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Lower Quadriceps Rate of Force Development Is Associated With Worsening Physical Function in Adults With or at Risk for Knee Osteoarthritis: 36-Month Follow-Up Data From the Osteoarthritis Initiative

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Abstract

Objective: To determine the association between quadriceps rate of force development (RFD) and decline in self-reported physical function and objective measures of physical performance.

Design: Longitudinal cohort study.

Setting: Community-based sample from 4 urban areas.

Participants: Osteoarthritis Initiative participants with or at risk for knee osteoarthritis, who had no history of knee/hip replacement, knee injury, or rheumatoid arthritis (N = 2630).

Interventions: Not applicable.

Main Outcome Measures: Quadriceps RFD (N/s) was measured during isometric strength testing. Worsening physical function was defined as the minimal clinically important difference for worsening self-reported Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) physical function subscale score, 20-m walk time, and repeated chair stand time over 36 months.

Results: Compared with the slowest tertile of RFD, the fastest tertile had a lower risk for worsening of WOMAC physical function subscale score at 36-month follow-up, with an odds ratio (OR) of .68 (95% confidence interval [CI], .51–.92) after adjustment for age, sex, body mass index, depression, history of chronic diseases, and knee pain. In women, in comparison with the slowest tertile of RFD, the fastest tertile had a lower risk for worsening of WOMAC physical function subscale score at 36-month follow-up, with an adjusted OR of .57 (95% CI, .38–.86). This decreased risk did not reach statistical significance in men (OR, .81; 95% CI, 0.52–1.27). No statistically significant associations were detected between baseline RFD and walk or chair stand times.

Conclusions: Our results indicate that higher RFD is associated with decreased risk for worsening self-reported physical function but not with decreased risk for worsening of physical performance.

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This article was prepared using an OAI public use data set and does not necessarily reflect the opinions or views of the OAI investigators, the National Institutes of Health, or the private funding partners.

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Knee osteoarthritis (OA) is a major public health issue, and worsening of physical function (eg, walking) is common among individuals with knee OA. Muscle weakness is closely related to knee OA, in that both men and women with radiographic knee OA have lower quadriceps strength, and specific torque regardless of pain status, suggesting that weakness may predate development of knee OA, rather than be a result of pain inhibition. Studies of multiple cohorts have revealed that quadriceps weakness is associated with elevated risk for incident symptomatic knee OA, progression of tibiofemoral joint space narrowing, worsening knee pain, and knee replacement in women. Muscle weakness is also associated with a reduction in self-reported physical function, and has been hypothesized as a causal factor for functional limitations.

Rate of force development (RFD), a measure of explosive muscle strength, is calculated from the slope of the isometric force-time curve at different intervals and strongly depends on fast neuromuscular activation. Cross-sectional studies demonstrate that RFD is closely associated with performance of both daily functional and sport-specific tasks. In addition, RFD is associated with unfavorable mobility outcomes over 2 years in older primary care patients. However, longitudinal investigation is needed to determine the relation between RFD and functional limitations in community-dwelling adults, with or at risk for knee OA.

Exercise therapy is widely used for knee OA to improve muscle strength. However, no consensus exists on the optimal types and intensity of exercise that should be prescribed. A better understanding of the relation between RFD and functional limitations would be helpful to direct rehabilitation interventions toward minimizing functional loss.

The objective of this study was to determine the association between RFD and decline in self-reported physical function and objectively measured functional performance in community-acquired adults with or at risk for knee OA over 36 months. We hypothesized that poor RFD would be a risk factor for worsening of physical function.

**Methods**

**Participants**

Data used in the preparation of this article were obtained from the Osteoarthritis Initiative (OAI) database, which is available for public access online (available at: http://oai.epi-ucsf.org/dataload). OAI offers high-quality longitudinal data with detailed information on 4796 participants with or at risk for developing symptomatic knee OA. The large sample size provides adequate power to examine the relation between RFD and worsening of physical function. We excluded the following participants: (1) healthy reference subjects without knee OA or risk factors for knee OA in both knees; (2) participants who had a knee replacement at baseline, and participants who had a hip replacement at baseline or follow-up; (3) participants who had knee injury at follow-up; and (4) participants who had rheumatoid arthritis or some other type of inflammatory arthritis at baseline or follow-up.

**Assessment of RFD**

RFD was measured using the Good Strength Chair (test-retest reliability: .88–.92) during isometric contractions on each side independently, with the knee fixed at 60° knee extension based on knowledge from prior studies that maximal isometric knee extensor strength should be measured at this angle. Participants completed 3 measurement trials on each side. The highest value of 3 maximum forces was selected after gravity correction. Because RFD is maximal with training loads between 30% and 90% of 1 repetition maximum (RM), time to produce 30% maximum forces and time to produce 90% of maximum forces was captured once the trial with the highest maximum force was selected. RFD was calculated with the following equation:

\[
\text{RFD} = \frac{\text{maximum force (N) at 90% RM} - \text{maximum force (N) at 30%RM}}{\text{time to produce 90% maximum forces (sec)} - \text{time to produce 30% of maximum forces (sec)}}
\]

RFD for the limb with greatest knee pain was used as the indicator variable in our analyses.

**Assessment of baseline to 36-month physical function outcomes**

Functional performance was assessed using the 20-m walk, repeated chair stand test, and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) physical function subscale. The timed 20-m walk test measures the time it takes a participant to walk 20m at their usual walking pace. The 20-m walk was measured twice during the examination. Average of the 2 measurements was used in analyses. The repeated chair stand test is a widely used performance-based measure of functional performance related to thigh strength. The time required for subjects to stand up 5 times from a seated position as quickly as possible was recorded with a stopwatch. This measure was repeated twice, and the average was used in analyses. The WOMAC physical function subscale is a validated self-report instrument with 17 questions related to physical function (0–68 range, with higher numbers on the scale indicating worse function). These functional outcome measures were repeated at the 36-month follow-up visit using the same procedures as at baseline.

**Minimal clinically important difference of physical performance measurements**

Worsening of functional performance was defined by minimal clinically important difference (MCID) to detect clinically

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**List of abbreviations:**

- BMI: body mass index
- CI: confidence interval
- MCID: minimal clinically important difference
- OA: osteoarthritis
- OAI: Osteoarthritis Initiative
- OR: odds ratio
- RFD: rate of force development
- RM: repetition maximum
- WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index

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relevant differences in physical function. Worsening 20-m walk was defined as an absolute decrease in gait speed of $\geq 14$ m/s. The MCID for worsening WOMAC physical function subscale was defined as an absolute increase of 9 (0–68 Likert scale). We are unaware of a validated MCID for the repeated chair stand test; therefore, we used an approximation of meaningful change, the 90% confidence interval (CI) for the minimal detectable change. The 90% CI for the minimal detectable change for worsening of repeated chair stand was defined by the following equation:

$$\text{Minimal detectable change} = 2.33 \times \text{SD} \times \sqrt{1 - \text{reliability}}$$

The SD for repeated chair stand tests at baseline in OAI was 3.99. Curb et al reported that reliability was .80 for 5 chair stands. Therefore, worsening repeated chair stand test was defined as an absolute increase of 4.16 seconds in our study.

In addition to the definitions previously mentioned, participants who underwent knee surgery on either knee or underwent replacement of either knee within the 36-month follow-up period were defined as having worsened, given evidence for a strong relation between knee replacement and functional decline.

**Assessment of potential confounders**

Age, sex, and body mass index (BMI) have been found to be related to functional performance in several studies, and were entered as potential confounders in multivariate analyses for exploring the relation between RFD and physical function. Depression and history of chronic diseases have proven to be associated with functional limitations. In OAI, depression was measured by the Center for Epidemiologic Studies Depression Scale, a short self-report scale designed to measure depressive symptomatology in the general population. History of chronic diseases (eg, heart attack, stroke) was measured by the Charlson Comorbidity Index score. Taking into account the number of participants in each score, the history of chronic diseases was converted into 2 categories (yes if score is not 0; no if score is 0). Depression and history of chronic diseases were treated as potential confounders.

WOMAC pain subscale (0–20 scale), adapted by OAI to score pain separately for each knee, was followed up every 12 months over the 36 months. In our study, WOMAC pain subscale at baseline was used to select the knee with greater pain and as a covariate in analyses of the relation between RFD and physical functional outcome measurements.

**Statistical analyses**

RFD data at baseline were divided into tertiles. Continuous variables at baseline were compared using analysis of variance or the appropriate nonparametric tests by RFD tertiles. The frequencies of categorical variables were compared using the chi-square tests. Logistic regression models were used to evaluate the association.
between RFD tertiles (predictor) and dichotomous worsening physical function, after adjusting for confounding factors (age, sex, BMI, depression, history of chronic diseases, and knee pain). The strength and direction of the associations were indicated with odds ratios (OR) and corresponding 95% CIs. Indicator variables were created from polytomous variables. Additional subgroup analyses were conducted by sex.

Knee pain was measured by the WOMAC pain subscale and was adjusted for in the logistic regression model. If pain was a major determinant of physical function, a correlation between the pain and function subscales could adversely affect our analyses. Therefore, sensitivity analyses were completed with and without adjustment for knee pain in the logistic regression model, to identify the effects of correlation. Additional sensitivity analyses were performed (1) defining knee replacement, but no other knee surgeries, as worsening; and (2) including participants who were unable to complete functional performance tests at follow-up as having worsened, and the overall results did not change substantially. Analyses were completed using SAS software version 9.4.

### Results

After applying the exclusion criteria, 3623 participants were included. However, because of missing data for either RFD at baseline or functional outcomes at follow-up, data were available for 2238 participants for the timed 20-m walk, 2017 participants for the repeated chair stand time, and 2630 participants for the WOMAC physical function subscale analyses. Baseline characteristics were compared between participants with missing data in different RFD groups to justify changes on participants’ characteristics by missing data. No differences were found in age ($P = .26$), BMI ($P = .93$), depression ($P = .37$), and history of chronic diseases ($P = .86$). However, WOMAC pain subscale scores in the highest tertile of RFD were lower than the subscales in the lowest tertile of RFD in participants with missing data ($P = .01$). Baseline characteristics of the participants are reported by tertile of RFD in table 1. There were no meaningful correlations between baseline RFD and baseline measures of physical function or functional performance (all $r < .14$).

The results for the logistic regression, adjusting for age, sex, BMI, depression, history of chronic diseases, and knee pain at baseline, are presented in table 2. Compared with the lowest tertile of RFD, the highest tertile had a lower risk for worsening of WOMAC physical function subscale score at 36-month follow-up with an adjusted OR of .68 (95% CI, .51–.92). Although the magnitude of reduction in the risk estimate was similar in the middle tertile of RFD (OR, .79; 95% CI, .60–1.05), this did not reach statistical significance. In sensitivity analyses unadjusted for knee pain, the ORs of the highest and middle tertiles were .64 (95% CI, .48–.85) and .78 (95% CI, .59–1.03), respectively.

Sex-stratified analyses are presented in table 3. Women with complete datasets for all outcome variables ($n = 1497$) in the highest tertile of RFD had a lower risk for worsening of WOMAC physical function subscale score at 36-month follow-up, in comparison with women in the lowest tertile (adjusted OR, .57; 95% CI, .38–.86). This decreased risk was not found in the middle tertile of RFD (adjusted OR, .72; 95% CI, .50–1.04). However, for men with complete datasets for all outcome variables ($n = 1133$), statistically significant reductions in risk for worsening of WOMAC physical function subscale score at 36-month follow-up were not detected in the middle or highest tertiles when compared with the lowest tertile of RFD (adjusted OR, .93; 95% CI, .59–1.47; OR, .81; 95% CI, .52–1.27, respectively).

### Discussion

Our results reveal that higher RFD was associated with reduced risk of worsening of WOMAC physical function subscale scores at 36-month follow-up in 45- to 79-year-old participants. We found no association between RFD and worsening of objective measures of physical performance (20-m walk time and repeated chair stand time) after 36 months.
Several studies have investigated the association of quadriceps RFD and self-reported physical function in patients with knee osteoarthritis. Maffulli et al. explored the association of quadriceps RFD and self-reported physical function in 31 patients (17 women, 66.3±7.1 years old) 6±1 months after undergoing total knee replacement. RFD was measured using the same Good Strength Chair system used in our study. Self-reported physical function was evaluated using the Knee Outcome Survey Activities of Daily Living Scale. The total Knee Outcome Survey Activities of Daily Living Scale score correlated with all RFD asymmetry variables. Winters and Rudolph conducted a comparative study between an OA group and a control group, involving a total of 49 subjects, to determine if RFD would improve the prediction of self-reported physical function. RFD was measured using a testing chair that was equipped with a SM-250 force transducer.

Self-reported physical function was evaluated by the function in daily living subscale from the Knee Injury and Osteoarthritis Outcome Score and a timed stair climbing test. The results of a hierarchical regression indicated that force at highest peak RFD explained 19.7% of the variance in the Knee Injury and Osteoarthritis Outcome Score function in daily living scale (P<.007). No association was found between RFD and stair climb time. Ward et al. identified neuromuscular impairments associated with unfavorable self-reported physical function outcomes in 391 community-dwelling primary care patients (261 women, 76.5±7.1 years old) with self-reported mobility modifications. Predictors of mobility change included leg strength and speed of movement (leg velocity, reaction time, and rapid leg coordination). Self-reported physical function was evaluated using the lower extremity function scales of the Late-Life Function and

### Table 2

<table>
<thead>
<tr>
<th>Measure of Physical Function or Performance</th>
<th>Lower RFD (&lt;224.8)</th>
<th>Middle RFD (224.8–491.6)</th>
<th>Higher RFD (&gt;491.6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-m walk n (%)</td>
<td>131 (17.8)</td>
<td>133 (18.1)</td>
<td>120 (15.6)</td>
</tr>
<tr>
<td>Univariate</td>
<td>ref</td>
<td>1.01 (0.77–1.31)</td>
<td>0.84 (0.64–1.11)</td>
</tr>
<tr>
<td>Multivariate</td>
<td>ref</td>
<td>1.03 (0.78–1.34)</td>
<td>0.89 (0.68–1.18)</td>
</tr>
<tr>
<td>Without knee pain</td>
<td>ref</td>
<td>1.01 (0.77–1.33)</td>
<td>0.86 (0.65–1.13)</td>
</tr>
<tr>
<td>Repeated chair stands</td>
<td>40 (6.4)</td>
<td>34 (5.0)</td>
<td>41 (5.7)</td>
</tr>
<tr>
<td>Univariate</td>
<td>ref</td>
<td>0.78 (0.49–1.25)</td>
<td>0.89 (0.57–1.40)</td>
</tr>
<tr>
<td>Multivariate</td>
<td>ref</td>
<td>0.78 (0.48–1.25)</td>
<td>0.94 (0.59–1.50)</td>
</tr>
<tr>
<td>Without knee pain</td>
<td>ref</td>
<td>0.78 (0.48–1.26)</td>
<td>0.85 (0.54–1.35)</td>
</tr>
<tr>
<td>WOMAC-PF*</td>
<td>130 (15.1)</td>
<td>108 (12.3)</td>
<td>93 (10.5)</td>
</tr>
<tr>
<td>Univariate</td>
<td>ref</td>
<td>0.79 (0.60–1.04)</td>
<td>0.66 (0.50–0.88)</td>
</tr>
<tr>
<td>Multivariate</td>
<td>ref</td>
<td>0.79 (0.60–1.05)</td>
<td>0.68 (0.51–0.92)</td>
</tr>
<tr>
<td>Without knee pain</td>
<td>ref</td>
<td>0.78 (0.59–1.03)</td>
<td>0.64 (0.48–0.85)</td>
</tr>
</tbody>
</table>

Note: Adjusted for age, sex, BMI, and knee pain (WOMAC) in multivariate analyses. Values are n (%) or OR (95% CI).

### Table 3

<table>
<thead>
<tr>
<th>Measure of Physical Function or Performance</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lower RFD (≤224.8)</td>
<td>Middle RFD (224.8–491.6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-m walk n (%)</td>
<td>45 (18.3)</td>
<td>57 (17.3)</td>
</tr>
<tr>
<td>Univariate</td>
<td>ref</td>
<td>0.93 (0.61–1.44)</td>
</tr>
<tr>
<td>Multivariate</td>
<td>ref</td>
<td>0.93 (0.60–1.44)</td>
</tr>
<tr>
<td>Without knee pain</td>
<td>ref</td>
<td>0.90 (0.58–1.39)</td>
</tr>
<tr>
<td>Repeated chair stands</td>
<td>12 (5.7)</td>
<td>16 (5.3)</td>
</tr>
<tr>
<td>Univariate</td>
<td>ref</td>
<td>0.93 (0.43–2.00)</td>
</tr>
<tr>
<td>Multivariate</td>
<td>ref</td>
<td>0.88 (0.40–1.92)</td>
</tr>
<tr>
<td>Without knee pain</td>
<td>ref</td>
<td>0.87 (0.40–1.90)</td>
</tr>
<tr>
<td>WOMAC-PF*</td>
<td>44 (15.2)</td>
<td>50 (13.1)</td>
</tr>
<tr>
<td>Univariate</td>
<td>ref</td>
<td>0.84 (0.54–1.30)</td>
</tr>
<tr>
<td>Multivariate</td>
<td>ref</td>
<td>0.93 (0.59–1.47)</td>
</tr>
<tr>
<td>Without knee pain</td>
<td>ref</td>
<td>0.88 (0.56–1.38)</td>
</tr>
</tbody>
</table>

Note: Adjusted for age, sex, BMI, and knee pain (WOMAC) in multivariate analyses. Values are n (%) or OR (95% CI).

Abbreviations: ref, reference; WOMAC-PF, WOMAC physical function subscale.

* P<.05 for chi-square trend test in women.
Disability Instrument. The results indicated that slower leg velocity predicted a greater likelihood of persistently poor function over 2 years. The observed associations between RFD and self-reported physical function concur with our findings, as did the lack of association of RFD with functional performance.

We did not find significant associations between RFD and worsening of physical performance as determined by 20-m walk time, or repeated chair stand time at the 36-month follow-up. One reason for the apparent discrepancy between WOMAC physical function subscale and the 20-m walk time is that during the physical performance test, participants were instructed to walk at their usual pace. Therefore, it is a measure of their usual walking pace, rather than their maximal walking pace. In addition, 36-month follow-up may be too short given the slow rate of functional decline. Batsis et al reported small changes in physical function (.07 m/s in gait speed and .02s in chair stand) over 6 years in older adults (≥60y of age). Therefore, the availability of only 3 years of follow-up may have resulted in the lack of statistically significant associations in our study. Finally, the participants in our study were younger (average age, 61y) than participants in the other 3 studies previously mentioned. Because functional limitations are usually occurring with older age, the relation between RFD and worsening of physical performance might not be present until later in the population of our study.

Knee OA is a leading cause of functional limitations. The relation between RFD and worsening of WOMAC physical function subscale would be helpful when designing rehabilitation interventions for knee OA. First, RFD determined by rapid muscle activation is closely related to physical performance and more sensitive to changes in physical performance. Muscle activation will be rapidly altered by difficult and complex physical performance (eg, during fast walking, stair negotiation). Maffiuletti et al have reported that RFD is better correlated with performance of both sport-specific and daily functional tasks than maximal voluntary contraction. Some studies have found that RFD was more sensitive to detect acute and chronic changes in neuromuscular function. Second, RFD can be improved by training. Both high-load strength training and explosive-type power training have a strong stimulatory effect on RFD. For example, in sedentary healthy men, Vila-Cha et al detected a 33% increase in knee extensor RFD after 6 weeks of lower-limb strength training. If a similar effect could be elicited, it is possible that exercise programs aimed at improving RFD may be useful in attenuating risk for worsening of physical function in people with knee OA. This is important not only to researchers in the field of human and exercise physiology but also for the prescription of exercise for preservation of physical function by practitioners in the fields of physical training and rehabilitation.

Through sex-specific subgroup analyses, we found the positive effects of RFD were driven by an association in women. In general, women also often report more substantial reductions in function than men in addition to greater pain and reductions in quality of life because of knee OA. Although sex differences in the association of muscle weakness and worsening of physical function is still unclear, some clues can be found in previous research. Significantly lower knee extensor strength prior to knee replacement was only observed in female patients compared with matched controls. In addition, a decreased risk of knee replacement from 0 to 84 months was only found in women with higher knee extensor strength at baseline. Some of the most common explanations for the sex differences are sex hormones and menopause. Studies have indicated that estrogen replacement therapy can decrease the risk of OA in postmenopausal women. However, another study demonstrated that systemic estrogen alone cannot explain the observed sex differences, and the assumed relation between the female hormonal status and OA remains to be explored further. In addition to sex hormones, other factors (eg, bone strength, alignment, ligament laxity, pregnancy, neuromuscular strength) could explain the sex difference. It is likely that a combination of mechanical, hormonal, and neural events in the joint are all involved in the explanation of sex differences. However, the association between these factors and sex difference in OA needs be investigated further.

Study limitations
Several limitations exist in this study. First, RFD was only assessed isometrically. However, strong correlations between isometric, isotonic, and isokinetic measures suggest similar results would have been likely to be detected irrespective of the mode of strength assessment. Second, our data cover only a 36-month period. The associations we found might be stronger if the intervals between the baseline assessment of RFD and follow-up assessment of physical function were longer. Third, OAI is a community-acquired sampling of people with or at risk for knee OA, allowing the results of this study to be generalizable only to that population. Fourth, some data were missing because a number of participants did not have RFD data collected at baseline or functional outcome data at follow-up. For participants with missing data, we found that WOMAC pain scores were lower for those in the highest tertile of RFD than in those in the lowest tertile of RFD (P = .01). In that case, participants without missing data in the highest tertile of RFD should be at higher risk for worsening physical function than participants without missing data in the lowest tertile of RFD because greater knee pain is closely associated with reduced physical function. Our results show that higher RFD at baseline is associated with reduced risk of worsening of WOMAC physical function subscale score at 36-month follow-up. It does not appear that absence of data influenced the direction of the association between RFD and risk for worsening physical function. However, the accuracy of estimates of risk reduction would be influenced by exclusion of participants with missing data from the analyses.

Conclusions
These data indicate that higher RFD at baseline is associated with reduced risk of worsening of WOMAC physical function subscale score at 36-month follow-up in older adults with or at risk for knee OA. Therefore, RFD may be a useful clinical predictor for worsening of physical function and could be a useful target for rehabilitation therapies aimed at maintaining or improving physical performance.

Suppliers
a. Good Strength Chair; Metitur.
b. SAS software version 9.4; SAS Institute.
c. SM-250 force transducer; Interface.
Keywords
Knee; Muscle Strength; Osteoarthritis; Quadriceps muscle; Rehabilitation; Sports Medicine

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