Comparing Sex-Specific Outcomes After Medial Patellofemoral Ligament Reconstruction for Patellar Instability

A Systematic Review

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Background: The impact of patient sex on outcomes after medial patellofemoral ligament reconstruction (MPFLR) has not been well studied.

Purpose: To conduct a systematic review to determine sex-based differences in outcomes after MPFLR for patellar instability and the proportion of studies examining this as a primary or secondary purpose.

Study Design: Systematic review; Level of evidence, 4.

Methods: A systematic review was performed using the PubMed, Cochrane Library, PubMed Central, Ovid, and Embase databases according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Studies were included if they were written in English, were performed on humans, consisted of patients who underwent MPFLR with allograft or autograft, evaluated at least 1 of the selected outcomes comparing male and female patients, and had statistical analysis available for relevant findings. Excluded were case reports, review studies or systematic reviews, studies that did not evaluate at least 1 sex-specific outcome, studies that included other injuries associated with patellofemoral instability injury, cadaveric studies, and those in which patients underwent concomitant procedures.

Results: The initial search yielded 3470 studies; 2647 studies remained after removing duplicates. Of the 401 studies that underwent full-text review, 10 met all inclusion criteria and were included for quantitative analysis. A meta-analysis could not be performed given the heterogeneity within the data set. Of the 2647 studies evaluated in this study, only 2 (0.08%) studies examined the impact of patient sex on MPFLR outcomes as a primary purpose and only 8 (0.30%) studies explored it as a secondary purpose.

Conclusion: Only 0.38% of the articles compared outcomes between male and female patients after MPFLR. The limited data available were too heterogenous to draw any concrete conclusions about the impact of patient sex on outcomes after MPFLR. Further research in this area is warranted, as findings may influence treatment plans and improve patient outcomes.

Keywords: patellar instability; medial patellofemoral ligament reconstruction; sex; male; female

The primary stabilizer preventing lateral patellar displacement is the medial patellofemoral ligament (MPFL), which is often torn as a result of patellar dislocations. Since its introduction, MPFL reconstruction (MPFLR) has become one of the most common treatments of patellar instability. One study found that MPFLR constituted 75% of all patella-stabilizing surgical procedures within the Danish healthcare system in 2014. There is a large body of literature that has studied the efficacy of this procedure, examined patient outcomes, and determined the ideal techniques and protocols in the treatment of patients with patellar instability. However, there is a paucity of information on the impact of patient sex on outcomes after MPFLR.

Studies often use “sex-adjusted” scores or “sex-matched” control groups, or they simply neglect to analyze data differentiating by patient sex. Differences in male and female knee anatomy and physiology have been previously described, including differences in the height of the anterior aspects of both the lateral and medial femoral condyles,
Q-angle, medial-lateral/anterior-posterior aspect ratio, cartilage volume and surface area, and patellofemoral joint biomechanics. Previous studies have demonstrated that female patients have a 5.45 times greater risk of any postoperative complications; higher 1-, 5-, and 8-year risk of recurrent dislocation or instability; and worse postoperative outcome scores after MPFLR. Despite known differences in male and female knee anatomy and physiology and preliminary evidence that patient sex impacts outcomes after MPFLR, there is a paucity of literature that comprehensively examines this concept. The purpose of this study was to perform a systematic review to evaluate the impact of patient sex on outcomes after MPFLR and to analyze the proportion of studies exploring this phenomenon.

METHODS

Search Strategy and Study Selection

This study was conducted according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement. A manual search and study selection were performed using the PubMed, PubMed Central, Cochrane Library, Ovid, and Embase databases. The following search terms were used: “Patellar instability” OR “Patellar dislocation” OR “MPFL reconstruction” OR “Medial Patellofemoral Ligament Reconstruction” AND “Sex” OR “Gender” OR “Male” OR “Female.” The search performed included all of the databases’ articles from inception to April 2020. Articles from each search were compiled into a reference management software (EndNote, version X9.3) to remove duplicates. Titles and abstracts were then screened for relevance. The full texts of the remaining articles were reviewed to determine eligibility for inclusion in the study using the criteria described in the next section. In all stages of screening and selection, all articles were reviewed by 2 authors (A.J.F. and A.J.H.) to determine inclusion or exclusion based on the following criteria, with discrepancies resolved by a third author (M.L.V.).

Eligibility Criteria

We included studies that were published in the English language, consisted of patients who underwent MPFLR with allograft or autograft, were performed on humans, and evaluated at least 1 of the following outcomes: postoperative patellar dislocation rate, postoperative patellar instability, reoperation rate, postoperative range of motion, postoperative stability, tibial tuberosity–trochlear groove distance, return to sport or work, rate of return to sport, visual analog scale (VAS) for pain, type of graft used based on patient sex, Beighton score, and any other postoperative functional outcomes or postoperative complications. Additionally, studies that were included provided a statistical analysis of sex-based claims. Studies were excluded if they were case reports, review studies or systematic reviews and if any of the following were present: published in non–English language, performed on animals, performed on cadavers, included any other associated injuries with patellar instability injury (meniscal injury, multiligamentous injury, quadriceps/patellar tendon rupture), did not evaluate at least 1 of the listed outcomes and compare male and female patients’ results, and included any concomitant procedures such as meniscal repair and anterior cruciate ligament reconstruction.

Data Extraction and Quality Appraisal

Each study selected for inclusion in the final analysis had the following data extracted if reported: patient characteristics including age, body mass index, workers’ compensation status, level of athletic activity, and sport type, as well as any outcome data listed in the eligibility criteria. Additionally, studies that examined the impact of patient sex on outcomes after MPFLR as one of their initial intentions within the title or abstract were recorded as “examining the impact of patient sex as a primary purpose.” Studies that compared outcome data between male and female patients but did not identify this within their title or abstract as a primary purpose were recorded as “examining the impact of patient sex as a secondary purpose.” Studies that did not compare outcome data between male and female patients or that reported that “sex did not have a significant influence” without providing further explanation or analysis were recorded as “not examining the impact of patient sex in MPFLR outcomes.”

Statistical Analysis

Descriptive statistics were conducted; categorical data were summarized with frequencies and percentages, and
The initial search yielded 3470 studies. After all detectable duplicates had been removed, 2647 studies were manually screened via title and abstract; 2246 studies were excluded for not meeting the criteria described previously. Full-text analysis was performed on 401 articles to determine eligibility for inclusion in this study’s quantitative analysis. Of the 2647 total articles evaluated, 10 (0.37%) met all inclusion criteria. As shown in Figure 1, several articles were excluded because they did not compare outcome data by patient sex.

Data were extracted from all 10 articles and compiled for statistical analysis; however, because of the heterogeneity of the data set, no meaningful statistical analysis could be performed. Demographic information for these 10 articles is shown in Table 1. Of all 2647 studies evaluated in our study, only 2 (0.08%) examined the impact of patient sex on outcomes after MPFLR as a primary purpose and only 8 of 2647 (0.30%) studies explored the impact of patient sex on outcomes after MPFLR as a secondary purpose. Three of 2647 (0.11%) studies examined the influence of patient sex on the rates of various postoperative complications. Five (0.19%) studies compared myriad functional outcome scores by patient sex. Two (0.08%) studies compared graft failure rates by patient sex.

### Postoperative Complications

After the evaluation and selection process, 3 of 2647 (0.11%) studies remained that compared male and female patients by recurrent patellar dislocation and instability. In a retrospective review of the Danish National Patient Registry from 1996 to 2014, Gravesen et al. collected data on 1770 patients undergoing isolated MPFLR. This study examined the risk of persistent patellar mortality, which they defined as “new patellar-related contact to health care system more than a year after surgery.” The authors reported that the 1-year risk of persistent patellar mortality was 8.5% (95% CI, 6.2-10.7) for men and 11.6% (95% CI, 9.9-13.3) for women; the 5-year risk was 17.3% (13.5-21.0) for men and 21.0% (18.4-23.5) for women; and the 8-year risk was 17.3% (13.5-21.0) for men and 22.4% (19.1-25.5) for women ($P = .029$). Similarly, Kita et al. performed a case-control study of 42 patients (9 male and 33 female) with patellar instability and no history of surgical treatment who underwent isolated MPFLR. After dividing the patients into those with postoperative patellar instability and those without, the authors found that 23.5% of the patients without postoperative patellar instability were men, as opposed to 10.0% of the patients with postoperative instability. Through single linear regression analysis, they determined that patient sex was not significantly related to residual patellar instability ($β = .146$, $P = .363$, $R^2 = 0.020$, $r = 0.141$). Additionally, in this study, no male patients suffered a re-dislocation and only 2 female patients had a re-dislocation of their patella postoperatively.

Parikh et al. performed a retrospective registry study of all patients undergoing MPFLR between 2005 and 2011 at the Cincinnati Children’s Hospital Medical Center. The authors found that 26% (24/91) of female patients had an identifiable complication and 5% (3/63) of male patients had a complication. Thus, female patients were shown to have a 5.45 times greater risk of complication (95% CI, 1.74-17.60; $P < .001$). Complications included recurrent lateral patellar instability (8 patients; 5.2%), knee motion stiffness with flexion deficits (8 patients; 5.2%), patellar fractures (6 patients; 3.9%), and patellofemoral arthrosis/pain (5 patients; 3.2%), among others.

### Functional Outcome Scores

After the filtering and selection process, of 2647 studies, 5 (0.19%) remained that compared male and female outcome scores. Hopper et al. performed a prospective case
series on 68 patients (18 male and 50 female) who underwent MPFLR at the Glasgow Royal Infirmary. Mean postoperative Kujala, Lysholm, and Tegner scores were reported as 76.2, 73.8, and 3.6, respectively. While no sex-specific data were reported, these 3 scores were compared for male and female patients via the Fisher exact test. The authors found that there were no statistically significant differences in Kujala, Lysholm, and Tegner scores between male and female patients (\(P = .065, .073, \) and .063, respectively).10

Howells et al11 performed a prospective cohort study of all patients undergoing MPFLR at the Bristol Royal Infirmary from 2005 to 2010. They evaluated functional outcome scores in 211 patients (92 male and 119 female) postoperatively and reported the mean score for male and female patients (Table 2). The authors found that women had significantly worse outcomes than men in all 8 outcome scores examined. However, they also compared male and female mean scores stratified into surgical indication groups of “traumatic injury” and “atraumatic injury” and

| Table 1 |
| Study Information* |

| Lead Author (Year) | Study Type (LOE) | Population | Graft Type | Outcome Summary |
|--------------------|------------------|------------|------------|----------------|
| Gravesen (2019)6  | Retrospective registry review (4) | All MPFLRs in Denmark from 1996 to 2014 | Mixed | Female patients had statistically significant increased 1-, 5-, and 8-y risk of persistent patellar morbidity |
| Kita (2015)12     | Prospective case control (3) | 44 (42 patients) isolated MPFLRs in a single Japanese hospital with mean follow-up of 36 mo | Auto | No statistically significant difference noted in patient sex between patients with postoperative patellar instability and those with no postoperative patellar instability |
| Parikh (2013)17   | Retrospective case series (4) | 179 (154 patients) MPFLRs at a single U.S. hospital over 6-y span | Auto | Female patients were found to have a 5.45 times greater risk of postoperative complications |
| Hopper (2014)10   | Retrospective case series (4) | 72 (68 patients) isolated MPFLRs at a single British hospital | Auto | No statistically significant difference in Kujala, Lysholm, and Tegner scores between male and female patients |
| Howells (2012)11  | Prospective cohort (3) | 211 (193 patients) isolated MPFLRs at a single British hospital | Auto | Female patients had significantly worse outcome scores than male patients in many categories |
| Hiemstra (2019)7  | Prospective case control (3) | 298 (298 patients) isolated MPFLRs at a single Canadian hospital | Auto | No statistically significant difference between male and female BPII scores |
| Bouras (2019)1    | Prospective cohort (2) | 57 (56 patients) isolated MPFLRs at a single British hospital | Auto | Female patients reported lower Kujala, EQ-5D, and VAS scores, but differences were not statistically significant |
| Neri (2019)15     | Retrospective case series (4) | 112 (107 patients) isolated MPFLRs at a single French hospital with a mean follow-up of 59 mo | Auto | Female patients had similar changes in Kujala and IKDC scores as their male counterparts |
| Sappey-Marinier (2019)19 | Retrospective case series (4) | 211 (206 patients) isolated MPFLRs at a single French hospital over 6-y span | Auto | Female patients had an increased odds of graft failure, although difference was not statistically significant |
| Puzziello (2019)18 | Retrospective case series (3) | 51 (50 patients) isolated MPFLRs at a single U.S. hospital over 7-y span | Mixed | Approximately equal numbers of male and female patients within study group experienced graft failure |

*Examining sex-based outcomes was the primary study purpose in Kita et al (2015)12 and Hiemstra and Kerslake (2019)7; in all other studies, it was a secondary purpose. Auto, autograft; BPII, Banff Patellofemoral Instability Instrument; EQ-5D, European Quality of Life 5-dimensional questionnaire; IKDC, International Knee Documentation Committee; LOE, level of evidence; MPFLR, medial patellofemoral ligament reconstruction; VAS, visual analog scale.

| Table 2 |
| Mean Outcome Scores as Reported by Howells et al11 |

| Outcome Measure | Mean Score | Mean Score for Patients With Atraumatic Injury |
|-----------------|------------|-----------------------------------------------|
|                 | Male       | Female | \(P\) | Male       | Female | \(P\) |
| IKDC            | 81.37      | 70.25  | <.001 | 82.98      | 72.78  | .001  |
| Kujala          | 87.54      | 77.16  | <.001 | 89.42      | 79.95  | <.001 |
| OKS             | 43.36      | 39.73  | <.001 | 44.45      | 41.22  | .002  |
| WOMAC           | 95.89      | 89.86  | <.001 | 97.20      | 92.45  | .013  |
| Fullerson       | 89.05      | 78.36  | <.001 | 90.73      | 80.82  | <.001 |
| Tegner          | 6.00       | 4.78   | <.001 | 5.66       | 4.75   | .003  |
| SF-12 PCS       | 52.25      | 49.10  | .009  | 52.25      | 49.86  | .123  |
| SF-12 MCS       | 56.99      | 52.16  | <.001 | 57.46      | 53.14  | .001  |

*IKDC, International Knee Documentation Committee; MCS, Mental Component Score; OKS, Oxford Knee Score; PCS, Physical Component Score; SF-12, Short Form 12; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.
found that in the patients with atraumatic injury, male and female differences in outcome scores were significant ($P < .05$) on all measures except the Short Form 12–Physical Component Score. No significant differences in outcome scores were observed in the traumatic group. Additionally, the study demonstrated that female patients had significantly worse subjective responses for improvement rate ($P = .011$), willingness to undergo the same procedure again after a similar injury ($P = .028$), likelihood of recommending the procedure to others ($P = .016$), rate of recurrent symptoms ($P = .011$), presence of residual symptoms ($P = .031$), and rate of resuming sports ($P = .026$).11

Hiemstra and Kerslake7 performed a prospective cohort study of 298 patients (73 male and 225 female) undergoing MPFLR at Banff Sport Medicine from 2010 to 2016. This study compared male and female data based on the following criteria: mean age of first dislocation; mean age at surgery; percentage of patients with no, low-grade, and high-grade trochlear dysplasia; WARPS/STAID (weak, atraumatic, risky anatomy, pain, and subluxation/strong, atraumatic, anatomically normal, instability, and dislocation) score; and mean Banff Patellofemoral Instability Instrument (BPII) score evaluated before surgery and at 12 and 24 months postoperatively (Table 3). The impact of patient sex on BPII was assessed via 2 linear regressions: one unadjusted and the other adjusted for WARPS/STAID score, grade of trochlear dysplasia, knee hyperextension, and age at first dislocation. Both of these models indicated no significant effect of patient sex on BPII scores.7

Table 3: Patient Age, Degree of Dysplasia, WARPS/STAID Score, and BPII Scores Reported by Hiemstra and Kerslake7

|                  | Total (N = 298) | Female (n = 225) | Male (n = 73) |
|------------------|-----------------|------------------|--------------|
| Mean age at first dislocation, y | 15.4            | 15.1             | 16.5         |
| Mean age at surgery, y            | 24.5            | 24.6             | 24.0         |
| No trochlear dysplasia, %         | 13.8            | 16.2             | 6.9          |
| Low-grade trochlear dysplasia, %  | 43.8            | 44.3             | 42.5         |
| High-grade trochlear dysplasia, % | 42.4            | 39.5             | 50.7         |
| WARPS/STAID score                | 5.1             | 4.8              | 5.8          |
| Mean BPII preoperatively          | 26.2            | 26.3             | 25.9         |
| Mean BPII at 12 mo               | 64.9            | 63.8             | 68.5         |
| Mean BPII at 24 mo               | 66.6            | 65.4             | 69.8         |

*BPII, Banff Patellofemoral Instability Instrument; WARPS/STAID, weak, atraumatic, risky anatomy, pain, and subluxation/strong, atraumatic, anatomically normal, instability, and dislocation.

scores, as seen in the following correlation coefficients of female sex with each outcome score: Kujala = –8.8 (95% CI, –15.1 to –2.6); EQ-5D index = –0.12 (–0.20 to 0.05); EQ-5D VAS = –7.6 (–15.5 to 0.2) (all P values were nonsignificant).1

Neri et al15 performed a prospective study of 112 patients (53 male and 59 female) undergoing MPFLR at the University Hospital of Saint Étienne. This study examined outcomes for MPFLR by collecting preoperative and postoperative International Knee Documentation Committee (IKDC) and Kujala scores. The change in these scores after surgery (dKujala and dIKDC) was compared with a number of potential demographic predictors by univariate correlation analysis to determine the influence of different factors on the change in the 2 selected functional scores. The correlation values of patient sex with dKujala and dIKDC were –0.034 and –0.037, respectively. Thus, patient sex was reported to have a statistically nonsignificant influence on dKujala and dIKDC.15

Failure Rates

After the filtering and selection process, 2 studies comparing male and female graft failure rates remained. Sappey-Marinier et al19 performed a prospective study of 211 MPFLR procedures from 2008 to 2014. The study reported an odds ratio of preoperative failure risk comparing women to men of 2.9 (95% CI, 0.8-14.2; $P = .119$). As suggested by the $P$ value, this difference was determined to be statistically insignificant. Puzzitiello et al18 performed a retrospective review of all patients with patellar instability who underwent MPFLR at a single center between 2008 and 2015. They reported that 11 of 51 total patients experienced a graft failure and that 6 of these patients were male while...
5 were female. The study reported that sex did not have a significant impact on failure rates.

Qualitative Bias Analysis

A risk of bias analysis was performed on each article according to procedures and criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions. Each article was evaluated by 2 authors (A.J.F. and A.J.H.), with discrepancies resolved by a third author (M.L.V.). The results of this analysis are displayed in Figure 2. Many of the articles included in this study demonstrated similar risk of bias profiles. This was primarily the result of a lack of blinding and randomization inherent to both surgical studies retrospective registry reviews.

DISCUSSION

To our knowledge, this is the first systematic review performed with the primary purpose of examining the impact of patient sex on outcomes after MPFLR for treatment of patellar instability. Only 2 of the 2647 (0.08%) studies identified examined the impact of patient sex as a primary purpose, and only 8 (0.30%) examined the impact of patient sex as a secondary purpose. Many studies,5,14,16,20 created sex-controlled experimental groups or used sex-adjusted scores and analyses. The studies that did examine the impact of sex tended to do so in a variety of ways, typically only examining one of the many different metrics used to evaluate patient outcomes after MPFLR.

Among the 5 (0.19% of 2647 total) studies comparing postoperative functional outcome scores between male and female patients, only 1 (0.04%) study found a statistically significant difference, while 4 (0.15%) did not find any statistically significant differences. The high degree of heterogeneity between data sets and variance in methods used to evaluate postoperative outcomes among these 5 studies is reflective of a larger trend within the orthopaedic literature comparing sex-specific outcomes. All of the articles within this section had similar risk-of-bias profiles, and the higher risk of bias was primarily a result of the lack of randomization and blinding inherent to many surgical studies.

Four of the 5 studies (0.15% of 2647 total), each with reasonably sized samples, suggested there was no statistically significant difference in male and female outcome scores. Although the conclusions of these studies were similar, the lack of uniformity in methodology used weakens their claim. The 1 study that did find statistically significant differences in functional outcome scores between male and female patients was performed by Howells et al.11 This study based its conclusion on a data set spanning 5 years, clearly displayed all of the data used, and thoroughly explained the analysis performed to reach that conclusion. Additionally, this study found that when it further stratified male and female functional outcome scores by surgical indication (traumatic vs atraumatic injury), the difference was present only among the male and female patients who had atraumatic patellar instability events.11

The WARPS/STAID classification identifies the 2 distinct patient subtypes that exist in patellar instability. Previous studies have demonstrated a statistically significant association between female sex and the WARPS classification in patients with recurrent patellar instability.6 The alternative classification of patellar instability is STAID. Additionally, significant differences between male and female knee anatomy have been previously demonstrated.2-4 This may help explain the findings by Howells et al11 in which the difference in male and female functional outcome scores after MPFLR was only present among patients in the atraumatic group. It is highly probable that for patients in this atraumatic injury group, anatomy was the primary cause of their injury. This would then support the idea that anatomic differences, and thus patient sex, played an important role in the patients’ response to MPFLR and ultimately the functional outcome scores used to measure that response. This is in contrast to the traumatic group, in which it is less likely that anatomic differences contributed to the initial injury and patient response to MPFLR. Hopper et al,10 Hiemstra and Kerslake,7 and Bouras et al1 all noted that female patients on average reported worse functional outcome scores but the differences were not statistically significant. It is possible that the results from these 3 studies may be confounded by the variable of traumatic/atraumatic injury and/or type of patellar instability, and that stratification of their male and female data into atraumatic and traumatic injury groups might lead them to the same conclusion as that reported by Howells et al.11

Limitations

There are several limitations to this study. First, the only data available were what had been previously published in the studies collected in our initial search. Because of the heterogeneity of the data regarding the impact of patient sex on outcomes after MPFLR, no meaningful statistical analyses were able to be performed and no formal meta-analysis could be conducted. This limited our study to a qualitative analysis of the articles examined. The lack of quantitative analysis combined with the heterogeneity among articles that were included limited our ability to draw conclusions on the impact of patient sex on outcomes after MPFLR. Additionally, the studies included in this review were primarily of lower levels of evidence, with only 1 study having level 2 evidence. Finally, the high risk of bias among the articles included in this analysis is compounded, resulting in a high risk of bias for this study.

CONCLUSION

There are limited data regarding the impact of patient sex on outcomes after MPFLR. Only 0.38% of articles compared outcomes between male and female patients after MPFLR. The limited data available are too heterogeneous to draw any concrete conclusions about the impact of patient sex on outcomes after MPFLR. Further research in this area
is warranted as this may influence treatment plans and improve patient outcomes.

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