Risk of Knee Osteoarthritis Over 24 Months in Individuals Who Decrease Walking Speed During a 12-Month Period: Data from the Osteoarthritis Initiative

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ABSTRACT. ***Objective.*** To assess the association between change in walking speed over a 12-month period and risk of developing radiographic knee osteoarthritis (rKOA) over a 24-month period.

Methods. We included participants without rKOA from the Osteoarthritis Initiative. Change in walking speed was determined from a 20-m walk assessment, calculated using walking speed at 12-month followup minus baseline speed and/or 24-month followup walking speed minus 12-month speed. Incident rKOA was defined as progressing to Kellgren-Lawrence arthritis grading scale ≥ 2 within 24 months (i.e., incidence between 12 and 36 mos or 24 and 48 mos). Self-reported significant knee injury during the exposure period, age, body mass index (BMI), and Physical Activity Scale for the Elderly (PASE) score were adjusted for analytically.

Results. We included 2638 observations among 1460 unique participants (58% women; aged 59 ± 9 yrs, range 45–79). The mean change in walking speed over 12 months was 0.001 ± 0.13 m/s (range –0.6271 to 1.4968). About 5% of the sample (n = 122) developed rKOA over a 24-month period. After controlling for significant knee injury, age, BMI, and PASE score, we found an 8% relative increase in risk of developing rKOA for every 0.1 m/s decrease in walking speed over a 12-month period (risk ratio 1.08, 95% CI 1.00–1.15, p = 0.05).

Conclusion. Evaluating change in speed over a 12-month period using a 20-m walk test may be useful in identifying individuals at increased risk of developing rKOA over the subsequent 24 months. Identification of patients at high risk for developing rKOA would allow medical providers to implement early interventions to maximize joint health. (J Rheumatol First Release June 1 2017; doi:10.3899/ jrheum.170093)

Key Indexing Terms:
OSTEOARTHRITIS GAIT KNEE

Knee osteoarthritis (KOA) is the 11th leading cause of global disability[1]. There are no disease-modifying interventions for KOA. One explanation for our failure to identify a disease-modifying intervention is that we primarily test patients late in the disease process when it may be too late. Therefore, early identification of risk factors associated with the incidence and progression of KOA has become paramount in preventing disease onset or progression, as well as associated physical disability[2,3]. Clinical strategies are needed that can easily be implemented to predict the incidence of radiographic KOA (rKOA). Reliable and efficient clinical measures would be beneficial to identifying individuals at increased risk of developing rKOA.

Walking speed is a readily observable and stable objective measure of physical function. Habitual walking speed is typically a stable measure that only varies 1% per decade on average until individuals reach about 62 years of age[4]. Individuals with symptomatic KOA demonstrate a rapid

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decrease in walking speed of as much as 2.75% per year[5]. Decreased walking speed is associated with decreased confidence in knee function[6] in those with KOA and predicts the likelihood that an individual with KOA will elect to undergo a knee replacement[7]. In addition, slower walking speed associates with higher concentrations of serum-based markers of type II collagen breakdown in individuals following anterior cruciate ligament reconstruction[8] who are at higher risk of developing rKOA[9,10,11].

Previous authors have demonstrated that slower habitual walkers without rKOA demonstrated higher odds of developing rKOA at 6-year followup[12]. However, change in walking speed may provide a more sensitive measure of future OA risk than an assessment of gait pace at a single timepoint. To date, to our knowledge, no prospective studies have examined longitudinal changes in walking speed and risk of rKOA. The ability to predict an individual's risk of developing rKOA by measuring a change in walking speed may provide clinicians with a cost-effective measurement tool that could be used at subsequent clinic visits. While walking speed is known to decrease in those with symptomatic KOA[5], it remains unknown whether a decrease in walking speed among those without rKOA over 1 year is identifiable prior to rKOA development or progression.

The overall goal of our analysis was to determine whether changes in a simple 20-m walk test, evaluated during annual clinical examinations, could be used as a marker of those who will develop rKOA within the following 2 years. To accomplish this goal, we assessed the association between a change in walking speed over a 12-month period among individuals without OA and the risk of developing rKOA over a subsequent 24-month period using data from the Osteoarthritis Initiative (OAI). We hypothesized that a decrease in walking speed over a 12-month period would be associated with an increase in rKOA risk over the subsequent 24 months.

MATERIALS AND METHODS

Study design. Data used in the preparation of our article were obtained from the OAI database, available for public access at www.oai.ucsf.edu[13]. Briefly, the OAI was a multicenter, longitudinal, prospective observational study of KOA in the United States[13]. Clinical staff recruited 4796 men and women between the ages of 45 to 79 years who primarily had symptomatic KOA or were at increased risk for developing symptomatic KOA between February 2004 and May 2006[13]. For our analyses, we used data from the OAI baseline and the first 4 annual followup visits (12-mo through 48-mo followup). This study was approved by the University of North Carolina at Chapel Hill Institutional Review Board under IRB 16-1678.

Inclusion criteria. We included OAI participants without tibiofemoral rKOA in both knees [Kellgren-Lawrence arthritis grading scale (KL) ≤ 1] and who had at least 2 walking speed assessments, separated by 12 months, prior to the 24-month OAI visit (Figure 1). Eligible participants also needed to have knee radiographs scored during the exposure period and at the OAI visit that occurred 24 months after the last assessment of walking speed. Participants were excluded if they demonstrated rKOA in either knee at any time during exposure assessment or if they had any knee arthroplasty in either knee, had any hip arthroplasty in either hip, had any type of prosthesis surrounding the knee, or reported using an ambulatory aid other than a single straight cane for more than 50% of their time during ambulation. We excluded participants with a self-reported history or clinical suspicion of rheumatoid arthritis during our study period.

Walking speed. The 12-month change in walking speed was determined from the pace of a 20-m walk assessment, using the "AllClinical" files. The 20-m walking speed assessment has been recommended to assess physical function in individuals with rKOA[14]. Participants were instructed to walk at their usual walking speed from the start to finish points of a marked 20-m distance[15]. As previously reported[15,16], 2 trials were collected and the mean of these trials was used for data analysis. We included 2 periods of exposure assessment to determine change in walking speed, resulting in 2 potential observations for each participant. Exposure assessment 1 was calculated from the Baseline AllClinical file (version 0.2.2) and the 12-month AllClinical file (version 1.2.1). Exposure assessment 2 was calculated from the 12-month AllClinical file (version 1.2.1) and the 24-month AllClinical file (version 3.2.1). To maximize the number of unique assessments of walking speed change, walking speed was calculated as a continuous variable from either (1) the baseline visit to the 12-month followup (Exposure Assessment 1: 12-mo speed – baseline speed) or (2) from the 12-month followup to the 24-month followup (Exposure Assessment 2: 24-mo – 12-mo speed; Figure 2). Walking speed was measured in meters per second (m/s).

Knee radiographs. We assessed the incidence of rKOA over 24 months at the 36-month or 48-month OAI visit for exposure assessments 1 and 2, respectively (Figure 2). Incident tibiofemoral rKOA was determined as having a KL grade ≥ 2 in either knee 24 months following no presence of rKOA (KL ≤ 1) at any time during exposure assessment. If either or both knees developed rKOA over the 24 months following exposure assessment, that participant was considered to have incident rKOA. Central readers scored KL grades on bilateral weight-bearing, fixed-flexion, posterior-anterior knee radiographs. Readers were blinded to the sequence of followup images. A study of image assessment in the OAI found good reliability for KL grading between baseline and the 36-month followup visit, with κ values of about 0.70 to 0.80[17]. In addition, agreement of readings was similar for the 48-month followup visit radiographs.

Potential confounders. To assess the association between change in walking speed and incident rKOA, we included in our initial analysis demographic information on age at baseline, sex, and body mass index (BMI) at baseline. Additionally, physical activity level was measured at the 12-month timepoint of the exposure assessment using the Physical Activity Scale for the Elderly (PASE; Figure 2)[18]. Finally, we included information about knee pain, ankle pain, back pain, hip pain, knee injury, and history of a fall as potential confounders. Knee, ankle, and hip pain were dichotomous variables for self-reported pain, aching, or stiffness for more than half the days in the past 30 days from the second walking speed assessment. Self-reported back pain in the past 30 days was also recorded during the 12-month timepoint of the exposure assessment. Knee injury was a dichotomous variable defined as "a serious enough knee injury to limit the ability to walk for at least 2 days" during the 12-month exposure assessment period. We also included self-reported history of a fall, which was defined as any fall to the floor or ground. All covariates were calculated from the Baseline AllClinical file (version 0.2.2), the 12-month AllClinical file (version 1.2.1), and the 24-month AllClinical file (version 3.2.1). Based on the minimally sufficient adjustment set identified from a directed acyclic graph, the following confounders were included in our analysis: knee injury, age, BMI, and PASE score.

Statistical analysis. Descriptive statistics were calculated for all variables of interest, including counts and proportions for dichotomous variables, and means and SD as well as medians and interquartile ranges (IQR) for continuous variables. Comparisons of continuous walking speed between those who developed rKOA and those who did not were performed using a 2-sample Student t test because of large sample size and normally distributed data. We determined *a priori* to assess the linear characteristic of the relationship prior to formal statistical analyses using functional form analysis techniques.

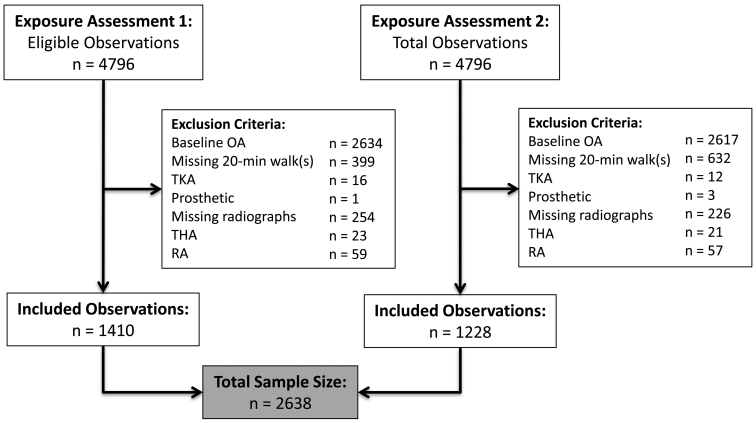

Figure 1. Flow diagram of study enrollment for OAI participants included in the analysis of the association between 12-month change in walking speed and 24-month risk for incident rKOA. OA: osteoarthritis; OAI: OA Initiative; rKOA: radiographic knee OA; TKA: total knee arthroplasty; THA: total hip arthroplasty; RA: rheumatoid arthritis.

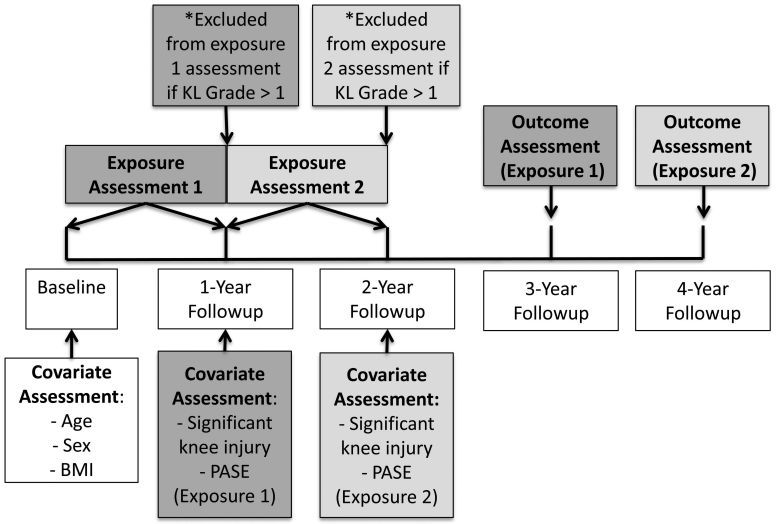

Figure 2. Exposure, outcome, and covariate assessment diagram for participants included in the analysis of the association between 12-month change in walking speed and 24-month risk for incident rKOA. rKOA: radiographic knee osteoarthritis; KL: Kellgren-Lawrence arthritis grading scale; BMI: body mass index; PASE: Physical Activity Scale for the Elderly.

Results of the functional form analysis indicated a relatively linear relationship between change in walking speed and incident rKOA. Therefore, multivariable log-binomial regression was used to assess the association between continuous walking speed and incident rKOA. An adjusted risk ratio (RR) was also calculated to estimate the effect of a –0.1 m/s decrease in walking speed on rKOA incidence (0.10 m/s change in walking speed has previously been reported as the minimal clinically important difference for change in walking speed over time) while controlling for the potential confounders (knee injury, age, BMI, and PASE score) for our primary analysis[19]. An interaction term was added to assess potential effect measure modification of the association between walking speed and rKOA incidence by reported knee injury. To account for the correlation within participants who were included in both exposure assessments, a generalized estimating equation analysis with robust standard errors was used. We used Statistical Analysis Software (SAS version 9.4) for all analyses with an *a priori* significance set at $p \leq 0.05$.

RESULTS

There were 2638 12-month walking speed change observations among 1460 unique participants included in our analysis. Descriptive characteristics of the included participants are listed in Table 1. Overall, average walking speed increased 0.001 ± 0.133 m/s (range –0.627 to 1.497 m/s) during the 12-month exposure period for observations included in our sample. The median change in walking speed was 0.001 m/s (IQR –0.075 to 0.075). Walking speed

Table 1. Descriptive characteristics for participants who were included in the analysis of the association between 12-month change in walking speed and 24-month risk for incident ROA (n = 1460 participants, 2638 observations). Values are n (%) unless otherwise indicated.

Variable	n	Value	Range
Age, yrs, mean (SD)	1460	59 (9)	45–79
BMI, kg/m^2, mean (SD)	1460	27.1 (4.5)	17.6–45.4
Sex	1460		
Male		618 (42)	
Female		842 (58)	
PASE score, mean (SD)	2624	166 (82)	7–464
Knee pain	2606	685 (26)	
Ankle pain	2624	236 (9)	
Back pain	2632	442 (17)	
Hip pain	2626	624 (24)	
Knee injury	2635	75 (3)	
History of fall	1211	380 (31)	

ROA: radiographic osteoarthritis; BMI: body mass index; PASE: Physical Activity Scale for the Elderly.

decreased in 1309 observations (50%), and increased in 1329 (50%) observations over the exposure period.

About 5% of the sample (122 participants) developed rKOA over a 24-month period. The average 12-month change in walking speed among those who developed rKOA was –0.012 ± 0.119 m/s compared with 0.002 ± 0.133 m/s among those who did not develop rKOA (p = 0.26). The risk of developing rKOA over 24 months was 1.08× higher (95% CI 0.94–1.23, p = 0.26) for every 0.1 m/s decrease in walking speed over a 12-month period. After controlling for significant knee injury, age, BMI, and PASE score, we found an 8% relative increase in risk of developing rKOA for every 0.1 m/s decrease in walking speed over a 12-month period (RR 1.08, 95% CI 1.00–1.15, p = 0.05; Table 2). Among observations in which no knee injury was reported (n = 2560), there was an 8% relative increase in risk of developing rKOA for every 0.1 m/s decrease in walking speed over a 12-month period (RR 1.08, 95% CI 1.00–1.17, p = 0.05); however, among observations where an injury was reported (n = 75), there was relatively no association between a change in walking speed and risk of developing rKOA over a 24-month period (RR 1.01, 95% CI 0.83–1.23, p = 0.91).

DISCUSSION

The results of our study support the hypothesis that individuals who decrease their walking speed over a 12-month period in the absence of rKOA are at increased risk for developing incident rKOA over the following 24-month period. Specifically, we found that for every 0.1 m/s decrease in walking speed over a 12-month period with no evidence of rKOA, the relative risk of developing rKOA over the subsequent 24-month period increased by 8%, when controlling for significant knee injury, age, BMI, and PASE score. We found the same relative increase in risk among participants who did not report a knee injury (RR 1.08, 95% CI 1.00–1.17, p = 0.05); however, among participants who did report a knee injury, there was no association between walking speed change and risk of incident rKOA (RR 1.01, 95% CI 0.83–1.23, p = 0.91).

These findings are in line with previous studies that suggested an association between habitual walking speed and incident rKOA[12,20]. Purser, *el al*[12] analyzed a community-based cohort for the effect of average habitual walking speed on the odds of developing rKOA over a 6-year period, and found a 12% decrease in odds of developing rKOA for participants with a 0.1 m/s increase in habitual walking speed. Our study corroborated and added to these findings by studying a change in walking speed over time in the absence of rKOA, as opposed to assessing walking speed at 1 timepoint. Therefore, a simple, repeated 20-m walk test, which could be easily evaluated during annual clinical examinations, could be used to indicate increased risk of developing rKOA within the following 2 years, particularly among adults without a reported knee injury. This simple indicator may help identify at-risk patients, allowing for an opportunity to intervene to prevent disease onset and associated disability.

Previous work has assessed the ability of walking speed to predict rKOA onset by characterizing slow walkers as those with a habitual walking speed of < 1.00 m/s. Others have predicted a clinically meaningful improvement in function over 30 months by dichotomizing individuals into those who were and were not able to improve walking speed by 1.0 m/s. In our cohort, the range of change in walking speed over 12 months was –0.627 m/s to 1.497 m/s, with an average change in walking speed of essentially 0 m/s. The

Table 2. Multivariable log-binomial regression results and comparison of covariates for participants who developed incident ROA over the 24-month study period compared with those who did not (n = 1460 participants, 2638 observations). Values are mean (SD) unless otherwise indicated.

Variable	Incident ROA		No ROA		RR	95% CI
	n	Value	n	Value		
Walking speed	122	–0.0121 (0.1188)	2516	0.0016 (0.1335)	1.08	1.00–1.15
Age, yrs	122	59.3 (8.4)	2516	59.0 (9.0)	1.00	0.98–1.03
BMI, kg/m^2	122	28.3 (4.9)	2516	27.0 (4.4)	2.03	1.33–3.10
PASE score	122	162.7 (87.5)	2501	166.5 (82.0)	1.00	1.00–1.00
Knee injury, n (%)	122	8 (6.5)	2513	67 (2.7)	1.38	0.76–2.49

ROA: radiographic osteoarthritis; RR: risk ratio; BMI: body mass index; PASE: Physical Activity Scale for the Elderly.

IQR for change in walking speed in our sample was –0.075 m/s to 0.075 m/s, suggesting that < 25% of our sample had a change in walking speed > 0.1 m/s in a 12-month period. Therefore, the 1.0 m/s change used previously is likely not clinically relevant because a very small proportion of people have that drastic of a change in walking speed over the course of 1 year. In contrast, a change of 0.10–0.20 m/s in habitual walking speed has been identified as a minimally clinically important difference for change in walking speed[19]. Our data suggested that a decrease of 0.1 m/s over a 12-month period was associated with an 8% relative increase in risk of developing rKOA over the subsequent 24 months. A change of –1.59 s has been reported to be the smallest detectable difference for the 20-m walking speed assessment[21], which would be a 0.07 m/s decrease in walking speed in individuals who initially walked at 1.00 m/s[21]. Therefore, the 20-m walking speed assessment appears to demonstrate the appropriate precision to detect a change of 0.1 m/s in this patient population. Our current study also improves upon previous research because evaluation of a 0.1 m/s change in walking speed over a 12-month period assesses risk of developing rKOA in a shorter period (over 24 mos) compared with a previous study that predicted rKOA onset over a 6-year followup[12]. The ability to provide information to patients and providers about increased risk over a shorter period may motivate more immediate further evaluation or lifestyle changes necessary to mitigate the risk of rKOA.

While the mechanisms that link slower walking speeds and rKOA onset remain unknown, it can be hypothesized that slower walking speeds may be a biomechanical adaption to the effect of early metabolic changes at the knee[8,12]. Slower walking speeds are associated with a lesser loading rate and magnitude of loading during the initial peak in the ground reaction force during the stance phase of gait[22,23,24,25]. Greater impulsive loading has been found to damage articular cartilage and weaken the extracellular cartilage matrix[26]. Alternatively, it is possible that decreased loading secondary to pain or inactivity may lead to deterioration and hasten the OA disease process. Decreasing habitual walking speed may be a subconscious protective strategy aimed at minimizing the magnitude and rate of loading on knee cartilage to maximize the longevity of tissue health. Additionally, slower gait speeds may increase the duration in which the knee cartilage is loaded during the stance phase of gait[27]. While slower speeds decrease the magnitude and loading rate of the first half of stance phase, these slower walking speeds increase the magnitude in which the extremity is loaded during the second half of the stance phase of gait[23,24,25]. Thereby, slower walking speeds and increased magnitude and duration of loading in the second half of the stance phase of gait may also cause increased cartilage breakdown. Further research is needed to determine whether slower walking speeds are protective of deleterious changes in joint tissue metabolism prior to rKOA onset or a contributor to these harmful changes that influence rKOA onset. Regardless of whether the change in walking speed that was appreciated in our study is an early indicator of prevalent OA or a causal component of its development, we believe our findings are meaningful because these data may be used to develop an early clinical indicator of patients who are at risk for developing rKOA before structural joint changes are detected radiographically.

While our study supports the use of walking speed as a clinical indicator of incident rKOA, limitations must be considered when interpreting the results of our study. We only included participants who completed the longitudinal evaluations, who may be inherently different from other participants who did not participate in at least 3 consecutive study visits. Additionally, the results of our current study are most generalizable to a subset of the population who meet the OAI inclusion criteria, including increased risk for developing OA; however, OAI provides a rich dataset that allows for control of potential confounders in a large study sample. In addition, our study focused on the development of tibiofemoral rKOA, and the results cannot be generalized to patients with patellofemoral rKOA. The exposure in our study was change in walking speed over a 12-month period, which was measured objectively during clinical 20-m walk analysis at 2 timepoints and may not adequately represent the true change in walking speed over a 12-month period. Nevertheless, this is a realistic representation of screening of this simple indicator in a clinician's office during annual visits. Overall, very little missing data (< 1% for most variables) was noted in this analysis, with no missing data for either exposure or outcome, but there is potential for measurement error for several of the covariates assessed using self-reported methods (i.e., history of fall, history of knee injury, pain in the knee, back, hip, or ankle in the last 30 days). The outcome of incident rKOA was determined based on radiographic assessment, and as is common in such studies, it was not possible to determine the exact time of rKOA development during the 24-month followup period. Additionally, inclusion into the study cohort relied on KL grade < 2 during the exposure period. While good reliability for KL grading between baseline and the 36-month followup visit (κ 0.70–0.80) was identified in a previous study[17], the reliability was lower among KL grade < 2. Therefore, it is possible that some individuals included in our analysis had existing OA. It is possible that important potential confounders exist for the relationship between walking speed and incident rKOA that were not measured in OAI. Multiple previous studies[15,16,28] have been published using the 20-m walk times from the OAI, yet we are not aware of any published reliability data on this physical function outcome at the different OAI sites. While measuring 20-m self-selected walking pace is a commonly collected clinical outcome of physical performance, a previous study[21] has described a learning effect in which individuals with rKOA

walked faster in the first trial compared to the second. Additionally, the OAI protocol[29] does not indicate whether standardized acceleration and deceleration space was provided to the participants, as well as verbal encouragement during the test.

Our study found that for every 0.1 m/s decrease in walking speed over a 12-month period, the relative risk of developing rKOA over the subsequent 24 months increased by 8%, when controlling for significant knee injury, age, BMI, and PASE score. For example, a patient who decreases walking speed by 0.4 m/s over a 1-year period has a 32% greater risk of developing rKOA within the next 2 years compared with a patient with no change in walking speed. Evaluating a change in walking speed during serial clinical followups using a 20-m walk test may be useful in identifying which patients are at risk for developing rKOA over the subsequent 24 months. Early identification of these patients at the highest risk for developing knee OA would allow for medical providers to implement early interventions to maximize joint health.

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