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ORIGINAL RESEARCH

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, 0.81; 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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Knee osteoarthritis (OA) is a major public health issue,¹ and worsening of physical function (eg, walking) is common among individuals with knee OA.^{2,3} Muscle weakness is closely related to knee OA, in that both men and women with radiographic knee OA have lower quadriceps strength,⁴ and specific torque regardless of pain status,⁵ 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,^{6,7} progression of tibiofemoral joint space narrowing,⁸ worsening knee pain,⁹ and knee replacement in women.¹⁰ Muscle weakness is also associated with a reduction in self-reported physical function,¹¹ and has been hypothesized as a causal factor for functional limitations.¹²

Rate of force development (RFD), a measure of explosive muscle strength, is calculated from the slope of the isometric force-time curve at different intervals¹³ and strongly depends on fast neuromuscular activation.¹⁴ Cross-sectional studies demonstrate that RFD is closely associated with performance of both daily functional¹⁵⁻¹⁷ and sport-specific tasks.¹⁸ In addition, RFD is associated with unfavorable mobility outcomes over 2 years in older primary care patients.¹⁹ 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.²⁰ However, no consensus exists on the optimal types and intensity of exercise that should be prescribed.²¹ A better understanding of the relation between RFD and functional

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 (fig 1).

Assessment of RFD

RFD was measured using the Good Strength Chair^a (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.²² 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),²³ 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:

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

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/datarelease>). OAI

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.²⁴ 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).²⁵ 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

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

Fig 1 Flowchart of the identification of participants for study inclusion.

relevant differences in physical function. Worsening 20-m walk was defined as an absolute decrease in gait speed of $\geq .14\text{m/s}$.²⁶ The MCID for worsening WOMAC physical function subscale was defined as an absolute increase of ≥ 9 (0–68 Likert scale).²⁷ 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.²⁸ 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 al²⁹ 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.³⁰

Assessment of potential confounders

Age, sex, and body mass index (BMI) have been found to be related to functional performance in several studies,^{31,32} and were

entered as potential confounders in multivariate analyses for exploring the relation between RFD and physical function. Depression³³ and history of chronic diseases³⁴ have proven to be associated with functional limitations. In OAI, depression was measured by the Center for Epidemiologic Studies Depression Scale score,³⁵ 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.³⁶ 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

Table 1 Characteristics of participants for each outcome

Variable	Participants for Worsening of 20-m Walk Time (n=2238)	Participants for Worsening of Repeated Chair Stands (n=2017)	Participants for Worsening of WOMAC-PF (N=2630)
RFD (N/s)	345.9 (185.0–611.4)	355.9 (192.2–624.9)	344.1 (184.1–608.0)
Age (y)	61.5±9.1	61.1±9.0	61.7±9.2
Sex, male	982 (43.9)	893 (44.3)	1133 (43.1)
BMI (kg/m ²)	28.1±4.5	28.1±4.5	28.2±4.6
CES-D	4.0 (1.0–8.0)	4.0 (1.0–8.0)	4.0 (1.0–8.0)
History of chronic diseases, yes	453 (20.2)	395 (19.6)	555 (21.1)
Baseline 20-m walk time (s)	15.1±2.1	15.1±2.1	15.3±2.2
Baseline repeated chair stand time (s)	10.8±2.7	10.7±2.6	10.9±2.8
Baseline WOMAC-PF subscale	4.0 (0.0–12.0)	3.2 (0.0–11.7)	4.0 (0.0–13.0)
Baseline WOMAC pain subscale	2.0 (0.0–4.0)	2.0 (0.0–4.0)	2.0 (0.0–4.0)
20-m walk time at 3-y follow-up (s)	15.2±2.2	15.1±2.1	15.2±2.3
Repeated chair stand time at 3-y follow-up (s)	10.4±2.4	10.4±2.4	10.4±2.5
WOMAC-PF subscale at 3-y follow-up	2.0 (0.0–10.0)	2.0 (0.0–9.0)	2.0 (0.0–10.0)
WOMAC pain subscale at 3-y follow-up	1.0 (0.0–4.0)	1.0 (0.0–4.0)	1.0 (0.0–4.0)

NOTE. Values are mean ± SD, median (quartile 1–quartile 3), or n (%).

Abbreviations: CES-D, Center for Epidemiologic Studies Depression Scale; WOMAC-PF, WOMAC physical function subscale.

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 substantively. Analyses were completed using SAS software version 9.4.^b

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, 0.79; 95% CI, 0.60–1.05), 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 0.78 (95% CI, 0.59–1.03), 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, 0.72; 95% CI, 0.50–1.04). 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, 0.93; 95% CI, 0.59–1.47; OR, 0.81; 95% CI, 0.52–1.27, 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.

Table 2 ORs for worsening of physical function by tertile of RFD at baseline

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

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.

Few studies are available for comparison. Maffiuletti et al³⁷ explored the association of quadriceps RFD and self-reported physical function in 31 patients (17 women, 66.3 ± 7.1 y 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.³⁷ Winters and Rudolph³⁸ conducted a comparative study between an OA group (14 men and 12 women, 65.3 ± 7.8 y old) and a control group (12 men and 11 women, 63.09 ± 7.66 y old), 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.^c

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 al¹⁹ identified neuromuscular impairments associated with unfavorable self-reported physical function outcomes in 391 community-dwelling primary care patients (261 women, 76.5 ± 7.1 y 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 3 Sex-specific ORs for worsening of physical function by tertile of RFD at baseline

Measure of Physical Function or Performance	Men			Women		
	Lower RFD (≤ 224.8)	Middle RFD (224.8–491.6)	Higher RFD (>491.6)	Lower RFD (≤ 224.8)	Middle RFD (224.8–491.6)	Higher RFD (>491.6)
20-m walk n (%)						
n (%)	45 (18.3)	57 (17.3)	58 (14.3)	86 (17.8)	76 (18.7)	62 (17.0)
Univariate	ref	0.93 (0.61–1.44)	0.74 (0.49–1.14)	ref	1.06 (0.76–1.50)	0.95 (0.66–1.36)
Multivariate	ref	0.93 (0.60–1.44)	0.74 (0.48–1.15)	ref	1.06 (0.75–1.50)	1.01 (0.70–1.45)
Without knee pain	ref	0.90 (0.58–1.39)	0.70 (0.45–1.08)	ref	1.06 (0.75–1.49)	0.99 (0.69–1.42)
Repeated chair stands						
n (%)	12 (5.7)	16 (5.3)	24 (6.3)	28 (6.7)	18 (4.8)	17 (5.1)
Univariate	ref	0.93 (0.43–2.00)	1.12 (0.55–2.29)	ref	0.71 (0.38–1.30)	0.74 (0.40–1.37)
Multivariate	ref	0.88 (0.40–1.92)	1.07 (0.52–2.21)	ref	0.73 (0.39–1.37)	0.82 (0.43–1.56)
Without knee pain	ref	0.87 (0.40–1.90)	1.00 (0.49–2.07)	ref	0.74 (0.40–1.37)	0.70 (0.38–1.32)
WOMAC-PF*						
n (%)	44 (15.2)	50 (13.1)	52 (11.3)	86 (15.0)	58 (11.7)	41 (9.6)
Univariate	ref	0.84 (0.54–1.30)	0.71 (0.46–1.09)	ref	0.75 (0.53–1.07)	0.60 (0.41–0.90)
Multivariate	ref	0.93 (0.59–1.47)	0.81 (0.52–1.27)	ref	0.73 (0.51–1.04)	0.60 (0.40–0.89)
Without knee pain	ref	0.88 (0.56–1.38)	0.71 (0.46–1.11)	ref	0.72 (0.50–1.04)	0.57 (0.38–0.86)

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 al³⁹ reported small changes in physical function (.07m/s in gait speed and .02s in chair stand) over 6 years in older adults (≥ 60 y 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.⁴⁰ 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).^{41,42} Maffiuletti et al⁴³ 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.^{44,45} 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 al⁴⁶ 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.⁴⁷ 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.¹⁰ 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.⁴⁸

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.^{49,50} However, another study demonstrated that systemic estrogen alone cannot explain the observed sex differences,⁵¹ and the assumed relation between the female hormonal status and OA remains to be explored further.⁵² In addition to sex hormones, other factors (eg, bone strength, alignment, ligament laxity, pregnancy, neuromuscular strength) could explain the sex difference.⁴⁰ It is likely that a combination of mechanical, hormonal, and neural events in the joint are all involved in the explanation of sex differences.⁵³ However, the association between these factors and sex difference in OA needs to 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.⁵⁴ 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

- Good Strength Chair; Metitur.
- SAS software version 9.4; SAS Institute.
- SM-250 force transducer; Interface.

Keywords

Knee; Muscle Strength; Osteoarthritis; Quadriceps muscle; Rehabilitation; Sports Medicine

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References

- Guccione AA, Felson DT, Anderson JJ, et al. The effects of specific medical conditions on the functional limitations of elders in the Framingham Study. *Am J Public Health* 1994;84:351-8.
- van Dijk GM, Dekker J, Veenhof C, van den Ende CH; Carpa Study Group. Course of functional status and pain in osteoarthritis of the hip or knee: a systematic review of the literature. *Arthritis Rheum* 2006;55:779-85.
- van Leeuwen DM, Peeters GM, de Ruiter CJ, et al. Effects of self-reported osteoarthritis on physical performance: a longitudinal study with a 10-year follow-up. *Aging Clin Exp Res* 2013; 25:561-9.
- Segal NA, Zimmerman MB, Brubaker M, Torner JC. Obesity and knee osteoarthritis are not associated with impaired quadriceps specific strength in adults. *PM R* 2011;3:314-23.
- Conroy MB, Kwok CK, Krishnan E, et al. Muscle strength, mass, and quality in older men and women with knee osteoarthritis. *Arthritis Care Res (Hoboken)* 2012;64:15-21.
- Segal NA, Torner JC, Felson D, et al. Effect of thigh strength on incident radiographic and symptomatic knee osteoarthritis in a longitudinal cohort. *Arthritis Rheum* 2009;61:1210-7.
- Oiestad BE, Juhl CB, Eitzen I, Thorlund JB. Knee extensor muscle weakness is a risk factor for development of knee osteoarthritis. A systematic review and meta-analysis. *Osteoarthritis Cartilage* 2015; 23:171-7.
- Segal NA, Glass NA, Torner J, et al. Quadriceps weakness predicts risk for knee joint space narrowing in women in the MOST cohort. *Osteoarthritis Cartilage* 2010;18:769-75.
- Glass NA, Torner JC, Frey Law LA, et al. The relationship between quadriceps muscle weakness and worsening of knee pain in the MOST cohort: a 5-year longitudinal study. *Osteoarthritis Cartilage* 2013;21:1154-9.
- Culvenor AG, Wirth W, Ruhdorfer A, Eckstein F. Thigh muscle strength predicts knee replacement risk independent of radiographic disease and pain in women: data from the Osteoarthritis Initiative. *Arthritis Rheumatol* 2016;68:1145-55.
- Ruhdorfer A, Wirth W, Eckstein F. Relationship between isometric thigh muscle strength and minimum clinically important differences in knee function in osteoarthritis: data from the osteoarthritis initiative. *Arthritis Care Res (Hoboken)* 2015;67:509-18.
- Pisters MF, Veenhof C, van Dijk GM, Heymans MW, Twisk JW, Dekker J. The course of limitations in activities over 5 years in patients with knee and hip osteoarthritis with moderate functional limitations: risk factors for future functional decline. *Osteoarthritis Cartilage* 2012;20:503-10.
- Aagaard P, Simonsen EB, Andersen JL, Magnusson P, Dyhre-Poulsen P. Increased rate of force development and neural drive of human skeletal muscle following resistance training. *J Appl Physiol* (1985) 2002;93:1318-26.
- de Ruiter CJ, Kooistra RD, Paalman MI, de Haan A. Initial phase of maximal voluntary and electrically stimulated knee extension torque development at different knee angles. *J Appl Physiol* (1985) 2004;97: 1693-701.
- Mayson DJ, Kiely DK, LaRose SI, Bean JF. Leg strength or velocity of movement: which is more influential on the balance of mobility limited elders? *Am J Phys Med Rehabil* 2008;87:969-76.
- Bean JF, Kiely DK, LaRose S, Leveille SG. Which impairments are most associated with high mobility performance in older adults? Implications for a rehabilitation prescription. *Arch Phys Med Rehabil* 2008;89:2278-84.
- Sayers SP, Guralnik JM, Thombs LA, Fielding RA. Effect of leg muscle contraction velocity on functional performance in older men and women. *J Am Geriatr Soc* 2005;53:467-71.
- Tillin NA, Pain MT, Folland J. Explosive force production during isometric squats correlates with athletic performance in rugby union players. *J Sports Sci* 2013;31:66-76.
- Ward RE, Beauchamp MK, Latham NK, et al. Neuromuscular impairments contributing to persistently poor and declining lower-extremity mobility among older adults: new findings informing geriatric rehabilitation. *Arch Phys Med Rehabil* 2016;97:1316-22.
- Rannou F, Poiraudou S. Non-pharmacological approaches for the treatment of osteoarthritis. *Best Pract Res Clin Rheumatol* 2010;24: 93-106.
- Bartholdy C, Juhl C, Christensen R, Lund H, Zhang W, Henriksen M. The role of muscle strengthening in exercise therapy for knee osteoarthritis: a systematic review and meta-regression analysis of randomized trials. *Semin Arthritis Rheum* 2017;47:9-21.
- Lord JP, Aitkens SG, McCrory MA, Bernauer EM. Isometric and isokinetic measurement of hamstring and quadriceps strength. *Arch Phys Med Rehabil* 1992;73:324-30.
- Kawamori N, Rossi SJ, Justice BD, et al. Peak force and rate of force development during isometric and dynamic mid-thigh clean pulls performed at various intensities. *J Strength Cond Res* 2006;20:483-91.
- Bohannon RW. Test-retest reliability of the five-repetition sit-to-stand test: a systematic review of the literature involving adults. *J Strength Cond Res* 2011;25:3205-7.
- Bellamy N, Bensen WG, Ford PM, Huang SH, Lang JY. Double-blind randomized controlled trial of flurbiprofen-SR (ANSAID-SR) and diclofenac sodium-SR (Voltaren-SR) in the treatment of osteoarthritis. *Clin Invest Med* 1992;15:427-33.
- Perera S, Mody SH, Woodman RC, Studenski SA. Meaningful change and responsiveness in common physical performance measures in older adults. *J Am Geriatr Soc* 2006;54:743-9.
- Tubach F, Ravaud P, Baron G, et al. Evaluation of clinically relevant changes in patient reported outcomes in knee and hip osteoarthritis: the minimal clinically important improvement. *Ann Rheum Dis* 2005;64:29-33.
- Tilson JK, Sullivan KJ, Cen SY, et al. Meaningful gait speed improvement during the first 60 days poststroke: minimal clinically important difference. *Phys Ther* 2010;90:196-208.
- Curb JD, Ceria-Ulep CD, Rodriguez BL, et al. Performance-based measures of physical function for high-function populations. *J Am Geriatr Soc* 2006;54:737-42.
- Wise BL, Niu J, Felson DT, et al. Functional impairment is a risk factor for knee replacement in the Multicenter Osteoarthritis Study. *Clin Orthop Relat Res* 2015;473:2505-13.
- Michl GL, Katz JN, Losina E. Risk and risk perception of knee osteoarthritis in the US: a population-based study. *Osteoarthritis Cartilage* 2016;24:593-6.

32. Zheng H, Chen C. Body mass index and risk of knee osteoarthritis: systematic review and meta-analysis of prospective studies. *BMJ Open* 2015;5:e007568.
33. Kouzis AC, Eaton WW. Emotional disability days: prevalence and predictors. *Am J Public Health* 1994;84:1304-7.
34. McKnight-Eily LR, Elam-Evans LD, Strine TW, et al. Activity limitation, chronic disease, and comorbid serious psychological distress in U.S. adults—BRFSS 2007. *Int J Public Health* 2009;(54 Suppl 1):111-9.
35. Irwin M, Artin KH, Oxman MN. Screening for depression in the older adult: criterion validity of the 10-item Center for Epidemiological Studies Depression Scale (CES-D). *Arch Intern Med* 1999; 159:1701-4.
36. Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. *J Clin Epidemiol* 1994;47:1245-51.
37. Maffiuletti NA, Bizzini M, Widler K, Munzinger U. Asymmetry in quadriceps rate of force development as a functional outcome measure in TKA. *Clin Orthop Relat Res* 2010;468:191-8.
38. Winters JD, Rudolph KS. Quadriceps rate of force development affects gait and function in people with knee osteoarthritis. *Eur J Appl Physiol* 2014;114:273-84.
39. Batsis JA, Zbehlik AJ, Barre LK, Bynum JP, Pidgeon D, Bartels SJ. Impact of obesity on disability, function, and physical activity: data from the Osteoarthritis Initiative. *Scand J Rheumatol* 2015;44:495-502.
40. Johnson VL, Hunter DJ. The epidemiology of osteoarthritis. *Best Pract Res Clin Rheumatol* 2014;28:5-15.
41. Schmitz A, Silder A, Heiderscheit B, Mahoney J, Thelen DG. Differences in lower-extremity muscular activation during walking between healthy older and young adults. *J Electromyogr Kinesiol* 2009; 19:1085-91.
42. Larsen AH, Puggaard L, Hamalainen U, Aagaard P. Comparison of ground reaction forces and antagonist muscle coactivation during stair walking with ageing. *J Electromyogr Kinesiol* 2008; 18:568-80.
43. Maffiuletti NA, Aagaard P, Blazevich AJ, Folland J, Tillin N, Duchateau J. Rate of force development: physiological and methodological considerations. *Eur J Appl Physiol* 2016;116:1091-116.
44. Angelozzi M, Madama M, Corsica C, et al. Rate of force development as an adjunctive outcome measure for return-to-sport decisions after anterior cruciate ligament reconstruction. *J Orthop Sports Phys Ther* 2012;42:772-80.
45. Penailillo L, Blazevich A, Numazawa H, Nosaka K. Rate of force development as a measure of muscle damage. *Scand J Med Sci Sports* 2015;25:417-27.
46. Vila-Cha C, Falla D, Farina D. Motor unit behavior during sub-maximal contractions following six weeks of either endurance or strength training. *J Appl Physiol* (1985) 2010;109:1455-66.
47. Zhang W, Nuki G, Moskowitz RW, et al. OARSI recommendations for the management of hip and knee osteoarthritis: part III: changes in evidence following systematic cumulative update of research published through January 2009. *Osteoarthritis Cartilage* 2010;18: 476-99.
48. Skou ST, Wise BL, Lewis CE, et al. Muscle strength, physical performance and physical activity as predictors of future knee replacement: a prospective cohort study. *Osteoarthritis Cartilage* 2016;24: 1350-6.
49. Spector TD, Nandra D, Hart DJ, Doyle DV. Is hormone replacement therapy protective for hand and knee osteoarthritis in women?: The Chingford Study. *Ann Rheum Dis* 1997;56:432-4.
50. Zhang Y, McAlindon TE, Hannan MT, et al. Estrogen replacement therapy and worsening of radiographic knee osteoarthritis: the Framingham Study. *Arthritis Rheum* 1998;41:1867-73.
51. Boyan BD, Hart DA, Enoka RM, et al. Hormonal modulation of connective tissue homeostasis and sex differences in risk for osteoarthritis of the knee. *Biol Sex Differ* 2013;4:3.
52. de Klerk BM, Schiphof D, Groeneveld FP, et al. No clear association between female hormonal aspects and osteoarthritis of the hand, hip and knee: a systematic review. *Rheumatology (Oxford)* 2009;48: 1160-5.
53. Boyan BD, Tosi LL, Coutts RD, et al. Addressing the gaps: sex differences in osteoarthritis of the knee. *Biol Sex Differ* 2013;4:4.
54. Sharma L, Cahue S, Song J, Hayes K, Pai YC, Dunlop D. Physical functioning over three years in knee osteoarthritis: role of psychosocial, local mechanical, and neuromuscular factors. *Arthritis Rheum* 2003;48:3359-70.