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Sex differences in patients with different stages of knee osteoarthritis

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Abstract

Objective—To quantify the differences in physical impairments, performance-based and patient-reported outcomes in men and women seeking non-operative management of symptomatic moderate knee osteoarthritis (OA) and those with symptomatic end-stage knee OA scheduled for total knee arthroplasty compared to healthy controls.

Design—Cross-sectional analysis from individuals referred to physical therapy, community participants, and subjects from a 2-year longitudinal study

Setting—University research department

Participants—Cross-sectional analysis of 289 participants consisting of moderate (MOD) OA group (n=83), Severe OA group (n=143), and healthy control group (n=63).

Interventions—Not applicable

Main Outcome Measures—Quadriceps strength, Timed Up and Go (TUG), Stair Climbing Test (SCT), 6-min walk test (6MW), Knee Outcome Survey-Activities of Daily Living Scale (KOS-ADLS), and Physical Component Summary (PCS) of the Medical Outcomes Study Short Form-36 (SF-36).

Results—Women had worse scores than men for physical impairment and performance-based measures ($p<0.001$). In the MOD Group, women had significantly lower KOS-ADLS ($p=0.007$)

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and PCS ($p=0.026$) scores than men with no differences seen between sexes in the other two groups for patient-reported measures.

Conclusions—Differences between women and men with knee OA on physical impairments and performance-based measures are not echoed in the differences seen in patient-reported measures. These measures signal different domains of knee function in patients with knee OA and should be used as part of a comprehensive functional evaluation.

Keywords

Osteoarthritis; Knee; Outcome Assessment; sex

Osteoarthritis (OA) of the knee is characterized by degeneration of the articular cartilage, morphological changes to the subchondral bone, and damage to the surrounding soft tissue.¹ These structural changes lead to joint pain, quadriceps muscle weakness, reduced range of motion, and joint instability.^{2, 3} As a result, most individuals with symptomatic knee OA report difficulty with walking, stair climbing, rising from a car, or carrying heavy loads.⁴

One of the challenges when studying patients with knee OA is capturing changes in impairments, activity limitations, and participation restrictions that occur over time but progress at different rates, depending on the participant. One method to address this challenge is through a cross-sectional design that permits researchers to study participants at similar stages of osteoarthritis. Studying patients at different stages of knee OA may provide critical information in how patients perform and function.

Although activity limitations and reduced quality of life are pervasive in this patient population, these deficits are most commonly assessed using patient self-report questionnaires.^{5–7} Patient-reported questionnaires are easy and cheap to administer in this population; however, these metrics tend to be driven by pain.^{8–11} Performance-based assessments are required to obtain a more complete picture of functional limitations in this patient population.^{9, 12} Therefore, performance-based and patient-reported outcome measures should be included as part of a comprehensive patient profile to accurately assess multiple domains of physical function and disability in patients with joint pain. A comprehensive physical assessment may enhance clinical decision-making, expedite recovery during rehabilitation, identify the need for additional interventions, or provide an objective assessment on the need for total joint replacement.

The prevalence and incidence of knee OA is influenced by sex differences. The prevalence and severity of knee OA are significantly higher in older women compared to older men.^{13, 14} Furthermore, the lifetime risk after the age of 25 of having a total knee arthroplasty (TKA) is higher in women than in men.¹⁵ Function and quality of life is also substantially reduced in women with knee OA compared to men with knee OA. Women who are candidates for TKA are weaker, and walk and climb stairs slower than their male counterparts.^{16, 17} The contribution of sex on different stages of knee OA may inform clinicians on its impact on knee function and on the rehabilitation management of patients with knee OA. The purpose of this study was to quantify the differences in physical impairments, performance-based and patient-reported outcomes in men and women seeking

non-operative management of symptomatic moderate knee OA and those with symptomatic end-stage knee OA scheduled for total knee arthroplasty compared to healthy controls. We hypothesized that women would have worse scores than men, regardless of whether they were seeking non-operative management for symptomatic moderate knee OA or TKA to manage the pain and symptoms of end-stage knee OA.

Methods

Participants

This is a cross-sectional analysis of 289 participants. The moderate OA group (MOD) (n=83) consisted of individuals with unilateral knee osteoarthritis who were referred to our clinic by their treating physician to obtain a functional assessment and to manage the pain and impairments associated with symptomatic knee OA. The Severe OA group (Severe) (n=143) had end-stage, unilateral knee osteoarthritis and were scheduled for unilateral total knee arthroplasty (TKA) within the next 2–4 weeks. These patients had participated in a 2-year longitudinal study investigating clinical and functional outcomes after TKA.¹⁷ Patients in MOD Group and Severe Group had symptomatic knee OA with at least Grade 3 on the Kellgren-Lawrence Grading Scale. All subjects in MOD Group were not seeking surgical intervention to manage their knee pain and symptoms, while subjects in Severe Group were all scheduled for TKA within 2 weeks. The control group (CON) (n=63) consisted of healthy individuals recruited through community advertisements. All subjects in the control group had no lower extremity joint pain or history of diagnosed knee abnormality and were eligible if they were in the same age ranges as the MOD and Severe groups. Exclusion criteria for the MOD and Severe Groups included any lower extremity musculoskeletal abnormalities other than unilateral knee OA, contralateral knee pain greater than 4/10 on verbal rating scale, and planned staged TKA on the contralateral knee. Exclusion criteria for all groups included cardiovascular disease, neurological impairments, or any other physical limitations that affected activities of daily living. Similar numbers of men (n=153) and women (n=136) were assessed. Demographic data for all groups is presented in Table 1. All subjects gave informed consent at the time of inclusion. The study was approved by the Human Subjects Institutional Review Board at the University of Delaware.

Measures

Patients were tested using one physical impairment measure (maximal quadriceps force), three performance-based tests (timed up and go (TUG), stair climbing test (SCT), and 6-min walk test (6MW)) and 2 patient-reported questionnaires (Knee Outcome Survey-Activities of Daily Living Scale (KOS-ADLS), and physical component scores (PCS) of the Medical Outcomes Study Short Form-36 (SF-36)). These tests and questionnaires are components of the Delaware Osteoarthritis Profile and have been used to measure functional ability before and after TKA.^{12, 18}

Quadriceps strength testing

Quadriceps strength testing consisted of maximal voluntary isometric contraction (MVIC) on an electromechanical dynamometer.¹⁹ Patients performed up to a maximum of three MVICs. Verbal encouragement from the therapist and visual feedback from the

dynamometer's real-time visual display were used to help facilitate maximal effort. Customized software written code^b was used to determine the maximal voluntary isometric contraction force in Newtons (N) and then normalized to BMI (NMVIC).

Performance-based Measures

The timed up and go (TUG) test assesses the amount of time a patient can rise from an armed chair, walk 3 m as fast and safely as possible, turn around, walk back 3 m back to the chair, and return to the seated position.^{8, 20} Patients were permitted to use the arms of the chair to rise from and sit down in the chair. The time was recorded with a standard stopwatch. The test began on the command of the investigator and stopped when the patient returned to the full seated position. Measurements were recorded to the nearest 100th of a second with a standard stopwatch.

The stair climbing test (SCT) measures the time a patient is able to ascend, turn around and descend a flight of 12 stairs as fast and safely as possible.^{20–22} Patients were permitted to use one handrail if needed, but were encouraged to use only their legs for stair climbing. The stopwatch was started when the patient began up the stairs and stopped when the patient returned to the starting position. Measurements were recorded to the nearest 100th of a second with a standard stopwatch.

The 6-minute walk test (6MW) measures the distance a patient is able to walk on level surfaces in 6 minutes.^{8, 12, 20} The stopwatch was started when the patient started to walk and the distance was recorded when 6 minutes had elapsed. Patients were permitted to rest during the test, however, time on the stopwatch continued. For the TUG, SCT, and 6MW, the use of an assistive device was permitted if the task could not be performed safely or completely without its use.

Patient-reported Measures

The Knee Outcome Survey-Activities of Daily Living Scale (KOS-ADLS) is a patient-reported measure of functional limitations and impairments of the knee during activities of daily living.^{23, 24} The KOS-ADLS contains 6 items related to symptoms and 8 related to functional disability during activities of daily living. Each item is scored 0–5 and the total score is expressed as a percentage, with lower scores corresponding to greater disability.

The Medical Outcomes Survey Short Form-36 (SF-36) is a generic health questionnaire with 8 subscales of differing health domains.^{25, 26} Each domain scale is scored 0–100 with a score of 0 represents the worst possible score and 100 represents the best possible score. The Physical Component Summary (PCS) is a composite score for the physical aspects of the SF-36. The PCS scores are standardized normative scores based on the general population's score with an average of 50 ± 10 .

^aKin-Com, Chattanooga Corp., Chattanooga, TN

^bNational Instruments, Austin, TX

Data analysis

Initially, separate 2×3 way multivariate analysis of covariance (ANCOVA) was used to evaluate the interaction between sex and group (disease stage) with BMI and age as covariates for performance-based measures and patient-reported measures. A 2×3 ANCOVA was used to evaluate the interaction between sex and group (disease stage) with age as the covariate for quadriceps strength. For quadriceps strength testing, the involved limb NMVIC was used for comparison in the MOD Group and Severe Group and the averaged NMVIC of the right and left quadriceps was used for comparison in the CON group. If an interaction was found between sex and group, post-hoc paired t-tests were used to determine where the differences occurred between sexes. If the data were not normally distributed, nonparametric post-hoc analysis were used to determine where the differences occurred between sexes.

Results

The data for TUG and SCT were not normally distributed, therefore after the multivariate analysis, nonparametric post-hoc analysis was used to determine where the differences occurred between sexes. An interaction between sex and group, covaried by age and BMI, was seen for TUG ($p=.025$), SCT ($p=.037$), and 6MW ($p<.001$). Women had lower performance scores than men in the all groups for all performance-based measures, except TUG scores in the control group (Table 2). There was a main effect of quadriceps strength for sex ($p<.001$) and disease stage ($p<.001$). Women were weaker than men at each OA stage (Table 2). An interaction between sex and group was seen for KOS-ADLS ($p=0.033$) and PCS ($p=0.028$). In the MOD Group, women had significantly lower KOS-ADLS ($p=0.006$) and PCS ($p=0.015$) scores than men (Table 3). No differences were seen between sexes in the CON and Severe Group for all patient-reported measures (Table 3). For men, KOS-ADLS and PCS scores were significantly lower between disease stages ($p=.001$). For women, significant differences were seen between the CON and other two groups ($p<.001$) but no differences between MOD and Severe groups ($p<.22$).

Discussion

The purpose of this investigation was to quantify the differences in physical impairments, performance-based measures and patient-reported outcomes in men and women seeking non-operative management of symptomatic moderate knee OA and those with symptomatic end-stage knee OA scheduled for total knee arthroplasty. We had hypothesized that women would have worse scores than men, regardless of whether they were referred for non-operative or operative management of symptomatic knee OA. Our hypothesis was confirmed in physical impairments and performance-based measures, but only partially confirmed in patient-reported outcomes. Differences between performance-based measures and patient-reported outcomes have been reported in other studies.^{11, 12} Our findings indicated that differences between men and women exist on performance-based measures and patient-reported outcomes.

Performance and patient-reported outcomes are different between men and women. OA group-related changes in performance-based scores in men and women are similar. Men and

women demonstrated lower scores from Control group to Severe Group. Despite lower performance-based scores in men and women, patient-reported measures are distinctly different. Women seeking non-operative management had self-reported scores worse than men in the same group, but there was no difference between men and women for self-reported scores in those scheduled for TKA. Moreover, the self-reported scores for men were significantly worse in Severe Group compared to Mod Group; however there was no difference in self-reported scores for women between the groups.

When examining patient-reported outcomes, the differences between men and women are significant in MOD Group only. Women in MOD Group had worse scores in their perceived knee function than their male counterparts. Perceptions of disability in women occur earlier than men.^{27, 28} Self-reported outcomes largely are influenced by pain.^{11, 12} A recent study reported that women with knee OA had more pain, greater pain sensitivity, and worse performance and perceived function than men with knee OA.²⁹ Additionally for women, patient-reported outcomes between the MOD Group and Severe Group are not different, suggesting that other factors such as social or behavioral factors may play a role in lower scores in women. While patients likely seek medical treatment based on the subjective burden of knee OA, the time point that help is sought may be different between men and women. Women with knee OA may have been delayed in seeking treatment due to sex bias influenced by physician's clinical decision-making.³⁰ Therefore, these women may be more symptomatic and impaired. These findings suggest that clinicians may need to provide different counseling strategies in regards to treatment interventions for women compared to men. This highlights the need for more equitable care for women in terms of earlier and more proactive treatment of knee OA.

While performance-based measures can be influenced by pain (currently there are no functional assessments that can be performed without pain in this population), the lower scores between groups and sexes is consistent with the literature. For all strength and performance-based measures, women had lower or slower scores. Lower quadriceps strength in women compared to men has been reported in previous studies.^{31, 32} In our study, women were 22–25% weaker than men with knee OA even when quadriceps MVIC was normalized to body mass index to account for differences between men and women. Additionally, preoperative quadriceps strength is a predictor of performance-based function before and after TKA.^{33, 34} In the OA groups, women walked and negotiated stairs slower than men, similarly to Kennedy et al.¹⁶ A similar pattern emerged in the 6MW times. Women were slower than men with greater decrements in walking speed as one neared TKA. Our findings demonstrate that women with knee OA have worse functional performance than men with knee OA for all performance-based measures. Individuals with greater impairments and functional limitations are more likely to have poorer outcomes after joint arthroplasty.^{35, 36} Proactive targeted interventions to improve quadriceps strength and functional performance in women with knee OA are paramount in enhancing function and quality of life in these patients.

Study Limitations

This study does have some limitations. This is a cross-sectional study of participants with differing stages of knee osteoarthritis. While a prospective longitudinal study would allow us to investigate the changes of performance-based measures and patient-reported outcomes in men and women with progressive knee OA, a cross-sectional study design allowed us to categorize the groups based on the stage of knee OA as opposed to categorizing based on time. While subjects in MOD and Severe Groups had symptomatic knee OA with at least Grade 3 on the Kellgren-Lawrence (K-L) Grading Scale, information on the onset and duration of symptoms are not recorded. It may be that women waited longer to seek treatment for their symptoms or were delayed in seeking treatment.³⁰ The results of this study can only be generalized to participants these stages of knee OA and cannot be generalized to individuals with asymptomatic knee OA or with lower than Grade 3 on the K-L Scale. While the SF-36 PCS combines functional and pain items into one score, there is a strong relationship with perceived function and pain in individuals with knee OA and the use of the SF-36 PCS score is most appropriate to use in this population. Additionally, the SF-36 PCS is generally reported in the literature and provides the reader an opportunity to compare our findings to others.

Conclusions

In conclusion, the differences between men and women in each group on quadriceps strength and performance measures are not reflected in the differences between sexes in each group on patient-reported outcome measures. Despite lower scores and slower times in performance measures in each group, women only had larger perceived differences in their knee function once they decided to seek treatment for knee OA than men. The exclusive use of performance-based measures or patient-reported outcomes may not capture differences in physical function in patients with knee OA.¹² These results have significant clinical implications by providing rehabilitation specialists with crucial data pertinent to patients' current knee function based on sex and disease stage or the necessity for additional rehabilitation. Initiation of counseling strategies and treatment interventions should be targeted earlier in women to address impairments, activity limitations, and patient-reported limitations that may enhance patient outcomes.

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Abbreviations

OA	Osteoarthritis
TKA	Total knee arthroplasty
MOD	Moderate OA group
Severe	Severe OA group

CON	control group
NMVIC	Normalized maximal voluntary isometric contraction
TUG	timed up and go
SCT	stair climbing test
6MW	6-minute walk test
KOS-ADLS	Knee Outcome Survey-Activities of Daily Living Scale
SF-36	Medical Outcomes Survey Short Form-36
PCS	Physical Component Summary

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Table 1

Demographic data for All Groups (mean ± standard deviation)

	CON Group (n=63)	MOD Group (n=83)	Severe Group (n=143)
Men/Women	26/37	51/32	76/67
Age (in years)	63.00 ± 8.4	58.06 ± 10.00 *	65.09 ± 8.48
BMI (kg/m ²)	26.78 ± 4.26 **	31.49 ± 5.81	31.05 ± 5.15

* MOD group significantly different than CON and Severe Group (p<.05)

** CON group significantly different than MOD and Severe Group (p<.05)

Table 2
Quadriceps strength and performance-based differences between sexes for each stage of knee OA (Medians, (25% and 75% quartiles))

	Control		P	MOD		P	Severe		P
	Men	Women		Men	Women		Men	Women	
Quadriceps strength (Newton/BMI)	34.26 (28.01, 40.18)	24.87 (19.47, 29.98)	<.001	26.70 (21.14, 32.88)	16.31 (11.17, 20.77)	.001	21.96 (17.91, 27.53)	14.09 (10.71, 18.04)	<.001
TUG (sec)	6.12 (5.17, 7.21)	6.97 (6.09, 7.38)	.08	7.72 (6.66, 8.74)	9.10 (6.96, 11.15)	.001	9.13 (7.73, 10.29)	11.11 (9.17, 12.64)	<.001
SCT (sec)	8.54 (7.01, 9.43)	9.48 (8.60, 11.34)	.06	11.25 (8.93, 12.89)	14.140 (10.55, 24.77)	<.001	15.09 (11.61, 20.51)	21.16 (16.86, 29.59)	<.001
6 minute walk (m)	730.30 (647.40, 812.44)	616.31 (576.38, 686.41)	.001	567.54 (499.57, 647.85)	489.51 (377.38, 553.36)	<.001	495.75 (424.28, 587.27)	419.40 (356.00, 484.63)	<.001

Table 3
Patient-reported differences between sexes for each stage of knee OA (Medians, (25% and 75% quartiles))

	Control		P	MOD		P	Severe		P
	Men	Women		Men	Women		Men	Women	
KOS-ADLS	100.00 (96.96, 100.00)	100.00 (99.29, 100.00)	.11	65.71 (48.57, 81.00)	46.57 (33.31, 73.50)	.007	50.70 (40.35, 62.86)	48.57 (34.30, 60.00)	.32
SF-36 PCS	53.31 (49.76, 56.73)	56.43 (52.95, 57.95)	.07	38.18 (31.53, 46.95)	34.49 (26.01, 41.41)	.026	32.51 (26.83, 39.00)	29.56 (25.80, 36.28)	.07