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Authors

Schroeder, Allison
Wang, Na
Felson, David T
et al.

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Knee extensor and flexor torque variability during maximal strength testing and change in knee pain and physical function at 60-month follow-up: The Multicenter Osteoarthritis Study (MOST)

Allison Schroeder, MD,
University of Pittsburgh Medical Center

Na Wang, MA,
Biostatistics and Epidemiology Data Analytics Center (BEDAC) Boston University School of Public Health

David T. Felson, MD,
Boston University

Cora E. Lewis, MD, MSPH,
University of Alabama at Birmingham

Michael C. Nevitt, PhD, MPH,
University of California, San Francisco

Neil A. Segal, MD
University of Kansas Medical Center and The University of Iowa

Abstract

As the population ages, there is a growing burden due to musculoskeletal diseases, such as knee osteoarthritis, and subsequent functional decline. In the absence of a cure, there is a need to identify factors amenable to intervention to prevent or slow this process. The Multicenter Osteoarthritis (MOST) Study cohort was developed for this purpose. In this study, associations between variability in peak knee flexor and extensor torque at baseline and worsening of pain and physical function over the subsequent 60 months were assessed in a cohort of 2,680 participants. The highest quartile of baseline knee flexor torque variability was found to be associated longitudinally with worsening pain 4th quartile ß estimate±SE, (0.49±0.19; p=0.0115) with R^2=0.28 and p-for-trend across quartiles=0.0370} and physical function scores {4th quartile ß estimate±SE (1.39±0.64; p=0.0296) with R^2=0.25 and p-for-trend across quartiles=0.0371}, after adjusting for baseline knee OA and maximum knee flexor torque. There were no associations between baseline knee extensor torque and worsening pain or physical function by 60 months. The presence of greater variability in maximum knee flexor strength may identify patients who may benefit from therapies aimed at preventing worsening knee pain and physical function.

Correspondence: Dr. Allison Schroeder, UPMC Department of PM&R; 347 Fifth Ave., Kaufman Building Suite 910, Pittsburgh, PA 15213.

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Keywords

knee; strength; physical function; osteoarthritis

INTRODUCTION:

As the population ages, the burden of musculoskeletal diseases becomes even more apparent, contributing to a cycle of worsening pain, impaired strength, and functional decline. Osteoarthritis (OA) is a degenerative joint disease commonly affecting the knee that causes pain, impairs function, reduces quality of life, and may lead to secondary health complications and increased risk for mortality[1–6]. Despite several studies examining prognostic factors for development of pain and declining physical function in patients with OA, there is limited evidence supporting pain, BMI, age, and muscle torque as prognostic factors for future functional limitations [2,7–10]. Maintaining sufficient quadriceps strength, measured by knee extensor torque, is one factor that has been found to be associated with lower risk for incident and progressive knee OA[11–13] and correlates with higher levels of physical function[14]. Although maintaining quadriceps strength is often a target of rehabilitation and exercise programs aiming to prevent and treat knee OA, additional factors likely contribute to worsening pain and physical function in those with or at risk for knee OA.

Inconsistent generation of muscle torque could contribute to worsening pain or physical function, as ambulation and daily activities require torque that exceeds a critical threshold, though this critical threshold has not yet been defined. Ability to consistently produce muscle torque is required with each step and the quadriceps and hamstrings work together to allow for proper knee mechanics during gait and other activities of daily life [15,16]. Most research regarding muscle function in the context of knee OA has focused on quadriceps or hamstring weakness by measuring the magnitude of muscle contraction, such as peak torque about the knee joint during maximal muscle contraction[11,13,17–19]. Frequently, muscle function is reported as the average torque measurement over multiple attempts. This type of measurement has revealed that impairments in knee extensor torque are associated with worsening pain and function[11,13,18,20]. However, selecting only the peak or average value obscures the degree of consistency of muscle torque testing. The ability to consistently generate torque may be a relevant factor, as this has been shown to be associated with worsening function in lumbar spine extension torque testing in patients with low back pain[21] and variability in test performance has predicted clinical outcomes better than the magnitude of the measurements in a variety of other domains[22–25].

Variability in strength of the muscles that control the knee may be a potential prognostic factor for future functional decline. Several studies have shown that steadiness, variability in knee extensor strength at a sub-maximal level, is associated with knee osteoarthritis[26–28] or impaired mobility[29] in adults. The ability to control knee extensor strength output has been investigated in community-dwelling adults, in individuals pre-and post- anterior cruciate ligament reconstruction, and in adults with knee OA[26–31]. Hortobagyi and colleagues studied patients with knee OA compared to age-and sex-matched controls and found that

those with knee OA had 155% greater variation in force production[26]. Other studies have shown variation in sub-maximal extensor torque (measure of strength over an arch) differed between those with OA and healthy controls[27] and decreased after total knee arthroplasty[28]. However, there is no gold standard measure for knee muscle torque variability, with different studies using different measures of variability, such as mean absolute error (evaluates absolute differences)[26], standard deviation (square of the absolute differences)[27] and coefficient of variation (standard deviation divided by the mean)[28]. These studies on sub-maximal torque all differ from the current study, but do not examine consistencies in generating maximal knee torque.

Previous studies have demonstrated associations between increased sub-maximal knee extensor variability and progression of knee OA[26–28] but the study of variability in maximal knee muscle torque and how this relates to longitudinal changes in physical function and performance remains unclear. To our knowledge, variability in muscle torque about the knee has not been examined in sample sizes large enough to control for several potential confounding factors (all less than 40 participants)[26,27]. None of the prior studies examined maximal torque variability, which may be important as a population ages and utilization of maximum strength may be needed in daily life. Additionally, only knee extensor torque variability has been studied[26–29], and knowledge gaps exist regarding possible contributions of flexor torque variability as a potential predictor of worsening pain, physical function and performance. Therefore, the objective of this study was to assess muscle function in a sufficiently large sample to determine whether peak knee extensor or flexor torque variability during maximal muscle torque testing is associated with changes in pain, physical function and physical performance at 60-month follow-up. The finding that greater variability in maximal torque efforts is associated with decline in functional outcomes would allow one to measure torque variability in clinic or with physical therapy and stratify patients for those adverse outcomes.

METHODS:

Study sample:

The Multicenter Osteoarthritis (MOST) Study is an NIH-funded longitudinal observational study of risk factors for knee OA[32] and disablement. At baseline, the MOST cohort consisted who were with or at risk of having knee OA and were made up of: 60.1% women, age 50-79 years old who had at least one of the following characteristics: were overweight or obese, had a history of injury that made it difficult to walk for at least one week, or had a previous knee surgery. Participants were recruited from the areas surrounding Birmingham, Alabama and Iowa City, Iowa, where the respective institutional review boards approved the study in compliance with the Declaration of Helsinki. All participants who completed 60-month follow-up and who had baseline strength measurements were included in the analysis. Baseline age, sex, body mass index (BMI), and study site were recorded as described previously[19,32]. All participants provided written informed consent to participate in the study, as approved by the institutional review boards (IRB). This study conforms to all STROBE guidelines and reports the required information accordingly.

Measurement of baseline knee extensor and flexor torque:

We measured peak muscle torque variability in the left lower limbs using a computerized isokinetic dynamometer (Cybex 350, Medway, MA, USA) on which participants' trunk, thigh and leg were fixed to the chair with straps. One limb (left) per participant was selected to avoid incomplete independence between sides within participants.

Peak concentric isokinetic left knee extensor and flexor torque were measured by trained operators at baseline, following a previously published protocol[11,13,18]. The participant was first instructed to complete three practice repetitions by pushing and pulling while giving 50% effort. After the participant was accustomed to the movement and the overall feel, a short rest of about 5 seconds was provided prior to completing the four repetitions for the measurement set.

For that, participants were instructed to push and pull as hard and as fast possible, while holding onto the handles firmly with both hands and not holding their breath during the test. Four repetitions of alternating flexion/extension maximal strength efforts were performed at 60°/second while the examiner provided a standardized script, encouraging to "Push, push, push! Pull, pull, pull!" during each of the repetitions. Visual feedback was provided, such that the participant could see the amplitude and slope of their isokinetic strength testing effort during each of the repetitions, superimposed on prior repetitions within the set. Quality control measures have been previously published and included certification of the testers in the MOST strength testing protocol, annual recertification, and a standardized script for participant testing[33]. Test-retest reliability of peak flexor and extensor torque was assessed through repeating the protocol for isokinetic strength testing once each month for 3 months in a random sample of the cohort included in this study and yielded an ICC of 0.94 (95% CI of 0.82–0.99) and a COV of 8% (95% CI of 6–12%)[19].

Calculation of torque variability:

Within-participant knee extensor and flexor torque variability was calculated as the coefficient of variation over the four trials. The coefficient of variation for baseline torque was calculated by dividing the standard deviation by the mean of the four peak strength measurements and multiplying by 100%.

Outcome measures:

Outcome measures included: self-reported pain measured on the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), self-reported WOMAC physical function, and physical performance measured with the repeated chair stand test and 20-meter walk times[32]. These were collected by trained researchers who were different from those performing the analysis. Measurements were recorded at baseline and 60-month follow-up and the differences were calculated.

Statistical Analyses:

Linear regression using generalized linear models with maximum likelihood estimation was used to fit baseline torque variability to each of the four outcome measures (i.e. 60-month change in WOMAC pain and function scores and chair stand and walk times) adjusting for

age, sex, BMI and study site. Data were stratified into quartiles of baseline torque variability (n=670 per group) to reduce data loss from a continuous scale compared to division into quartiles or dichotomization of data and the lowest quartile was used as the reference group. In order to minimize potential confounding bias, additional regression analyses were adjusted for baseline presence of knee OA (associations knee OA and variability was significant for knee flexors (chi-square=17.7027, p=0.0005) but not knee extensors (chi-square=5.2437, p=0.1547)) and baseline peak flexor and extensor torque magnitudes respectively (associations between peak torque and torque variability were −0.63 for both flexors and extensors). Analyses were completed using SAS version 9.4 (SAS, SAS Institute, Cary, NC, USA) with an alpha level of $p<0.05$.

RESULTS:

Baseline characteristics:

The left knees of 2680 participants (60.9% female; 15.5% non-white) were included in the analyses. Participants had an average age of 62.0±8.1 years and average BMI of 29.8 ± 5.8 kg/m^2. Average peak knee flexor torque variability was 14.9±12.8%. Average peak knee extensor torque variability was 10.1±13.2%. Participants' baseline characteristics are described in Table 1.

Flexor Torque Variability:

When adjusting for baseline age, sex, BMI, and study site, there was a significant association between higher baseline peak knee flexor torque variability and worsening of WOMAC pain score, WOMAC physical function, chair stand time, and 20-meter walk time (Table 2). After additional adjustment for baseline knee OA and maximum flexion torque, these significant associations persisted for worsening pain {4th quartile ß estimate±SE, (0.49±0.19; p=0.0115) with R^2=0.28 and p-for-trend across quartiles=0.0370} and physical function scores {4th quartile ß estimate±SE (1.39±0.64; p=0.0296) with R^2=0.25 and p-for-trend across quartiles=0.0371}. Significant associations did not persist for worsening of physical performance on the timed chair stand after adjustment for baseline peak flexor torque. WOMAC pain, physical function, chair stand time, and 20-meter walk time are displayed by quartile in Figure 1 and showed regression to the mean when comparing outcome measures at 60 months to baseline.

Extensor Torque Variability:

When adjusting for baseline age, sex, BMI, and study site, there were no significant associations between baseline peak knee extensor torque variability and worsening of pain, physical function, chair stand time, or 20-meter walk time (Table 2). When additionally adjusting for baseline knee OA and maximum extensor torque, absence of significant associations persisted.

DISCUSSION:

The goal of this study was to determine if baseline flexor and extensor torque variability was associated with worsening pain, physical function, and physical performance at 60-month

follow-up. It has been well documented that impaired maximum knee extensor torque is associated with a decline in physical function as patients age [34–36]. The goal of this study was to identify patients who could be at risk for developing worsening pain and functional decline that may not be identified by measurements of the magnitude of maximum torque measurements alone. This observational study was not designed to comprehensively evaluate the mechanism for the potential association that was identified. Additional research to examine the mechanism for the relationship would allow design of interventions to prevent and potentially mitigate the effect of variability in strength on worsening of pain and physical function. After adjustment for baseline factors including peak torque and presence of knee OA, this study provided evidence of an association between greater knee flexor torque variability and worsening pain and physical function. No such association was detected between knee extensor torque variability and these outcomes.

Impairments in maximum knee extensor torque have been shown to be associated with worsening pain and functional decline [17,37–39]. Although several studies have documented an association between sub-maximal knee extensor torque variability and OA or impaired mobility, these studies examined sub-maximal torque, included measurement of only extensor torque variability but not flexor torque variability, were limited by small sample sizes, and did not report variability after adjusting for baseline extensor torque magnitude, [26–29] a factor that we found to be associated with torque variability. In our study, with a much larger sample size and looking at maximum values, we did not find an association between extensor torque variability and worsening pain and function in patients who have or are at risk for knee OA. This suggests that measurement of maximal knee extensor torque without calculating variability between trials, is likely sufficient to identify individuals with or at risk for knee osteoarthritis who may experience worsening pain and physical function.

In contrast, although alteration in hamstring firing has been demonstrated in individuals with knee osteoarthritis [40–42], a clear association between maximum hamstring strength and those at risk for worsening pain and physical function has not been described. In this study, we found that variability in maximum knee flexor strength measurements was associated with worsening pain and self-reported physical function over 60-month follow-up, even after adjustment for baseline maximum flexor strength. Measurement of variability in maximum flexor strength may help clinicians identify the patients who are at particularly elevated risk for developing worsening pain and function and enroll them in a physical therapy program, though further studies are needed to determine the mechanism of this association.

Possible mechanisms by which higher variability in hamstring torque could contribute to worsening of pain and physical function derive from the biomechanics of the role of the hamstrings during gait. During terminal swing and initial contact phases of gait, the hamstrings eccentrically contract to decelerate the leg, thereby attenuating impulse loads and articular contact stress in the knee as the limb transitions into weight acceptance. A burst in hamstring muscle activity with loading response has been shown to occur in patients with knee osteoarthritis and pain [40–42]. Variability in ability for the hamstrings to fire at a consistent effort when decelerating the lower leg contributes to altered tibiofemoral contact forces and impaired knee mechanics, potentially resulting in worsening knee pain and could result in patients walking more slowly to minimize elevated forces in the joint, thereby

reducing physical function [43,44]. As maximal flexor torque may not be required in normal gait, further research is necessary to better elucidate the mechanism for the associations detected in our current study. Measurement of maximum knee flexor torque variability can be calculated easily from a brief series of maximum efforts, and patients with excessive variability may be identified as having particularly elevated risk for worsening pain and physical function. Excessive variability in flexor torque would best be defined by the 4th quartile of 50–79 year-olds in our study, as it was the quartile with the highest variability that appeared to be driving the overall study results (Table 2). These individuals may be at greatest risk for worsening pain and function. Additional research is needed to determine the underlying factors contributing to excessive flexor torque variability, including patient effort, fatigue, and discomfort. Identifying those at risk for worsening of pain and function is the first step in developing therapeutic approaches to prevent mobility limitations, particularly in an aging population. There is also a need for future studies in determining both a) whether interventional studies targeting reducing excessive flexor torque variability will prevent or slow onset or worsening of pain and physical functional decline, and, if so, b) the optimal rehabilitation program to target improvement in flexor torque variability.

Strengths of this study include the large sample of community-living older adults that is generalizable to other older adults, with average age of 62 years at baseline and 67 years at follow-up in this study. This study benefited from high test-retest reliability in knee flexor and extensor torque measurements. Limitations include the fact that isokinetic torque testing is not the usual way in which muscles are activated in daily functional activities but serves as a good research tool due to its wide use and internal consistency. Torque was calculated while grasping bars during testing which could impact maximum measurements; however, it likely did not affect variability between the maximum measurements, since all were performed in the same manner. Additionally, isometric sub-maximal torque testing, which was used by Hortobagyi[26] and Mau-Mueller [27] and maximal isokinetic torque testing, which was used in our study can yield different results. Isometric torque testing depends on a fixed knee flexor angle, while isokinetic torque testing measures torque over the functional range of motion. This methodological difference may not allow for direct comparison of the results, since participants may have more pain with tasks that move the knee vs. those that do not. In comparison with isometric testing, our use of isokinetic torque testing might be considered to be functionally relevant from the standpoint that daily activities are not performed at a fixed knee joint angle. Additionally, episodic self-reported pain and function, at baseline and 60-month follow-up visits, may not accurately reflect true pain/function over time. However, this is a measurement limitation of any study in which measurements cannot be acquired continuously and it is hoped that the large sample size averages out variability of the results. Only including left limbs also may be a limitation, although we selected one limb for consistency, and to minimize bias. Finally, the participants did hold onto bars during the strength testing, but all were performed in the same manner in a continuous flow without changing grip during the continuous arc of motion of the 4 alternating pushes and pulls.

CONCLUSION:

The main findings of this cohort study were that higher baseline knee flexor torque variability was significantly associated with worsening of self-reported pain and physical

function, and20-meter walk time. These associations persisted for self-reported pain and physical function after further adjusting for baseline maximum knee flexor torque. Thus, patients with higher knee flexor torque variability may potentially benefit from rehabilitation programs to attenuate risk for worsening of pain and physical function.

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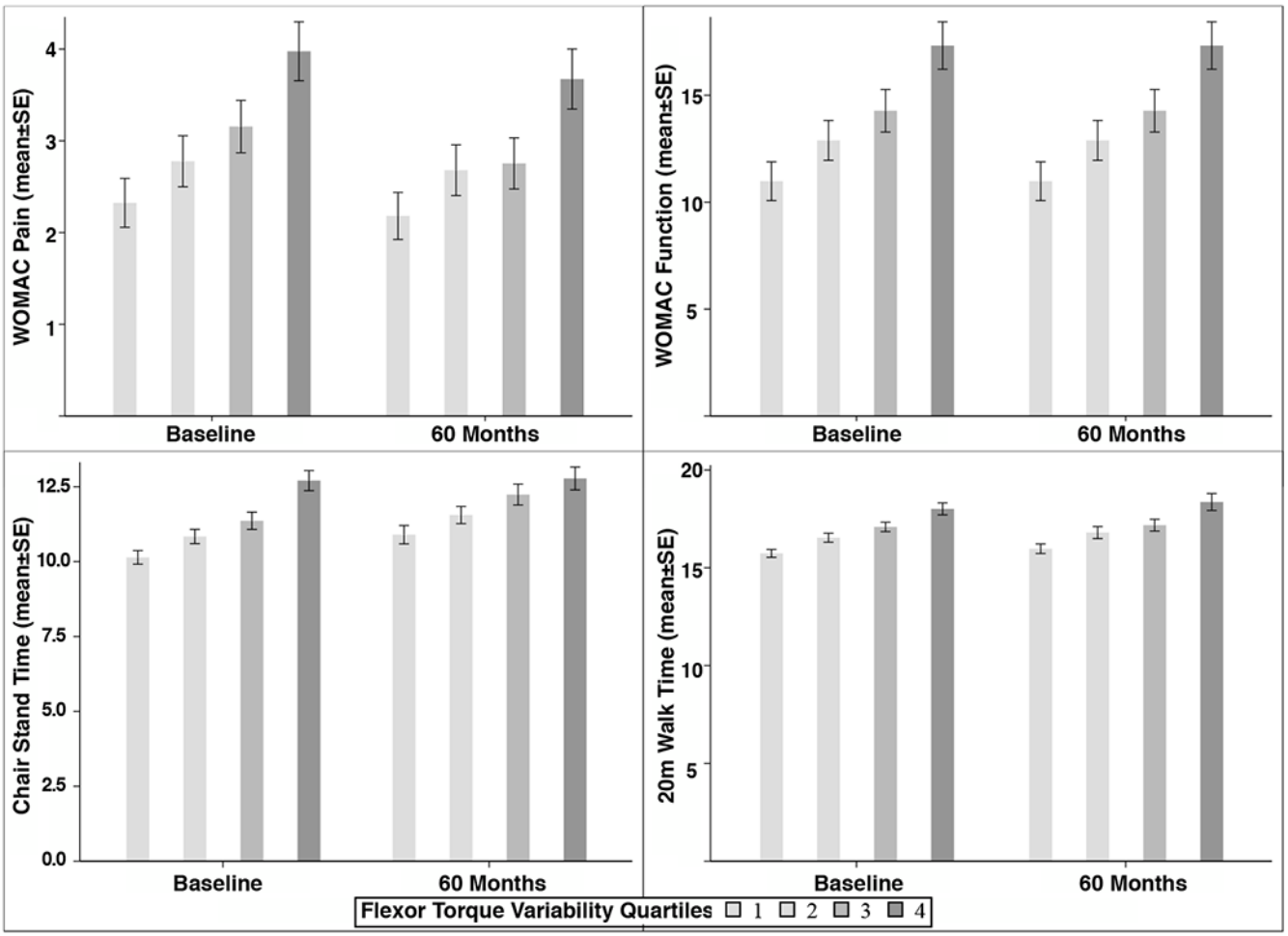

Figure 1:
Outcome measures at baseline and 60-month follow-up

Table 1:

Demographic and baseline characteristics of patient population

Variable	Value
Total participants	2680
% Women	60.9
% Non-white	15.5
Age (years)	62.0±8.1
BMI (kg/m^2)	29.8 ± 5.8
% Recruited from The University of Iowa clinical site	51.6
Peak knee flexor torque variability (%) (mean±SD)	14.9±12.8
Peak knee extensor torque variability (%) (mean±SD)	10.1±13.2
Flexor variance quartiles:	
1	0.00-6.74
2	6.75-11.10
3	11.10-18.41
4	18.43-127.66
Extensor variance quartiles:	
1	0.70-6.66
2	6.67-10.69
3	10.69-16.81
4	16.86-107.61

Table 2:

Adjusted associations of baseline flexor and extensor torque variability with changes in outcome measures between baseline and 60-month follow-up. The 2nd, 3rd, and 4th quartiles were compared to the first quartile for significance.

	Knee Flexor Torque Variability				Knee Extensor Torque Variability			
Predictor	**Pain**	**Physical Function**	**Chair Stand**	**20m Walk**	**Pain**	**Physical Function**	**Chair Stand**	**20m Walk**
2nd quartile ß estimate±SE	**0.12±0.17***	−0.05±0.58	0.14±0.19	0.12±0.17	−0.04±0.18	−0.40±0.59	0.32±0.20	0.15±0.17
3rd quartile ß estimate±SE	0.08±0.18	0.20±0.59	**0.41±0.20^**	0.08±0.17	0.10±0.18	−0.03±0.59	0.38±0.20	0.09±0.17
4th quartile ß estimate±SE	**.60±0.18***	**2.03±0.60***	0.36±0.21	**0.58±0.18***	0.23±0.18	0.41±0.60	0.39±0.20	0.10±0.17
R^2	**0.27**	**0.24**	**0.19**	**0.13**	.27	0.23	0.19	0.13
p-for-trend across quartiles	**0.0022**	**0.0011**	**0.0361**	**0.0026**	0.1506	0.4003	0.0537	0.6405

* = p <0.01,

^ =p<0.05.