Sex Differences in Factors Influencing Recovery from Arthroscopic Knee Surgery

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Abstract

Background Many factors affect recovery from arthroscopic partial meniscectomy, including patient sex. However, sex differences in time to maximal recovery of knee function and factors influencing differential rates of recovery are unknown.

Questions/purposes We determined (1) preoperative sex differences, (2) sex differences in rate and extent of recovery through 1 year postoperatively, and (3) clinical and fitness variables that could explain potential sex differences in recovery from partial meniscectomy.

Patients and Methods The study sample consisted of 180 patients undergoing arthroscopic partial meniscectomy. Sex, age, body mass index, history of prior injury, length of time between knee injury/impairment and surgical

evaluation, weekly exercise frequency, and self-reported fitness were assessed preoperatively, and extent of osteoarthritis was recorded postoperatively. We used the Tegner-Lysholm scale to assess knee function preoperatively and postoperatively at Weeks 1, 3, 8, 16, 24, and 48 followups.

Results Females had worse knee function and delayed maximal recovery, requiring 1 year, compared with males, who required only 4 months. History of prior knee injury and lower self-reported fitness were associated with slower recovery in females but not in males. Osteoarthritis was associated with slower recovery but not related to sex. Body mass index, length of time between injury/impairment and surgical evaluation, and weekly exercise frequency did not influence rate of recovery.

Conclusions Females have delayed recovery after arthroscopic partial meniscectomy. Prior knee injury and self-reported low fitness are associated with delayed recovery for females but not for males.

Level of Evidence Level I, prognostic study. See Guidelines for Authors for a complete description of levels of evidence.

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Each author certifies that his or her institution approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that written informed consent for participation in the study was obtained. This work was conducted at Yale University and University of Connecticut.

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Introduction

Factors affecting the rate of recovery from arthroscopic knee surgery include severity and chronicity of injury, specific tissue involvement, and degenerative joint changes [7, 17], location of injury and structures involved [2, 19], and age and activity levels [11, 18]. Sex differences in recovery also have been supported [18]. Sex differences appear to influence diverse aspects of musculoskeletal health, including growth and development; fractures and bone strength; and muscle, tendon, and ligament injury [21]. Females have a greater incidence of musculoskeletal injuries, such as fractures, ankle sprains, and ACL injuries [13, 21]. Females also reportedly tend to have lower preoperative and postoperative function for major orthopaedic surgery (ie, THA, TKA, laminectomy) [9] and worse pain [18].

In a previous study using a subset of the current study sample, Fabricant et al. examined whether patient age, sex, and body mass index (BMI), depth of meniscal excision, involvement of both menisci, extent of meniscal tear, and extent of osteoarthritis were associated with short-term rate of recovery from minimally invasive orthopaedic surgery, ie, arthroscopic partial meniscectomy [4]. They found only sex and extent of osteoarthritis were associated with slower rate of recovery through the 1-year postoperative period. That report, however, did not determine whether specific clinical and fitness factors were associated with rate of recovery. In addition, it did not determine whether clinical and fitness factors also were associated with sex such that sex and a particular factor need to be considered simultaneously to understand the rate of recovery.

We therefore posed three questions: (1) Would male and female patients differ preoperatively for the following clinical and fitness variables: history of prior injury to the same knee, length of time between injury/impairment and surgical evaluation, BMI, extent of osteoarthritis, self-reported fitness, and amount of weekly exercise? (2) Would female and male patients differ in rate and extent of recovery during the first postoperative year? (3) Would clinical and fitness variables assessed preoperatively be associated with rate and extent of recovery during the first postoperative year, and would sex differences in any of these variables account for some of the variability in short-term (1-year) recovery?

Patients and Methods

This prospective, longitudinal study included all patients from the study by Fabricant et al. [4] ($n = 126$) and an additional 54 patients from two university-affiliated sports medicine clinics. All patients had a preoperative diagnosis of

torn medial meniscus, torn lateral meniscus, or both based on history, physical examination, and confirmatory MRI. We included patients aged 17 to 80 years, nonsmokers, with no prior history of surgery on the knee, no chronic comorbid conditions resulting in restricted physical activity for greater than 6 months (eg, insulin-dependent diabetes mellitus or severe coronary obstructive pulmonary disease), no history of chronic pain conditions, and no emergency surgery. Of the 191 recruited patients completing a preoperative interview, four were excluded postoperatively owing to more extensive surgery than partial meniscectomy, and seven patients dropped out of the study within 3 weeks postoperatively, leaving 180 patients, including 79 (44%) females and 101 (56%) males. The mean age of the patients was 48.2 years (range, 17–78 years) and 93% ($n = 168$) were Caucasian. All 180 patients completed a minimum of two postoperative interviews between Weeks 1 and 48; 159 (88%) of the patients completed the final postoperative interview.

A power analysis was conducted for longitudinal analytic models for comparison of two groups (females versus males) with repeated clinical measurements over seven times and an expectation of a moderately correlated structure with time [5]. Assuming power = 0.80 and $p = 0.05$, this power analysis confirmed a sample of 180 is sufficient to detect a small difference in postoperative outcome (approximately 3.5 points or more) as measured on the Lysholm-Tegner scale with time for groups based on sex. Approval for all procedures was obtained from the Yale Human Investigations Committee and the University of Connecticut Health Center Institutional Review Board. Participation in the study was voluntary and did not affect delivery of health care in any way. All patients provided written informed consent.

Patients were screened and recruited over the telephone by trained research assistants after evaluation by an orthopaedic surgeon and the patient-physician decision to schedule arthroscopy for a torn meniscus. Patients completed a face-to-face preoperative psychosocial interview that lasted approximately 1 hour and was conducted by research staff 1 to 30 days before surgery. Demographic information (eg, age, race/ethnicity, education) was obtained during the preoperative structured interview. In addition, preoperative clinical history and fitness factors were assessed because of their potential relationship with recovery. Clinical history included a history of knee impairment (ie, prior injury to the same knee, length of time between knee injury/impairment and surgical evaluation). Physical measurements (height, weight) were taken to obtain BMI. Patient fitness was assessed via a measure of weekly exercise frequency (number of hours) and a rating of current self-reported fitness (0–10 scale) developed for the study; the measure has not been validated. The eight-item Tegner-Lysholm rating scale measured knee

function, combining mechanical function of the knee, pain, mobility, and ability to perform daily activities [20]. A summary score ranging from 0 to 100 points is generated, with a higher score reflecting better knee function. The Tegner-Lysholm rating scale is the most widely used patient-reported outcome instrument in orthopaedic research [6, 8, 15, 17, 22] and is acceptable, reliable, and valid [10]. Knee function was assessed preoperatively to provide a baseline knee function score.

All patients underwent partial meniscectomies. Patients who underwent more extensive surgery were excluded from the study after surgery.

Postoperatively, an independent structured home exercise program was followed by all patients as described on a printed handout of specific exercises given to each patient before surgery. These included quadriceps, hip flexor, abduction and adduction, and hamstring exercises. A nurse provided detailed instructions regarding how to do the exercises, including body position, frequency, and number of sets to do for each exercise postoperatively.

Followup interviews were conducted at 1, 3, 8, 16, 24, and 48 weeks postoperatively. At each visit, patients were examined by their orthopaedic surgeon, followed by a brief psychosocial interview conducted by a trained research assistant. Severity of osteoarthritis in the knee was assessed through ratings of articular cartilage damage in three areas of the knee (ie, medial, lateral, patella), rated by physicians during surgery via a 0 to 4 modified Outerbridge articular surface grading scale (ASG) [1] and noted on a study form at the Week 1 followup. To avoid underestimation of degenerative changes in the joint, we used the worst of the three ASG scores as a measure of cartilage damage. Knee function was assessed postoperatively at each time using the Tegner-Lysholm scale to assess improvement in function with time. This was our measure of recovery.

To answer the first study question, we used T tests and chi square analyses to determine whether there were any preoperative sex differences in demographic, clinical, and fitness factors before surgery. To answer the second question, sex differences in rate of recovery with time were documented. Recovery was defined by improvement in the patients' Tegner-Lysholm scores across each of the postoperative visits. Mixed-model repeated-measures analysis was used to examine the rate of recovery. Mixed-model analytic strategies estimate missing observations through the use of model parameter estimates and therefore have several advantages over other repeated-measures models, including greater tolerance for missing data in the dependent variable. Missing data were limited, and generally the result of a missed followup appointment. Missing data were treated as follows: the mean score of each variable was entered for all missing variables except BMI, in which case the mean score for females or males was entered, as

appropriate; 13% had missing ASG values, 6% had missing BMI values, and less than 2% had missing values for the remaining variables. These analytic strategies offer solutions for other potential problems, including serial correlation, time-varying covariates, and irregular measurement periods. In addition, they can accommodate systematic person-specific deviations from average time trends [3, 12]. Three predictor variables were entered in this mixed-model repeated-measures analysis: sex, age, and time. We included sex and age to examine whether either of these demographic variables would be associated with rate of recovery. Time was included as a variable in the model to confirm knee function improved with time from surgery to 1 year postsurgery. Finally, a sex by time interaction term was included to examine whether there was any difference in the rate of recovery with time between males and females (ie, one group slower to recover). To answer the third study question regarding clinical and fitness factors associated with postoperative rate of recovery and what factors might be associated with sex differences in recovery, we conducted two mixed-model repeated-measures analyses. The first analysis included sex, age, time, and all clinical and fitness variables: history of prior injury to the same knee, length of time between injury/impairment and surgical evaluation, BMI, extent of osteoarthritis, self-reported fitness, and amount of weekly exercise. This analysis was conducted to test whether any of the clinical and fitness factors were associated with rate of recovery over time. If no study variable had a significant association with rate of recovery over time, the analyses would be completed. If any study variable had a significant association with rate of recovery over time, a second mixed-model analysis would be conducted adding interaction terms by sex (eg, sex by BMI, sex by self-reported fitness). Finally, post hoc analyses would be conducted to examine the nature of any significant interaction terms. This enabled us to specifically determine whether any factor was differentially associated with rate of recovery based on patient sex. SPSS[®] Version 16.0 (SPSS Inc, Chicago, IL, USA) was used for all analyses.

Results

The only difference in clinical and fitness factors before surgery between male and female patients was in preoperative knee function: females had lower Tegner-Lysholm scores than males (48.8 versus 62.1) (Table 1). There were no differences between male and female patients in their prior history of knee injury, length of time between injury and evaluation, preoperative BMI, extent of osteoarthritis, amount of weekly exercise, and self-reported fitness.

Table 1. Preoperative (baseline) gender differences in demographic, clinical, and fitness characteristics of study participants

Predictors	Females (n = 79)	Males (n = 101)	Statistic value	p Value
Demographic				
Age (years)	49.3 (12.9)	47.4 (11.1)	$t = 1.0$	0.293
Clinical				
Prior knee injury (number of patients)	24 (30.4%)	35 (34.7%)	$\chi^2 = 0.37$	0.544
Months since injury*	18.5 (52.8)	21.8 (56.2)	$t = 0.4$	0.696
Articular surface grading*	2.3 (1.1)	2.3 (1.0)	$t = 0.2$	0.862
Body mass index*	28.5 (7.4)	29.0 (4.7)	$t = 0.5$	0.586
Fitness				
Weekly hours of exercise*	3.7 (4.0)	3.6 (3.4)	$t = 0.1$	0.908
Self-reported fitness*	4.9 (2.4)	5.5 (2.2)	$t = 1.3$	0.115
Tegner-Lysholm score*	48.8 (16.7)	62.1 (16.9)	$t = 5.2$	< 0.001

* Values are expressed as mean, with SD in parentheses.

Fig. 1 Knee function as measured by Tegner-Lysholm scores are plotted by sex with time beginning with the presurgery (baseline) score and followed by Postoperative Weeks 1, 3, 8, 16, 24, and 48 scores. Data are expressed as mean $\pm$ standard error of the mean. Sex differences were found in the rate of recovery after partial knee meniscectomy through the first postoperative year, with females having worse knee function than males until 1 year postoperatively.

Time predicted recovery ($p = 0.001$), confirming there was a linear improvement in Tegner-Lysholm scores with time. We observed an association between sex and rate of recovery with time, with females having worse knee function than males until 1 year postoperatively (Fig. 1). However, results also revealed that the rate of recovery across time points differed depending on whether the

patients were male or female ($F = 4.36$; $p < 0.001$). Post hoc univariate analyses revealed that females showed improvement in Tegner-Lysholm scores at each time point compared with the previous one through Week 48 ($p < .001$ to $p = .021$), except for the period from Weeks 8 to 16 ($p = .230$), which appeared to be a 2-month plateau in progress. In contrast, males showed improvement from one visit to the next until Week 16 ($p < .001$ to $p = .032$) when they reached near-peak function. From Weeks 16 to 48, we observed no improvement in knee function for males ($p = .655$ and $.864$, respectively, for Weeks 15 to 24, and Weeks 24 to 48, respectively). By Week 48, male and female patients had comparable knee function.

Sex, history of prior injury, self-reported fitness score, and ASG score were associated with rate of recovery. The extent of osteoarthritis (ASG score) was associated with lower function with time but was not differentially associated with sex with time (Table 2), suggesting extent of osteoarthritis is associated with rate of recovery with time, independent of sex. History of prior injury and self-reported fitness, however, acted with sex over time in their influence on rate of recovery (Fig. 2). Females with a prior knee injury had worse ($F = 15.46$; $p < 0.001$) knee function postoperatively than females with no prior injury. Prior injury had no influence ($F = 0.44$; $p = 0.51$) on postoperative function for males. Males had better knee function than females, regardless of prior injury. Females with low baseline ratings of self-reported fitness had worse ($F = 8.26$; $p = 0.005$) knee function postoperatively than females with high fitness (Fig. 2). However, preoperative fitness level had only a marginal influence ($F = 3.52$; $p = 0.06$) on postoperative knee function for males. There was a difference ($F = 14.92$; $p < 0.001$) between females and males in average knee function for patients who were less fit, with males having better knee function even at lower levels of fitness.

Table 2. Demographic, clinical, and fitness factors as predictors of improved knee function with time

Effect source	Parameter estimate*	T value	p Value
Main effects			
Intercept	69.75	11.60	< 0.001
Time	0.32	15.26	< 0.001
Age	0.09	1.01	0.315
Gender	-7.88	-4.38	< 0.001
History of prior injury to same knee	5.96	3.07	0.002
Length of time between injury/impairment and surgical evaluation	0.00	0.100	0.921
Body mass index	-0.21	-1.28	0.202
Articular surface grading	-2.30	-2.22	0.028
Self-reported fitness	0.95	2.15	0.033
Mean hours of weekly exercise	0.20	0.76	0.451
Gender × predictor (interaction) effects			
Gender × prior injury	8.61	2.23	0.023
Gender × length of time between injury and evaluation	-0.48	-1.46	0.147
Gender × body mass index	-0.22	0.64	0.523
Gender × articular surface grading	-1.93	-1.01	0.316
Gender × self-reported fitness	1.72	1.99	0.049
Gender × mean hours of weekly exercise	-0.26	-0.49	0.625

* A parameter estimate (probability distribution for multiple measurements with time) was generated for each variable.

Discussion

Arthroscopic surgical outcome is influenced by diverse demographic [4, 18], clinical [4, 7, 17], neuroimmunologic [14], and psychosocial [16] factors. Empirical data suggest surgical outcomes may be influenced by sex [4, 18]. The exact nature of this relationship, however, is unknown, including sex differences in rate of postoperative recovery, and factors that may influence outcome depending on patient sex. Our objectives were to confirm and extend previous findings regarding sex differences in recovery by examining preoperative differences between males and females in clinical and fitness variables, determining rate and extent of recovery for males and females, and examining variables that might work together with sex to delay recovery with time.

We acknowledge several limitations to our study. First, all patients were sampled from academic sports medicine clinics in urban settings in the Northeast and therefore may not represent all patients undergoing partial meniscectomy. Future research is necessary to confirm whether results can be generalized to patients in rural, nonacademic medical

Fig. 2 Knee function (Tegner-Lysholm score) is stratified by sex for history of prior knee injury and self-reported baseline fitness. Data are expressed as mean $\pm$ standard error of the mean. The two variables were differentially associated with rate of recovery depending on sex. Females with no prior history of knee injury had higher postoperative knee function than females with prior history of knee injury but prior knee injury had no impact on postoperative knee function for males. Similarly, females with self-reported lower fitness had lower postoperative knee function than females with higher fitness but fitness level had no impact on postoperative knee function for males.

settings in different parts of the country where patient health practices may differ and potentially influence outcome. Second, the study sample was not ethnically diverse (< 8% ethnic minority). Although the ethnic homogeneity may be considered a strength of the study, it is also a limitation in that study results may not generalize to patients who are not Caucasian. Third, although the study sample excluded patients with substantial health comorbidities to increase sample homogeneity, study results may not generalize to patients with substantial health concerns. Fourth, our rating of self-reported fitness was developed for the study and was not a previously validated measure such as the Tegner-Lysholm scale. The fitness scale, however, correlated with other indirect measures of fitness in our study database, including amount of weekly exercise, providing some empirical support as a measure of fitness.

We found sex differences in preoperative knee function, with females having worse preoperative knee function than males. This finding is consistent with previous reports [4, 14]. Our study confirms preoperative sex differences in knee function cannot be attributed to differences in BMI, extent of osteoarthritis, history of prior injury, amount of weekly exercise, self-reported fitness, or length of time

elapsed between injury and surgical evaluation. Previous research suggests females are more likely to have osteoarthritis in the knee and more severe arthritis in the knee than males [12]; however, the extent of osteoarthritis did not differ between male and female patients in our study. This lack of sex difference in extent of osteoarthritis may be partially explained by a younger study sample (ie, mean age < 50 years). Although extent of osteoarthritis was not associated with preoperative sex differences in knee function, it was associated with rate of recovery for males and females.

Consistent with our previous findings [4, 14], we found sex differences in the rate of surgical outcome after arthroscopic knee surgery. We examined the sex differences in recovery trajectories in detail and investigated factors that could partially explain the differences in the rate of recovery. Female patients required 1 year for maximum recovery compared with male patients, who reached maximum recovery by approximately 4 months. The slower recovery to maximal knee function may be partially explained by (1) lower preoperative knee function in females and (2) differences in factors that act together with sex postoperatively with time. Females, overall, appear to have more factors that contribute to a slower rate of recovery than males after arthroscopic knee surgery. However, females eventually obtain the same level of knee function as males, despite lower preoperative knee function scores.

We found sex differences in two study variables: history of prior injury and fitness level. Although there were no preoperative differences between our female and male patients, both factors acted together with sex over time and were differentially associated with recovery. Females reporting knee injury or impairment before the index condition had a slower recovery. In addition, females reporting a lower preoperative fitness level took longer to recover. These factors were less critical to recovery in male patients. Although our study results support a history of prior injury and lower fitness level may contribute to female knee susceptibility manifested postoperatively in terms of slower recovery, it is unclear why females and not males are particularly sensitive to these factors. Anatomic, biomechanical, neuromuscular, and hormonal differences may contribute to this particular susceptibility.

Our data suggest the general preoperative and postoperative susceptibility of females facing partial meniscectomy and the particular association between female sex, history of prior injury, and self-reported lower fitness contribute to a delayed recovery process. Our study lays the groundwork for future research identifying sex differences in mechanisms that enhance the rate and extent of recovery. Future research needs to clarify the factors contributing to underlying preoperative sex differences in knee function and why

prior injury and lower level of self-reported fitness appear deleterious to the recovery process in females.

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