherent nature of ligament size and quality among females likely does not confer reduced knee stability after ACL reconstruction. In addition, ligament size may need to be considered with regard to size of the individual, not just in isolation.

### Limitations

This study is not without limitations. First is the small sample size, which limits the strength of the results. We sought to include only high-quality data from Level I

and II studies, but the exclusion of retrospective studies was 1 factor that limited the sample size. Second, heterogeneous graft sources, surgical techniques, patient-reported outcomes, and postoperative rehabilitation protocols used among the studies create substantial variability in the collected data. Additionally, patient-reported outcome measures could not be investigated because of lack of reporting. Another limitation is the lack of information about baseline laxity and antero-lateral procedures in all but one study.<sup>26</sup> There was also a lack of data from Lachman and pivot shift tests in all included studies except one.<sup>25</sup> One of the important biases is that the rate of loss to follow-up was significant (30%) in another study,<sup>27</sup> which can affect the results. Furthermore, most of the included studies were outdated. This is of concern because current trends of ACL reconstruction were not reflected. Even though most of the studies included in this study described that they performed anatomical reconstruction, nonanatomic or poorly placed graft tunnels could be a cause of laxity and graft failure. Additionally, the definition itself of failure as revision surgery does not account for symptomatic patients whose ACL graft is not satisfactorily functioning but never underwent surgical treatment for a plethora of reasons—including changes in activity profile, lower-demand patients, or patients who looked for a different surgeon after primary failure. Additionally, postoperative knee stability was measured through provider-documented physical examination tests rather than by objective quantitative measurement tools. Last, return to sport was not reported, which is ultimately the primary outcome of interest in this population.

### Conclusion

Female patients undergoing ACL reconstruction have higher reported rates of residual anterior instability with Lachman than male patients. However, no sex-based differences were identified with residual

pivot-shift on examination or rate of revision ACL surgery.

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