Comparing Sex-Specific Outcomes After Rotator Cuff Repair

A Meta-analysis

Andrew J. Fancher,[*†] BS, Anthony C. Mok,[‡] BS, Matthew L. Vopat,[†] MD, Kim Templeton,[§] MD, Brandon K. Kimbrel,[§] MD, Armin Tarakemeh,[§] BA, Mary K. Mulcahey,[||] MD, Scott Mullen,[§] MD, John P. Schroeppel,[§] MD, and Bryan G. Vopat,[§] MD

Investigation performed at University of Kansas School of Medicine, Kansas City, Kansas, USA

Background: Rotator cuff repair (RCR) is a well-studied procedure. However, the impact of patient sex on outcomes after RCR has not been well studied.

Purpose: To conduct a systematic review and meta-analysis of sex-based differences in outcomes after RCR and to record what proportion of studies examined this as a primary or secondary purpose.

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

Methods: A systematic review was performed using multiple databases according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Studies were included if they were written in English, performed on humans, consisted of patients who underwent RCR, evaluated at least 1 of the selected outcomes based on patient sex, and had statistical analysis available for their sex-based claim. Excluded were case reports, review studies, systematic reviews, cadaveric studies, and studies that did not report at least 1 sex-specific outcome or included certain other injuries associated with a rotator cuff injury.

Results: Of 9998 studies screened and 1283 full-text studies reviewed, 11 (0.11%) studies with 2860 patients (1549 male and 1329 female) were included for quantitative analysis. None of these 11 studies examined the impact of patient sex on outcomes after RCR as a primary outcome. Postoperative Constant-Murley scores were analyzed for 7 studies. Male patients had a postoperative Constant-Murley score of 76.77 ± 15.94, while female patients had a postoperative Constant-Murley score of 69.88 ± 17.02. The random-effects model showed that male patients had significantly higher scores than female patients, with a mean difference of 7.33 (95% CI, 5.21-9.46; $P < .0001$). Analysis of retear rates in 5 studies indicated that there was no difference in the retear rate between sexes (odds ratio, 0.91 [95% CI, 0.49-1.67]).

Conclusion: Female patients had lower postoperative Constant-Murley scores compared with male patients, but there was no difference in the retear rate. However, these results were based on an analysis of only 11 studies. The paucity of studies examining the impact of sex suggests that more research is needed on the impact of patient sex on outcomes after RCR.

Keywords: rotator cuff; rotator cuff repair; sex; male; female

A rotator cuff injury is the most common underlying cause of shoulder pain and disability.[15] Rotator cuff repair (RCR) is commonly performed in patients with rotator cuff tears who do not improve with physical therapy and anti-inflammatory medications. There is an abundance of literature comparing patient outcomes based on different implants, techniques, and patient comorbidities. However, few studies have examined the impact of patient sex on outcomes after RCR. Most studies tend to ignore patient sex when examining demographic trends in outcomes, report “sex-adjusted” statistics, or use sex-matched groups.[12] Despite this common practice, there have been studies demonstrating a significant difference in the postoperative outcomes of male and female patients after RCR, such as female patients reporting more disability,[15] male patients reporting higher Constant-Murley scores,[6] and male patients having higher odds of experiencing a retear.[18] The number of individual studies suggesting that sex may affect patient outcomes after this procedure begets the need for a comprehensive examination of these data focused on this demographic difference alone.

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The purpose of this study was to conduct a systematic review and meta-analysis to evaluate for any sex-based differences in outcomes after RCR and to record what proportion of studies include and report sex-disaggregated data. This study sought to aid physicians' practice by providing more information on the impact of patient sex in recovery after RCR as well as to highlight areas for future research.

METHODS

Search Strategy and Study Selection

This review was conducted according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.[8] 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: "Rotator Cuff Repair" OR "Rotator Cuff" AND "Outcome" 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 reference management software (EndNote Version X9.3; Clarivate) to remove duplicates. Titles and abstracts were then screened for relevance. The full texts of the remaining articles were reviewed to determine their eligibility for inclusion in the study using the criteria described below. In all stages of screening and selection, all articles were reviewed by 2 authors (A.F. and A.M.) to determine inclusion or exclusion, and discrepancies were resolved by a third author (M.V.).

Eligibility Criteria

Inclusion criteria were studies written in English, performed on humans, consisting of patients who underwent RCR, evaluating at least 1 of the selected outcomes based on patient sex, and having statistical analysis available for their sex-based claim. Excluded were animal studies, cadaveric studies, and studies that included the following concomitant procedures: Bankart repair, superior labral anterior-to-posterior repair, and fixation of traumatic fractures.

Data Extraction and Quality Appraisal

Each study selected for inclusion in the final analysis had the following data extracted if reported: age; body mass index; workers' compensation status; level of athletic activity; sport type; return to sport or work; return-to-sport rate; visual analog scale for pain score; postoperative range of motion; retear rate; postoperative complications; and any postoperative functional outcomes such as Constant-Murley, American Shoulder and Elbow Surgeons, Western Ontario Rotator Cuff Index, 12-Item Short Form Health Survey, and Disabilities of the Arm, Shoulder and Hand scores. Data available within all studies that met criteria were extracted; however, only the Constant-Murley score and retear rate were reported frequently enough to allow for statistical analysis.

Additionally, studies that examined the impact of patient sex on outcomes after RCR 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 a further explanation or analysis were recorded as "not examining the impact of patient sex in RCR outcomes."

Statistical Analysis

Descriptive statistics were used; categorical data were summarized with frequencies and percentages, and continuous variables were summarized with means. While this study sought to collect data on many more variables, the postoperative Constant-Murley score and retear rate were the only variables with enough studies reporting them in a similar enough manner to produce a meaningful quantitative analysis. All of the other variables that this study sought to collect were either reported too sporadically or too heterogeneously for quantitative analysis to be performed. Studies that reported postoperative Constant-Murley scores and retear rates were included in the meta-analysis. Random-effects models were used. For the Constant-Murley score, the mean difference between male

*Address correspondence to Andrew J. Fancher, BS, University of Kansas School of Medicine–Wichita, 1010 N Kansas St, Wichita, KS 67214, USA (email: dfancher2@kumc.edu).

†University of Kansas School of Medicine–Wichita, Wichita, Kansas, USA.

‡University of Kansas School of Medicine–Kansas City, Kansas City, Kansas, USA.

§Department of Orthopedic Surgery and Sports Medicine, University of Kansas Medical Center, Kansas City, Kansas, USA.

‖Department of Orthopaedic Surgery, Tulane University School of Medicine, New Orleans, Louisiana, USA.

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and female patients, along with the 95% CI, was calculated. The odds ratio (OR) and 95% CI were calculated for the difference in retear rates. Heterogeneity was examined using the I^2 statistic.[4] $P < .05$ was considered significant. R (Version 3.6.3) was used for all statistical analyses.

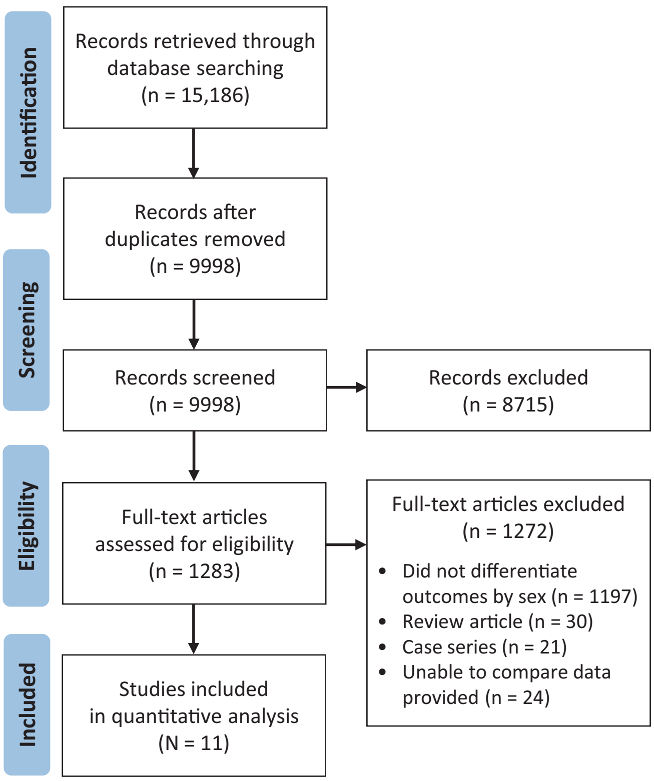

Figure 1. Flow diagram describing the article selection process.

Risk-of-Bias Assessment

Risk-of-bias analysis was performed on each article according to procedures and criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions*.[3] Each article was evaluated by 2 authors (A.F. and A.M.), with discrepancies resolved by a third author (M.V.).

RESULTS

The initial search yielded 15,186 studies; 9998 studies remained after removing duplicates. Titles and abstracts were screened, and 1283 full-text studies were reviewed, 11 (0.11%) of which met all inclusion and exclusion criteria and were included for quantitative analysis (Figure 1). The characteristics of these studies are shown in Table 1. These studies included 2860 patients, 1549 male and 1329 female, who underwent RCR. Of the 9998 studies examined in this study, 35 (0.35%) met all inclusion criteria. However, many of these articles reported their sex-based outcome findings in a format that did not allow for a comparison with data from other articles within the meta-analysis. Only 4 (0.04%) studies examined the impact of sex as a primary outcome,[2,14-16] while 31 (0.31%) examined the impact of sex as a secondary outcome. All of the articles included in the meta-analysis examined the impact of sex on RCR outcomes as a secondary outcome. The 4 articles examining the impact of sex as a primary outcome either reported data for a variable that not enough other studies evaluated as one of their outcome metrics, which prevented

TABLE 1
Characteristics of Included Studies[a]

Lead Author (Year)	Study Type (LOE)	No. of RCR Procedures	Age,[b] y	Follow-up, mo
Monesi[10] (2018)	Retrospective registry review (4)	49 at a single Italian hospital	59.5 ± 8.1	12
Aydin[1] (2017)	Prospective case-control study (3)	29 at a single Turkish hospital	55.2 ± 7.6	24
Kukkonen[6] (2015)	Retrospective case series (4)	576 at a single Finnish hospital	59.6 ± 9.6	12
Pauly[13] (2015)	Retrospective case series (4)	40 at a single German hospital	60.3 (42-75)	24
Linthoudt[9] (2003)	Prospective cohort study (3)	50 at a single Swiss hospital	58.5 ± 10.7	M: 80.76; F: 66.72[c]
Verma[20] (2010)	Prospective cohort study (3)	44 at a single US hospital	75.3 ± 4.2	36.1 (24.3-59.4)[d]
Witney-Lagen[21] (2019)	Prospective cohort study (2)	60 at a single British hospital	78 (75-86)	26
Jeong[5] (2018)	Case-control study (3)	112 at a single Korean hospital	65.6 ± 6.6	NR
Lee[7] (2013)	Retrospective case series (4)	62 at a single Korean hospital	56.1 (29-73)	27.4 (6-52)[d]
Rhee[17] (2014)	Case-control study (3)	238 at a single Korean hospital	64.5 ± 2.8 and 74.9 ± 2.5[e]	14.6 (12-62)[d]
Robinson[18] (2017)	Retrospective cohort study (3)	1600 at a single Australian hospital	59.0 ± 0.3	6

[a]All studies examined sex-based outcomes as their secondary purpose. F, female; LOE, level of evidence; M, male; NR, not reported; RCR, rotator cuff repair.
[b]Data are reported as mean ± SD or mean (range).
[c]Data are reported as mean values for male and female patients.
[d]Data are reported as mean (range) for all patients.
[e]This study did not report the mean age of the overall cohort but examined retear rates from 2 different age groups, combining these data for their sex-based comparison.

statistical analysis, or reported data in a way that was unusable for a statistical comparison.

Risk-of-Bias Assessment

Results of the risk-of-bias assessment are displayed in Figure 2. Of the studies included in this meta-analysis, 6 had an evidence level of 3, four had an evidence level of 4, and 1 had an evidence level of 2. Many of these studies were retrospective or lacked randomization because of the nature of surgical studies, leading to a high risk of bias.

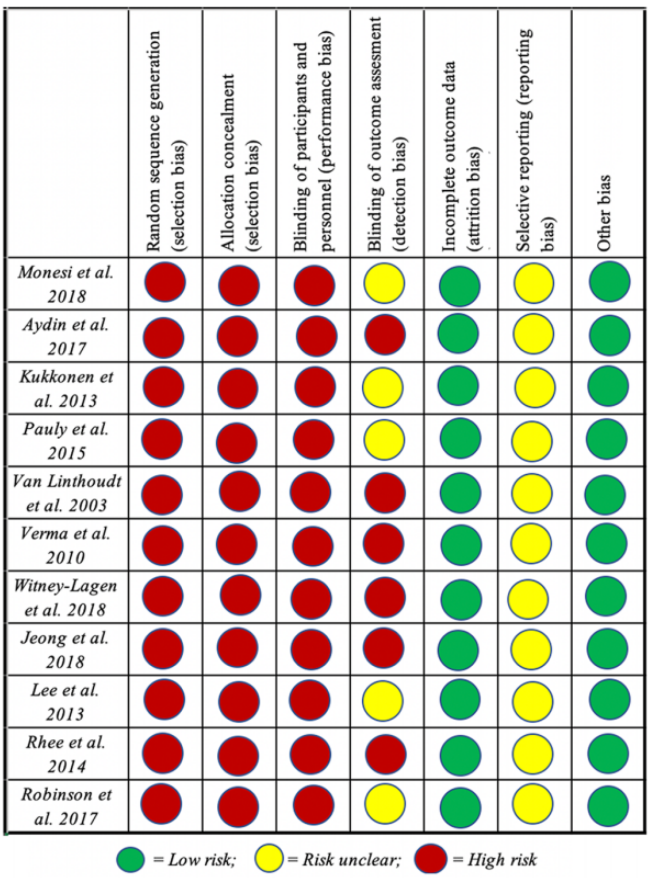

Figure 2. Results of risk-of-bias assessment.

Meta-analysis of Constant-Murley Score

Included in the meta-analysis of postoperative Constant-Murley scores were 7 studies[1,6,9,10,13,20,21] with a total of 482 male and 354 female patients. The mean postoperative Constant-Murley score was 76.77 ± 15.94 for male patients and 69.88 ± 17.02 for female patients. The random-effects model showed that male patients had a significantly higher score compared with female patients (mean difference, 7.33 [95% CI, 5.21-9.46]; $P < .0001$). Heterogeneity among the studies was very low ($I^2 = 0\%$).

Meta-analysis of Retear Rate

The retear rate analysis included 5 studies with 1067 male and 975 female patients.[5,7,13,17,18] There was no difference in the retear rate (OR, 0.91 [95% CI, 0.49-1.67]; $P < .01$). There was a high level of heterogeneity among the studies ($I^2 = 75\%$).

DISCUSSION

In this review, we examined nearly 10,000 studies relating to RCR and completed a meta-analysis of data collected, exploring the impact of patient sex on the postoperative Constant-Murley score and retear rate. The results of the meta-analysis indicated that male patients had significantly higher postoperative Constant-Murley scores than their female counterparts. Because the Constant-Murley score includes both objective and subjective measures, it is difficult to clearly identify why there may be a difference. One possible explanation is that 25% of the score is based on objective strength. The natural difference in male and female shoulder strength could explain the difference between sex-based Constant-Murley scores. However, this could also suggest that female patients may not benefit as much functionally from or have a more difficult time

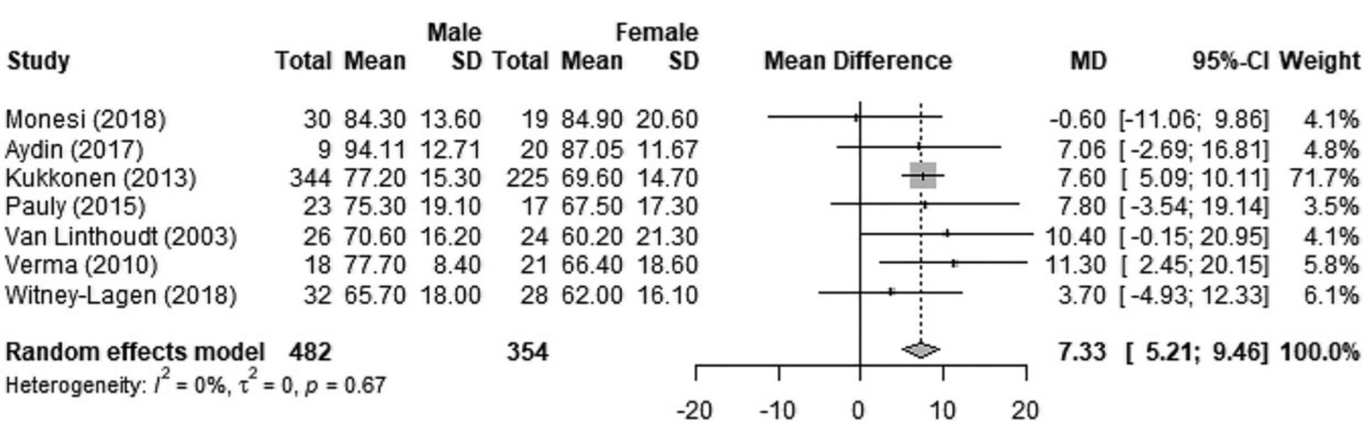

Figure 3. Forest plot of Constant-Murley scores. MD, mean difference.

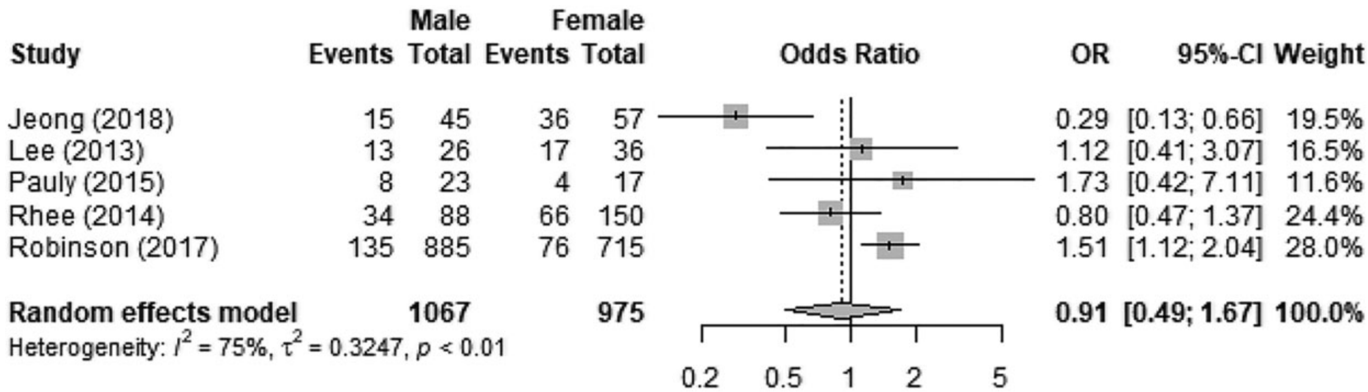

Figure 4. Forest plot of retear rates. OR, odds ratio.

recovering from RCR. Baseline data comparing strength between the sexes in those without a rotator cuff injury could help place this component of the Constant-Murley score into context.

Men and women experience the course of a rotator cuff injury and repair differently: a component of the score reflects subjective pain, and sex- and gender-based differences have been identified in the pain experience, which could affect reported outcomes.[19] Similar trends have been observed between male and female patients' functional outcomes after total knee arthroplasty, with women tending to have lower postoperative functional scores despite experiencing similar levels of improvement.[11] The data for total knee arthroplasty outcomes suggest possible gender-based factors such as unconscious physician bias causing delays in referring female patients for surgery or gender-based delays in seeking treatment. This same phenomenon may be occurring with RCR and more societal-based gender roles, and related delays in care, rather than sex-based differences, may be causing lower postoperative Constant Murley scores in female patients primarily because of lower preoperative functional scores.

The minimal clinically important difference (MCID) for the Constant-Murley score has been found to be 6.7 by Xu et al.[22] The difference between male and female postoperative Constant-Murley scores found in this meta-analysis (7.33 [95% CI, 5.21-9.46]; $P < .0001$) as shown in Figure 3, was higher than the MCID but near enough that the confidence interval crossed the threshold of clinical significance. However, this MCID was calculated on outcome data not stratified by patient sex. If patient sex does influence postoperative outcomes, it is reasonable to suggest that men and women may have different MCID values for the Constant-Murley score after RCR. Ultimately, the objective and subjective nature of the Constant-Murley score, in addition to the complex effect of biological sex and gender-based differences, makes it difficult to find a clear cause of female patients' lower postoperative scores, demonstrating the need for more research focused on the effect of patient sex in these procedures.

One possible solution to this would be the use of a modified Constant-Murley score unbiased by sex. This could be achieved by using an objective measure of strength as 25% of the score in addition to a measure of strength relative to the patient's healthy shoulder. A system could be created to compare the patient's postoperative shoulder strength to the preinjury shoulder strength. If previously recorded, the postoperative strength of the injured shoulder could be reported and contribute to the composite score as a percentage of preinjury strength. In the more likely case that this preinjury measure is not available, the uninjured shoulder's strength could be used as a surrogate for the injured shoulder's preinjury strength. In this scenario, the patient's postoperative injured shoulder strength would be reported as a percentage of his or her preinjury state. In either scenario, no bias of sex or overall strength differences could affect the score, as the recovery process is measured relative to preinjury strength rather than simply with objective strength. In addition, issues from differences in nociception and pain expression could be addressed by focusing the score more on functional levels rather than subjective pain scores. Another possible solution to the issue of sex bias in RCR outcome scores would be to begin collecting male and female data separately. Eventually, enough normative data for each sex would be available to better interpret outcome scores and potentially create new sex-based benchmarks. This type of sex-based data model is already used for bone density and other variables that have a demonstrated difference between male and female patients and could be implemented here.

This meta-analysis found that male patients were not significantly more likely to have a retear (OR, 0.91 [95% CI, 0.49-1.67]) as shown in Figure 4. This suggests that while male and female patients may vary in time to recovery and/or level of recovery, other factors besides patient sex alone likely play a larger role in repair failure. Among the studies included, Robinson et al[18] presented the strongest evidence with 1600 patients (885 male and 715 female), finding that male patients had a 1.51 odds of retearing. Lee et al,[7] Pauly et al,[13] and Rhee et al[17] all agreed with the meta-analysis finding of no statistically significant differences in male and female retear rates, although these studies had smaller sample sizes. Jeong et al[5] reported that male patients had a 0.29 odds of a retear, but they also had a smaller sample size compared with Robinson et al.[18] There was a great degree of heterogeneity among these studies ($I^2 = 75\%$), making it difficult to form any conclusive statements on male and female differences in the retear rate. However, with the exception of Pauly et al,[13] who did not report preoperative tear sizes, each of these studies also found a higher rate of retears among patients with larger preoperative tear sizes. Although each of these studies examined male and female retear rates, they did not compare male and female retear rates stratified by tear size. This could mean that preoperative tear size may be a confounding variable masking the impact of patient sex on retear rates. It is also possible that there is no impact of sex on the retear rate and that preoperative tear size is the more important risk factor, but ultimately, more research into sex-specific differences in the retear rate, while controlling for preoperative tear size, should be conducted.

There were 35 (0.35%) studies in our systematic review that met all inclusion criteria for our study. However, the data examining the impact of patient sex among 24 of these studies were too heterogeneous to be included in this meta-analysis. This exemplifies 3 trends among all the articles examined. First, most of the literature on RCR neglects to examine the impact of patient sex on outcomes after RCR or performs a study with sex-matched groups. Second, when studies do compare male and female outcomes, the way the data are presented varies greatly, with some studies providing detailed data on a number of outcomes and others reporting only the results of a linear regression that determined that patient sex did not have a significant impact on their results or P values to support that claim. Third, there are a wide variety of functional outcome tests and scores used within the literature with no standardization as to which metric of postoperative recovery and function should be used, preventing a statistical comparison of data. Of the 35 studies that met all inclusion criteria, only 4 (0.04% of 9998)[2,14-16] examined the impact of patient sex on outcomes after RCR as a primary outcome, and none of these were usable within this meta-analysis. The lack of literature examining the impact of patient sex and the heterogeneity of the data provided by the studies that do examine this impact demonstrate a strong need for further study into the impact of patient sex on outcomes after RCR.

Limitations

The main limitation of this study is the lack of information available to analyze. As previously discussed, few articles examined the impact of patient sex on outcomes after RCR, and when they did, the data were reported in a variety of ways that prevented all the studies that met inclusion and exclusion criteria from being included in the meta-analysis. Another limitation was the low level of evidence and the high risk of bias among the studies that were able to be included, with only 1 study having a level of evidence of 2. This is primarily because many of these studies were retrospective reviews or studies that lacked randomization and blinding, which are difficult to achieve in surgical studies.

CONCLUSION

The study findings indicated that female patients had lower postoperative Constant-Murley scores compared with male patients but that there was no difference in the retear rate. However, these results were based on 11 of 9998 (0.11%) studies collected for a systematic review. The finding of a statistically significant difference in male and female postoperative Constant-Murley scores and the paucity of studies examining the impact of sex suggest that more research needs to be conducted in examining the impact of patient sex on outcomes after RCR and perhaps the development of outcome measures that take inherent sex-based differences into account.

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