ACL Reconstruction: Do Outcomes Differ by Sex?

A Systematic Review

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Background: Anterior cruciate ligament (ACL) reconstruction is frequently performed to restore knee stability and function following ACL injury. Female sex is known to predispose to ACL injury; however, it remains unclear whether female sex predisposes to poor outcomes following ACL reconstruction. We hypothesized that male and female patients exhibit no differences in (1) graft failure risk, (2) contralateral ACL injury risk, (3) knee laxity, and (4) patient-reported outcome scores following ACL reconstruction.

Methods: A systematic review of the literature was performed to identify studies in which results of ACL reconstruction were reported by sex at a minimum of two years. Study findings were reviewed, and meta-analysis was performed when data were sufficiently homogenous.

Results: Thirteen studies were identified from the literature review. Meta-analysis revealed no difference in graft failure risk (eight studies), contralateral ACL rupture risk (three studies), or postoperative knee laxity on physical examination (six studies). There was no evidence of a clinically important difference in patient-reported outcomes according to sex.

Conclusions: Results of ACL reconstruction were similar in male and female patients. More high-quality studies are needed to further evaluate these findings.

The anterior cruciate ligament (ACL) is among the most commonly injured knee ligaments in young, active individuals, and it is the focus of substantial clinical resources and research efforts. A well-described and particularly salient aspect of ACL injury epidemiology is the observation that the risk of ACL injury is twofold to eightfold greater in female compared with male athletes\(^1\). Among other possible causes, this increased risk may be related to an increased prevalence of deficits in dynamic neuromuscular control of the knee recorded in female compared with male subjects\(^1\).

In young, active individuals, ACL reconstruction is frequently performed to facilitate a return to cutting and pivoting sports. Although the results of ACL reconstruction generally are favorable and allow a return to desired activities, outcomes are not always ideal. Graft failure, contralateral ACL rupture, and decreased patient satisfaction are frequently noted following ACL reconstruction\(^5,6\). Numerous authors have identified factors that adversely affect ACL reconstruction outcomes, including smoking\(^7\), the presence of associated meniscal or chondral injuries\(^8\), younger patient age\(^10,12\), and increased activity level\(^10,13\), as well as surgical factors such as the choice of graft type\(^10\) and size\(^7\). The influence of patient sex on the outcome following ACL reconstruction remains unclear, with some authors reporting poorer outcomes in female patients\(^7\) and others noting no difference\(^8\).

The specific goal of this systematic review was to determine whether the results of ACL reconstruction are influenced by patient sex. We hypothesized that, following ACL reconstruction, male and female patients exhibit no differences in

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(1) graft failure risk, (2) contralateral ACL injury risk, (3) knee laxity, and (4) patient-reported outcome scores.

Methods

Study Identification

A systematic review of the literature was performed to identify all studies in which the results of ACL reconstruction were reported by sex. The PubMed, CINAHL, Embase, and Cochrane Library databases were searched from their earliest entries through December 31, 2012. The search identified all articles containing the terms “ACL” or “anterior cruciate,” “sex” or “gender,” and “reconstruction.” This search yielded 291 studies. In addition, the “related citations” feature of PubMed and the reference list from each study were searched to determine whether any relevant studies had been missed by the search strategy. Five additional studies were identified. The titles and abstracts (and, when necessary, the full text) of the 291 studies were reviewed, and 279 studies were excluded (Fig. 1) on the basis of the inclusion and exclusion criteria (see Appendix). Included studies were published in English on primary ACL reconstruction in humans utilizing any technique and graft type, with outcomes reported by sex at a minimum of two years. Studies were excluded if they involved nonhuman subjects (forty-one), were in a language other than English (twelve), did not report outcome data by sex (146), were not ACL-related (twenty-four), were biomechanical in nature (twenty-four), were a review article without original data (twelve), were an imaging study (seven), focused on revision surgery (one), involved the skeletally immature (five), had less than two years of follow-up (five), or represented a cost analysis (two). In addition, four of the seventeen studies that satisfied the selection criteria were subsequently excluded because of duplicate or incomplete data. The remaining thirteen studies formed the basis of this systematic review.

Data Extraction

Data were extracted and spreadsheets were developed on the basis of accepted recommendations. Collected data included study design, patient demographics, surgical technique, incidence of graft and contralateral ACL rupture, objective laxity measurements on physical examination, instrumented laxity (arthrometer data), and patient-reported outcome scores. Two independent reviewers extracted data, and any discrepancies were resolved by consensus. Efforts were made to contact the original investigators when requisite data were lacking from the publications.

Statistical Analysis

Each outcome measure was qualitatively assessed for homogeneity. If the data appeared qualitatively heterogeneous, no statistical analysis of heterogeneity or meta-analysis was performed. If it appeared homogeneous, statistical (chi-square) testing of homogeneity was performed. If the observed variation was inconsistent with the null hypothesis of homogeneity (p < 0.1), no meta-analysis was performed.

For each outcome variable that was sufficiently homogeneous for meta-analysis, a Mantel-Haenszel analysis utilizing a random-effects model was performed with Review Manager software (version 5.0 [2008]; Copenhagen: The Nordic Cochrane Center, The Cochrane Collaboration) to pool results while accounting for the number of subjects in individual studies. Subgroup analyses were also performed according to graft tissue type (allograft or autograft).

Source of Funding

The authors received no funding in support of this study.

Results

Study Characteristics

All thirteen studies identified by the search were classified as retrospective comparative studies (Level-II evidence); however, prospective collection of data was reported in nine of these studies. All studies had a minimum of two years (range, two to seven years) of follow-up, and the mean follow-up rate across the studies was 70% (range, 23.5%-100%).
Eight of the thirteen studies did not include reporting of a power analysis. The thirteen studies reported on a total of 7559 patients, 4379 male and 3180 female. The mean patient age in the studies ranged from twenty-one to thirty years. Mean age was reported separately for male and female patients in five of the thirteen studies and was 2.5 years older, on average, in the male patients. A variety of surgical techniques and graft types were utilized (see Appendix).

**Graft Rupture Risk**

Graft rupture risk was reported by sex in seven of the thirteen studies, and communication with the author yielded data from one additional study. These studies included a total of 2518 patients (1485 male and 1033 female). Failure risk was 4.6% for males and 4.7% for females. Meta-analysis indicated no difference in the risk of graft failure according to sex (Fig. 2).

Included studies were subsequently stratified on the basis of the choice of graft type. Three studies utilized exclusively patellar tendon grafts. Failure risk was 4.0% for males and 4.7% for females. Meta-analysis indicated no difference in the risk of patellar tendon graft failure according to sex (Fig. 3). Four studies utilized exclusively hamstring grafts. Failure risk was 6.4% for males and 9.2% for females. Meta-analysis indicated no difference in the risk of hamstring graft failure according to sex (Fig. 4).

**Contralateral ACL Rupture Risk**

The risk of contralateral ACL rupture was reported by sex in three of the thirteen studies. These studies included 1793 patients, 923 male and 870 female. The failure risk was 5.3% for males and 5.4% for females. Meta-analysis indicated no difference in the risk of contralateral ACL rupture according to sex.
patients (1061 male and 732 female). The overall risk was 4.0% for males and 7.4% for females. Meta-analysis indicated no difference in the contralateral ACL rupture risk according to sex (Fig. 5).

Knee Laxity on Physical Examination
Lachman test findings were reported by sex in five of the thirteen studies. These studies included 774 patients (450 male and 324 female). A Lachman test grade greater than 0 (side-to-side difference >3 mm) was noted in 37.5% of males and 39.8% of females. Meta-analysis indicated no difference in the risk of increased anterior laxity according to sex (Fig. 6).

Pivot-shift test findings were reported by sex in five of the thirteen studies. These studies included 624 patients (356 male and 268 female). A pivot-shift test grade other than 0 was noted in 12.3% of males and 20.1% of females. Meta-analysis indicated no difference in the risk of increased rotational laxity according to sex (Fig. 7).

Instrumented Laxity
Laxity findings on instrument testing were reported by sex in seven of the thirteen studies. These studies included 948 patients (545 male and 403 female). Anteroposterior laxity was documented with a variety of instruments, including the KT1000 and KT2000 (MEDmetric, San Diego, California) as well as a computerized knee motion assessment device (OSI CA4000; Orthopedic Systems, Hayward, California). Two studies demonstrated significantly greater laxity in females; however, the mean difference in both studies was <1 mm. No significant difference was noted in the remaining five studies (see Appendix). The heterogeneity of measurement tools and lack of standard deviation values precluded meta-analysis.
Patient-Reported Outcomes

Patient-reported outcome scores were reported by sex in nine of the thirteen studies. These studies included 5,410 patients (3,085 male and 2,325 female). A variety of patient-reported outcomes tools were utilized, including the Lysholm score, subjective International Knee Documentation Committee (IKDC) score, Cincinnati knee score, Knee injury and Osteoarthritis Outcome Score (KOOS), and Hospital for Special Surgery (HSS) knee score (see Appendix). The only significant differences between the scores of male and female patients were in the study by Ageberg et al. and involved the KOOS sport and recreation function subdomain and the KOOS knee-related quality of life subdomain. These differences did not reach clinical importance. The heterogeneity of measurement tools precluded meta-analysis.

Activity scores were reported by sex in six of the thirteen studies. These studies included 1,175 patients (673 male and 502 female). Both Marx and Tegner activity scores were utilized. No study demonstrated a significant difference in the postoperative Tegner score according to sex. Preoperative Tegner scores were often not reported. The lack of consistency in the scoring instrument (Marx or Tegner) and in the nature of the outcome reporting (median or mean) precluded meta-analysis.

Discussion

This systematic review demonstrated that the results of ACL reconstruction were similar in male and female patients. Meta-analysis revealed no significant differences in the graft failure risk, contralateral ACL rupture risk, or postoperative knee laxity on physical examination, although there was nonsignificant evidence of increased laxity and increased contralateral ACL rupture risk in female patients. There was no evidence of a clinically significant difference in patient-reported outcomes between male and female patients.

In contrast to the findings of the present study regarding the risk of ACL graft rupture, it has been clearly demonstrated that female sex is associated with a greater risk of tearing of the native ACL. Although numerous factors likely contribute to this risk, an increased prevalence of deficits in dynamic neuromuscular control of the knee has been reported in female compared with male subjects and represents an important risk factor. Numerous authors have demonstrated that programs aimed at addressing neuromuscular control deficits and landing technique can reduce the risk of ACL tears in female subjects to approximately that of male subjects. The lack of a difference in the graft failure rate according to sex in the present study may reflect the efficacy of postoperative rehabilitation protocols in improving neuromuscular control following ACL reconstruction, particularly in female patients.

It is possible that there are significant differences between the outcomes of male and female patients following ACL reconstruction that were not detected in this review. Some authors have suggested that the degree of postoperative laxity and the graft rupture risk are highly dependent on the choice of graft type, with male and female patients responding differently to different graft types. Our stratified analysis demonstrated no difference in the failure risk according to sex for either hamstring or patellar tendon grafts, although the number of studies in each group was relatively small. Gobbi et al. did demonstrate increased anteroposterior laxity in female compared with male patients following ACL reconstruction with soft-tissue grafts but did not report whether this difference was significant. No difference in instrumented laxity was noted when patellar tendon grafts were used. Our analysis lacks sufficient power and detailed data from the included papers to fully answer this question. There are additional factors, such as activity level and age, that may also influence differences in outcome between male and female patients. Unfortunately, the relatively small number of graft ruptures in the included studies and the data heterogeneity precluded analysis of the impact of such factors on graft failure risk in the present study.

Further limitations of this study relate to the data contained within the individual included studies as well as the differences among those studies. Eight of the thirteen included studies did not include reporting of a power analysis. This raises the possibility that some of the included studies were underpowered, thereby introducing a detection bias. However, we believe that the included studies provide the best data currently available to answer this important question. The majority of the studies included in this review had relatively short-term follow-up of two to three years. It is unclear whether further differences between the outcomes of male and female patients will become apparent over time. In addition, the relative heterogeneity of the outcome instruments as well as the variety of methods of reporting the findings limited the pooling of data and potentially weakened our conclusion that the results of ACL reconstruction are similar in male and female patients.

Appendix

Tables showing the inclusion and exclusion criteria as well as the patient demographics, instrumented laxity, and patient-reported outcome and activity scores in the included studies are available with the online version of this article as a data supplement at jbjs.org.

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