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Relationship of Patellofemoral Osteoarthritis to Changes in Performance-based Physical Function Over 7 Years: The Multicenter Osteoarthritis Study

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ABSTRACT. ***Objective.*** To determine the relationship of patellofemoral osteoarthritis (PFOA) to changes in performance-based function over 7 years.

Methods. There were 2666 participants (62.2 ± 8.0 yrs, BMI 30.6 ± 5.9 kg/m^2, 60% female) from the Multicenter Osteoarthritis Study with knee radiographs at baseline who completed repeated chair stands and a 20-meter walk test (20MWT) at baseline, 2.5, 5, and 7 years. Generalized linear models assessed the relation of radiographic PFOA and radiographic PFOA with frequent knee pain to longitudinal changes in performance-based function. Analyses were adjusted for age, sex, BMI, tibiofemoral OA, and injury/surgery.

Results. Linear models demonstrated a significant group-by-time interaction for the repeated chair stands ($P = 0.04$) and the 20MWT ($P < 0.0001$). Those with radiographic PFOA took 1.01 seconds longer on the repeated chair stands ($P = 0.02$) and 1.69 seconds longer on the 20MWT ($P < 0.0001$) at 7 years compared with baseline. When examining the relation of radiographic PFOA with frequent knee pain to performance-based function, there was a significant group-by-time interaction for repeated chair stands ($P = 0.05$) and the 20MWT ($P < 0.0001$). Those with radiographic PFOA with frequent knee pain increased their time on the repeated chair stands by 1.12 seconds ($P = 0.04$) and on the 20MWT by 1.91 seconds ($P < 0.0001$) over 7 years.

Conclusion. Individuals with radiographic PFOA and those with radiographic PFOA with frequent knee pain have worsening of performance-based function over time. This knowledge may present opportunities to plan for early treatment strategies for PFOA to limit functional decline over time.

Key Indexing Terms: function, osteoarthritis, patellofemoral, rehabilitation

Pain and functional limitations (e.g., difficulty with walking and rising from a chair) associated with knee osteoarthritis (OA)[1] are important barriers to physical activity in individuals with knee OA.[2] This reduced mobility may contribute to the development of comorbidities such as cardiovascular disease associated with physical inactivity.[3] Thus, it is important to understand and address functional limitations associated with knee OA.

Knee OA can occur either in the tibiofemoral joint, patellofemoral joint, or both. Tibiofemoral OA is associated with poorer performance during walking and sit-to-stand activities relative to those without OA.[4] It is also associated with a decline in self-reported and performance-based function over time.[5,6] The patellofemoral joint is frequently affected in knee OA.[7] Patellofemoral OA (PFOA) is more prevalent than previously thought—half of individuals with knee pain or radiographic

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knee OA have patellofemoral involvement.[8] It is associated with substantial knee pain[7,9] and reduced quality of life (QOL).[10]

PFOA is associated with poor self-reported functional ability[7,11] and performance-based function (assessed by Timed Up and Go test [TUG], timed stair test, and single-leg rise test)[12,13]; however, the extent of longitudinal changes in performance-based function in those with PFOA is unknown. Considering the progressive nature of PFOA,[14,15] the knowledge about the course of decline in functional ability associated with PFOA is of clinical importance. In addition, symptomatic knee OA (defined as radiographic OA with knee pain) has been associated with lower self-reported function than radiographic knee OA without pain.[16] Therefore, it is important to investigate the association of radiographic and symptomatic PFOA with performance-based function over time. Treatment strategies targeting functional limitations associated with PFOA early in the disease process may improve outcomes. Therefore, we aimed to determine the relationship of both radiographic PFOA and radiographic PFOA with frequent knee pain with changes in performance-based function (assessed using the repeated chair stand test [CST] and 20-meter walk test [20MWT]) over 7 years. We hypothesized that individuals with PFOA will have greater decrease in performance-based function over 7 years than those without PFOA.

METHODS

Study population. Funded by the National Institutes of Health, the Multicenter Osteoarthritis Study (MOST) is a prospective cohort study of 3026 older adults, who were aged 50 to 79 years and had knee OA or were at risk of knee OA at the time of recruitment. Participants were recruited from 2 communities in the US: Birmingham, Alabama, and Iowa City, Iowa. Ethical approval was obtained from the institutional review boards of the University of Iowa (#201511711), University of Alabama at Birmingham (#000329007), University of California San Francisco (#10-00500), and Boston University Medical Center (#H-32956). Participants enrolled in MOST provided written informed consent. Details of the study population have been previously published.[17] Participants who had knee radiographs assessed at baseline and who completed the repeated CST and the 20MWT at baseline and at the 2.5-, 5-, and 7-year study visits were included in the present study. Participants who had a total knee/hip replacement at baseline were excluded from the analyses (n = 71), as function after these surgeries is highly variable and is unlikely due to baseline OA status. For participants who had total knee or hip replacement at 2.5-, 5-, or 7-year study visits, their performance-based function data were included in the analyses from study visits before their surgery.

Radiographic knee OA. Participants were classified by the presence of OA at baseline. We considered 2 definitions of PFOA: *radiographic OA*, defined by the presence of radiographic features; and *symptomatic OA*, which was defined by both radiographic features and the presence of knee pain. Bilateral knee radiographs were obtained at baseline. Radiographs included standing fixed-flexed posterior-anterior view as well as weight-bearing lateral view. The posterior-anterior views were scored on a scale of 0–3 based on the atlas of the Osteoarthritis Research Society International (OARSI),[18] and the lateral views were scored on a scale of 0–3 based on the atlas of the Framingham Osteoarthritis Study.[19] Radiographic tibiofemoral OA was defined as Kellgren-Lawrence grade ≥ 2 on posterior-anterior radiographs.[20,21] Radiographic PFOA was defined as grade ≥ 2 osteophytes on lateral view, or grade ≥ 2 joint space narrowing with grade ≥ 1 osteophytes, sclerosis, or cyst on lateral view.[18,21] Two raters independently scored all knee radiographs, and discrepancies were resolved by a panel of 3 adjudicators.[22]

Knee pain. At baseline, frequent knee pain was assessed in each knee by asking participants, "Do you have knee pain, aching, or stiffness on most days of the month?"

Performance-based function. The repeated CST[23] and the 20MWT[24] were used to assess performance-based function. For the repeated CST, participants were asked to stand up from a sitting position and sit down, with both arms crossed against the chest, 5 times as quickly as possible. The time required to complete 5 repetitions was recorded in seconds. The repeated CST is a measure of functional performance related to thigh strength.[25] For the 20MWT, participants were asked to walk 20 meters in an unobstructed hallway at their usual walking pace and the time needed to perform the test was recorded in seconds. The 20MWT is a commonly used performance measure to assess the walking speed and monitor physical functioning over time. As the repeated CST and 20MWT provide different information, these performance-based functional tests were studied independently. Those who were not able to perform the repeated CST and/or 20MWT were excluded from the analysis.

Statistical analyses. Since our 2 measures of performance-based function were person-specific (not knee-specific) measures, a person was considered to have PFOA if either knee had PFOA at baseline. We used generalized estimating equation (GEE) linear regression models to assess the effects of PFOA on changes in performance-based function over 7 years. Tukey-Kramer adjustments were used for multiple comparisons. Group (radiographic vs no radiographic PFOA) was included along with the assessment visit (4-level categorical variable representing each clinic visit) and their interaction (i.e., group by assessment visit) as the main predictors of performance-based function at each timepoint. We performed additional analyses to determine the relation of radiographic PFOA plus presence of frequent knee pain to changes in performance-based function. Analyses were adjusted for age, sex, BMI, history of injury/surgery, and baseline radiographic tibiofemoral OA. Analyses were conducted using SAS 9.4 (SAS Institute).

RESULTS

Participant characteristics. Of the 2737 participants who had radiographs assessed at baseline, 71 participants had a total hip or knee replacement in either knee at baseline, leaving 2666 participants eligible for the current study (Table 1). In total, 2623 and 2664 participants had at least 1 visit where the repeated CSTs and 20MWTs were assessed, respectively. For repeated CSTs, 1453 (54.5%) participants had data for all study visits, and 424 (15.9%), 544 (20.4%), and 202 (7.6%) had data for 3, 2, and 1 study visit, respectively. For 20MWT, 1531 (57.5%) participants had data for all study visits, and 428 (16.0%), 545 (20.5%), and 160 (6.0%) had data for 3, 2, and 1 study visits, respectively (Figure 1).

Relation of radiographic PFOA to changes in performance-based function. When comparing individuals with and without radiographic PFOA, there were no significant differences in the time to complete the repeated CST (mean difference [95% CI] 0.09 s [−0.28 to 0.47], $P = 0.99$) and the 20MWT (0.25 s [−0.14 to 0.64], $P = 0.91$) at baseline. There were also no significant differences at 2.5 years between individuals with and without radiographic PFOA (repeated CST 0.56 s [0.06–1.06], $P = 0.36$; 20MWT 0.56 s [0.16–0.96], $P = 0.11$). There were no significant differences in time to complete the repeated CST at 5 years (0.54 s [0.04–1.03], $P = 0.41$) and 7 years (0.90 s [0.26–1.54], $P = 0.10$) between those with and without radiographic PFOA; however, those with radiographic PFOA took significantly longer to complete the 20MWT at 5 years (1.08 s [0.60–1.55],

Table 1. Baseline characteristics.

	Overall, n = 2666	Radiographic PFOA, n = 607	No Radiographic PFOA, n = 2059	Radiographic PFOA With FKP, n = 533	No Radiographic PFOA and FKP, n = 2131
Age, yrs	62.2 ± 8.0	63.6 ± 8.0	61.8 ± 8.0	63.6 ± 8.0	61.8 ± 7.9
BMI, kg/m^2	30.6 ± 5.9	32.8 ± 6.7	29.9 ± 5.4	33.2 ± 6.9	29.9 ± 5.4
Female sex, %	60	65	42	68	58
Radiographic tibiofemoral OA, %	51	85	41	87	42
History of injury/surgery, %	31	37	29	37	29

Data are presented as mean ± SD, unless otherwise indicated. FKP: frequent knee pain; PFOA: patellofemoral osteoarthritis.

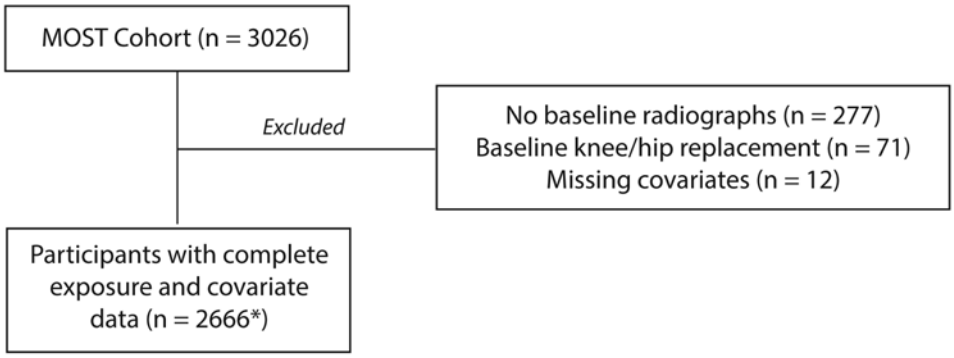

Figure 1. Flowchart of participant selection. * 2664 included in the 20-meter walk test model (2 participants had no data at any timepoint) and 2623 included in the repeated chair stand test model (43 participants had no data at any timepoint). MOST: Multicenter Osteoarthritis Study.

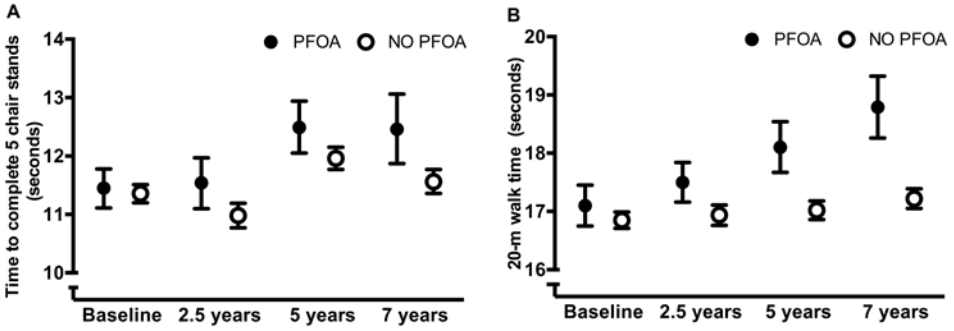

Figure 2. Mean time (seconds) to complete (A) 5 chair stands, and (B) 20-meter walk in those with and without radiographic PFOA from baseline to 7 years. PFOA: patellofemoral osteoarthritis.

P = 0.0002) and 7 years (1.57 s [1.00–2.13]; P < 0.0001; Figure 2).

Individuals with radiographic PFOA had worsening performance over time on the repeated CST (Figure 2A) and 20MWT (Figure 2B). There was a significant group-by-time interaction for the repeated CST (P = 0.04) and the 20MWT (P < 0.0001). From baseline to 7 years, those with radiographic PFOA took 1.01 seconds (95% CI 0.42–1.60, P = 0.02) longer on the repeated CST and 1.69 seconds (95% CI 1.18–2.20, P < 0.0001) longer on the 20MWT. On the other hand, individuals without radiographic PFOA took 0.21 seconds (95% CI 0.01–0.40, P = 0.43) longer on the repeated CST and 0.37 seconds (95% CI 0.23–0.52; P < 0.0001) longer on the 20MWT from baseline to 7 years.

Relation of radiographic PFOA with frequent knee pain to changes in performance-based function. Between individuals with and without radiographic PFOA with frequent knee pain, there were no significant differences in the time to complete the repeated CST (0.43 s [0.03–0.84], P = 0.42) or the 20MWT (0.42 s [–0.001 to 0.84], P = 0.51) at baseline. At 2.5 years, those with radiographic PFOA with frequent knee pain took significantly longer to complete the repeated CST (0.93 s [0.39–1.48], P = 0.02) and the 20MWT (0.89 s [0.46–1.32], P = 0.001) when compared with those without radiographic PFOA or knee pain. Individuals with radiographic PFOA with frequent knee pain also took significantly longer to complete the performance-based function tests at 5 years (repeated CST 0.87 s [0.32–1.43],

$P = 0.04$; 20MWT 1.39 s [0.86–1.93], $P < 0.0001$) and 7 years (repeated CST 1.33 s [0.59–2.08]; $P = 0.009$; 20MWT 1.96 s [1.31–2.60], $P < 0.0001$) when compared with those without radiographic PFOA or knee pain (Figure 3).

When examining the relation of radiographic PFOA with frequent knee pain to performance-based function, there was a significant group-by-time interaction for the repeated CST ($P = 0.05$; Figure 3A) and the 20MWT ($P < 0.0001$; Figure 3B). From baseline to 7 years, individuals with radiographic PFOA with frequent knee pain increased their time on the repeated CST and 20MWT by 1.12 seconds (95% CI 0.42–1.82, $P = 0.04$) and 1.91 seconds (95% CI 1.31–2.52; $P < 0.0001$), respectively. In those without radiographic PFOA with frequent knee pain, the time to complete the repeated CST (0.23 s [0.04–0.42], $P = 0.28$) did not significantly increase from baseline to 7 years, but the time to complete the 20MWT increased (0.38 s [0.23–0.52], $P < 0.0001$) from baseline to 7 years.

DISCUSSION

Our study revealed that participants with radiographic PFOA and those with radiographic PFOA with frequent knee pain had worsening of performance-based function over time. It has been reported that taking longer than 12 seconds to complete the repeated CST and walking slower than 1.22 m/s to complete the 20MWT may indicate inadequate physical ability to walk at least 6000 steps/day,[26] which is the daily step count threshold associated with risk of incident functional limitation in individuals with knee OA.[27] Our results showed that on average, individuals with radiographic PFOA (with or without frequent knee pain) took longer than 12 seconds to complete the repeated CST at 5 and 7 years, whereas those with PFOA walked with a gait speed of < 1.22 m/s at baseline and each study follow-up.

PFOA is associated with poor self-reported function[7,11] and performance-based function.[12] In the present study, individuals with PFOA at the study baseline took longer to complete the repeated CST and walked more slowly during the 20MWT during follow-up than those without PFOA at 7 years. The differences between individuals with and without radiographic PFOA with frequent knee pain were evident at the 2.5-year follow-up for the repeated CST and the 20MWT. The repeated CST is a measure of functional performance related to thigh strength[25] and previous research has reported that individuals with PFOA have reduced quadriceps volume and strength.[28] Further, activities that load the patellofemoral joint during weight bearing on a flexed knee can be more demanding for individuals with PFOA than level walking. Interestingly, the decline in performance appeared to be more prominent on the 20MWT than the repeated CST between those with and without radiographic PFOA with frequent knee pain at the 5- and 7-year follow-ups. These findings highlight the importance of using a variety of performance-based functional tasks, as different tests measure different aspects of physical health.

Walking speed has been identified as a functional sixth "vital sign" and it is an indicator of future health status and QOL.[29] For example, slower walking speed has been associated with incident radiographic and symptomatic knee OA.[30] A change in 20MWT time between −1.59 seconds (walking slower) and 0.15 seconds (walking faster) among individuals with knee OA is considered within the range of normal variability.[24] Individuals with radiographic PFOA increased the time to complete the 20MWT by 1.69 seconds from baseline to 7-year follow-up, and individuals with symptomatic PFOA increased the time to complete the 20MWT by 1.91 seconds, which is outside the normal variability for the 20MWT. This is of importance, as walking 0.2 m/s slower over time during the 20MWT has been associated with increased mortality in individuals with knee OA.[31] Individuals without PFOA also took 0.38 seconds longer to complete the 20MWT at 7 years than at baseline; however, this is within the normal variability for the test.

We are unaware of a validated minimal clinically important difference for the increase in repeated CST in individuals with knee OA. The minimal detectable change (MDC) for the repeated CST is 4.52 seconds based on community-dwelling adults aged ≥ 50 years (median age 66 yrs, range 51–89 yrs).[32] At all timepoints except one, we observed significant differences in individuals with radiographic PFOA (with or without frequent pain) and those without PFOA. These differences, however, were within the MDC for the repeated chair stands. In individuals without PFOA, there were significant fluctuations in time to complete the repeated CST over the 7 years; however, these were within the MDC value. When compared to baseline, there were no significant differences in the time to complete the repeated CST at 7 years in individuals without PFOA.

Individuals with PFOA have a decline in performance-based function over time. Thus, clinicians should monitor function in individuals with PFOA and target modifiable risk factors of

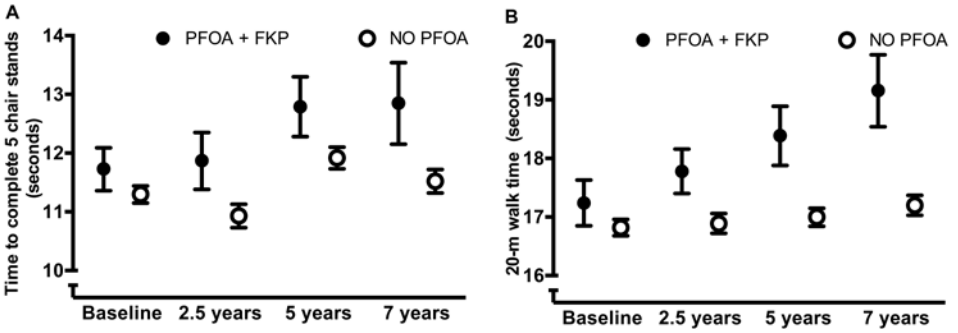

Figure 3. Mean time (seconds) to complete (A) 5 chair stands and (B) 20-meter walk in those with and without symptomatic PFOA from baseline to 7 years. FKP: frequent knee pain; PFOA: patellofemoral osteoarthritis.

physical function (such as quadriceps strength) to aid in reducing functional decline over time.[33] Further to this, researchers and clinicians should consider using a battery of functional tests. Different performance-based functional tests assess discrete and specific components of the performance on specific tasks, and thus, functional limitations may be more evident or may be evident earlier on some performance-based functional tasks than others. The OARSI-recommended set of performance-based tests of physical function for individuals with knee OA include the minimum core set (i.e., 30-s CST, 40-meter fast-paced walk test, stair climb test) and the recommended set (minimum core set, TUG, and 6MWT).[34] MOST was established prior to the OARSI recommendations regarding performance-based tests, and it does not include the entire minimum core set. Although we were unable to gain insights into stair-climbing function over time, we were able to determine how performance-based function changes over time based on a walking task (20MWT) and a chair task (repeated CST).

Our study has several strengths and clinical implications. We used data from a large cohort of individuals with or at risk of knee OA to investigate longitudinal changes in performance-based function. Individuals with PFOA have self-reported functional limitations; however, this is the first study, to our knowledge, to describe how individuals with PFOA are more likely to experience decline in performance-based function over time. The MOST study included individuals aged 50–79 years with or at risk of knee OA. PFOA is common in young and middle-aged adults[35,36] who have higher physical demands due to work and childcare-related activities; any decline in function may adversely affect work participation and QOL. Thus, it is important to investigate performance-based function over time in a younger cohort of individuals with PFOA. This could have important implications, as early rehabilitative treatments focusing on improving pain and functional limitations in younger and middle-aged individuals with PFOA may mitigate worsening over time. There are several other limitations that we encourage the readers to consider when interpreting the results. We focused on the presence of PFOA at baseline and its association with performance-based function. However, radiographic PFOA disease severity may influence patterns of performance-based function. Unfortunately, there were not enough numbers to analyze mild, moderate, and severe OA separately. We defined PFOA using only the lateral radiographs; this likely led us to miss cases of PFOA. Repeating our analysis in a cohort that also has a skyline view may lead to different results. We relied on the baseline assessment of OA in this study, although some participants without OA at baseline could develop OA during the follow-up period, and this may have reduced the observed group differences at later exams. Further to this, we accounted for age, sex, BMI, history of injury/surgery, and radiographic tibiofemoral OA in the models. However, there are several other factors such as comorbidities, depression, and physical activity, which may contribute to performance-based function over time. Last, 35% and 43% of participants did not have complete data for all study visits for the repeated CST and 20MWT, respectively. This may have influenced the results of our study, especially the precision of the estimates. However, the repeated measures linear regression analyses are valid under the same "missing at random" assumption that other approaches such as multiple imputation would require. The GEE analyses of longitudinal data allow inclusion of participants with some missing outcome values due to study dropout. If the dropout from the study is completely at random, then the estimates will be unbiased. If the dropout rate is low and variables predictive of dropout are included as independent variables, then any bias should be minimal. In addition, we found no differences in baseline participants' characteristics between individuals with complete data and those with missing data.

In conclusion, individuals with PFOA demonstrated worsening of performance-based function over 7 years. This information may present opportunities to plan for early treatment strategies for PFOA to limit functional decline over time.

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