



Determinants of six-minute walk test performance in individuals with knee osteoarthritis

Sivakami Mylvaganam¹, Philippa Nicolson², Ian Stanaitis³, Gillian Hawker^{1,3},
Lauren K. King^{1,4,*}

¹ Department of Medicine, University of Toronto, Toronto, Ontario, Canada

² Nuffield Department of Orthopaedics, Rheumatology & Musculoskeletal Sciences (NDORMS), University of Oxford, UK

³ Research and Innovation Institute, Women's College Hospital, Toronto, Ontario, Canada

⁴ Li Ka Shing Research Institute, St. Michael's Hospital, Unity Health Toronto, Toronto, Ontario, Canada

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ABSTRACT

Objective: The 6-minute walk test (6MWT), an Osteoarthritis Research Society International (OARSI)-recommended measure of physical function in knee osteoarthritis (OA), was originally developed to assess submaximal aerobic fitness in people with cardiovascular disease. The degree to which 6MWT performance reflects knee OA severity versus other patient factors remains unclear. Our objective was to assess the contributions of OA-related and non-OA-related patient characteristics to 6MWT performance in individuals with symptomatic knee OA.

Design: In this cross-sectional study, participants scheduled for total knee arthroplasty completed the 6MWT and standardized questionnaires. Participant characteristics were compared by tertiles of 6MWT distance. Multi-variable linear regression modelling was used to assess associations between patient factors and 6MWT distance.

Results: Among 278 participants (mean age 67.1 years, 65.5% female, mean WOMAC pain 57.0, and mean 6MWT distance 323.1m), older age (adjusted beta coefficient -4.0 per year, 95% confidence interval [CI] -5.4, -2.5), female sex (adjusted beta [95% CI] -43.0 [-67.3, -18.7]), presence of obesity (adjusted beta [95% CI] -44.4 [-68.2, -20.5]), greater knee pain (adjusted beta [95% CI] per unit increase in WOMAC pain -1.12 [-2.1, -0.2]), worse knee-OA related function (adjusted beta [95% CI] per unit increase in KOOS-PS -1.1 [-2.0, -0.1]) were associated with shorter 6MWT distance. Greater arthritis coping efficacy (adjusted beta [95% CI] 5.2 [1.4, 9.0]) was associated with longer 6MWT distance.

Conclusions: While 6MWT distance declines with greater knee OA symptom severity, other demographic, biomedical and psychosocial factors also significantly influence 6MWT performance. These should be considered when interpreting the 6MWT in this population.

1. Introduction

Knee osteoarthritis (OA) is a leading cause of pain and disability worldwide [1,2] and contributes to more walking difficulty than any other condition [3,4]. Walking difficulty is a primary reason people with knee OA seek care, including joint replacement [5]. Walking difficulty also represents a strong independent risk factor for adverse chronic disease outcomes in people with knee OA, including increased risk for all-cause mortality [6,7]. Being able to robustly measure walking ability in people with knee OA is therefore important for both clinical decision-making and research applications [8].

The Six-Minute Walk Test (6MWT), which assesses functional walking capacity, is an Osteoarthritis Research Society International (OARSI)-recommended performance-based measure of physical function [9,10]. In the 6MWT, participants walk as far as possible on a flat, hard surface over 6 minutes, with rests and gait aids permitted as needed [11]. The 6MWT was originally developed as an alternative to laboratory-based methods for assessing cardiovascular fitness [12] and was first applied in populations with cardiovascular and respiratory disease [13,14]. Its use in knee OA research began in the 1990s, first appearing in a study evaluating improvements in walking ability following a structured exercise program [15]. There has been

* Corresponding author. St. Michael's Hospital 30 Bond Street, Room 3-057, Toronto Ontario M5B 1W8 Canada.

E-mail addresses: s.mylvaganam@mail.utoronto.ca (S. Mylvaganam), philippa.nicolson@ndorms.ox.ac.uk (P. Nicolson), ian.stanaitis@wchospital.ca (I. Stanaitis), g.hawker@utoronto.ca (G. Hawker), l.king@utoronto.ca (L.K. King).

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subsequent rapid expansion of use of the 6MWT within the OA field [9, 16–18]. Despite this, there remains a limited understanding of what exactly the 6MWT measures in people with knee OA [16,19–23], given that walking ability is shaped by a wide range of physical, psychological, and social factors [24,25]. The extent to which OA severity contributes to 6MWT performance relative to other influences remains unclear, limiting the interpretation of the 6MWT as a measure of OA-related physical function.

To address this gap, we assessed the association between knee OA-related symptom severity and other patient-level biomedical, psychological and social factors with 6MWT distance in a cohort of individuals with symptomatic knee OA awaiting total knee arthroplasty (TKA). We hypothesized that, given the multidimensional nature of walking behaviour, 6MWT performance would be similarly influenced by both knee OA-related symptom severity and non-OA related patient-level factors.

2. Methods

2.1. Design and study participants

This cross-sectional study was nested within the BEST-Knee prospective cohort study [19,26]. The BEST-Knee study recruited adults aged 30 years and older with primary knee OA (confirmed by the surgeon based on history, physical examination and imaging) who were awaiting elective unilateral TKA at two provincial hip and knee clinics in Alberta, Canada. Participants with a diagnosis of inflammatory arthritis and those undergoing revision or bilateral TKA were excluded. All participants were required to have sufficient comprehension of English to provide written informed consent and to follow verbal instructions for the 6MWT.

At the Edmonton site, study participants scheduled for TKA were invited to complete the 6MWT as a secondary objective to enable comparison of patient-reported and performance-based TKA outcomes, aiming for a target of >200 participants based on study funding. Data for participants who completed the 6MWT were included in the current study.

The study was approved by the Research Ethics Boards of the Universities of Alberta (PRO-00051108) and Calgary (REB 14–1294), and from Women's College Hospital (REB 2014–0092) at the University of Toronto. All participants provided informed written consent. The reporting of this study was guided by the Strengthening the reporting of observational studies in epidemiology checklist [27].

2.2. Assessments

Participants completed standardized questionnaires one month prior to TKA, which assessed all exposure variables except for participant age, sex, height and weight (to calculate body mass index [BMI]) which were abstracted from clinical records. Participants also completed the 6MWT one month prior to TKA.

2.3. Exposures

Our study hypothesis was underpinned by a biopsychosocial model of walking ability [24,25] where, in addition to knee OA symptoms, other demographic, biomedical, psychological and social factors may contribute. Exposures of interest included:

Patient-reported knee OA symptom severity: Knee OA pain, assessed using the Western Ontario and McMaster Universities OA Index (WOMAC) pain subscale (higher score indicates worse pain [28,29]) and knee OA-related functional impairment, assessed using the Knee injury and OA Outcome Score physical function short form (KOOS-PS; scores were reverse coded such that higher scores indicated worse disability [3, 30,31]).

Other biomedical factors: Obesity (defined as BMI ≥ 30 kg/m²) [32, 33], number of physician-diagnosed medical comorbidities (yes/no from list of: cardiovascular disease, hypertension, diabetes, respiratory disease, stomach disease, liver disease, kidney disease, anemia and cancer) [34], total number of troublesome lower extremity joints (number of painful, aching, swollen or stiff lower extremity joints on a lower extremity joint homunculus, including the index knee) [34–36], and presence of lower back pain (yes/no) [37].

Psychological factors: Depressive symptoms, assessed using the eight-item Patient Health Questionnaire Depression Scale (PHQ-8) (higher scores indicate more severe symptoms) [31,34,38], arthritis coping efficacy, using the 4-item Perceived Arthritis Coping Efficacy scale, which evaluates an individual's perceived ability to manage arthritis-related challenges across physical, emotional and role functioning domains (higher scores indicate greater efficacy) [25,39], and pain catastrophizing using the 13-item pain catastrophizing scale (higher scores suggest more catastrophizing) [25,40].

Social factors: Level of education (post-secondary education, yes/no) and social support using the Lubben Social Network Scale (Lubben SNS) (lower scores suggest social isolation) [25,41].

Demographic factors: Age (years) [33] and sex assigned at birth [32, 42].

2.4. Outcome

Our outcome of interest was 6MWT distance. The 6MWT was administered approximately one month prior to TKA. It was performed with or without gait aids on a 45-m indoor flat loop with bright orange cones to mark turning points [11]. Participants were instructed to walk as quickly as possible to cover as much ground as possible in 6 min [11]. Test administrators provided encouragement to participants in 1-min intervals. At the end of 6 min, the distance was measured by noting the number of laps completed and adding partial lap distances measured using a measuring wheel. Normative values for 6MWT distance reported for healthy adults of a similar age typically exceed 480m [42,43].

2.5. Analysis

Participant characteristics were described using frequencies, means and standard deviations, overall and by tertile of 6MWT distance to allow for comparison across functional levels. Differences in characteristics between tertiles were analyzed using one-way ANOVA. Number of troublesome joints was categorized as 0–1, 2, and 3 or more, and number of non-musculoskeletal comorbidities was categorized as 0, 1, 2, and 3 or more conditions. WOMAC pain and KOOS-PS scores were normalized 0 to 100 (higher score representing worse symptoms).

We used multivariable linear regression to assess the association between knee OA symptom severity and other factors (biomedical, psychological, social and demographic) with 6MWT distance. We first modelled the association between knee OA symptom severity alone with 6MWT distance. In a second model, we included all exposures of interest. Adjusted R² was calculated for each model to quantify the proportion of variance in 6MWT distance explained by the included exposures. Exposures were assessed for multicollinearity using variance inflation factor (where >4 indicated presence of multicollinearity).

Analysis was performed using R version 4.4.3 (R Foundation for Statistical Computing, Vienna, Austria) and SAS Studio Version 3.1 (SAS Institute Inc., Cary, NC). A p-value of <0.05 was considered statistically significant.

3. Results

3.1. Characteristics of study participants

A total of 278 participants were included. Characteristics of participants are shown in Table 1. Their mean age was 67.1 years (standard

Table 1
Participant characteristics.

Characteristic	Overall (N = 278)	Terile of 6MWT Distance			p-value
		Lowest (N = 92)	Middle (N = 93)	Highest (N = 93)	
Demographics					
Age - years, mean (SD)	67.1 (8.5)	69.1 (9.8)	67.3 (7.7)	64.9 (7.5)	0.003
Female, n (%).	182 (65.5)	68 (73.9)	62 (66.7)	52 (55.9)	0.026
Biomedical comorbidities					
Body Mass index - kg/m ² , mean (SD)	32.2 (6.1)	32.9 (6.6)	33.0 (5.7)	30.7 (5.7)	0.012
Number of troublesome lower extremity joints, n (%)					0.054
0-1	81 (29.1)	19 (20.7)	30 (32.3)	32 (34.4)	
2	88 (31.7)	28 (30.4)	27 (29.0)	33 (35.5)	
3+	109 (39.2)	45 (48.9)	36 (38.7)	28 (30.1)	
Presence of lower back pain, n (%)	148/272 (54.4)	57/88 (64.8)	48/91 (52.7)	43 (46.2)	0.04
Number of non-musculoskeletal comorbidities, n (%)					0.09
0	73/276 (26.4)	17/90 (18.9)	21 (22.6)	35 (37.6)	
1	103 (37.3)	32 (35.6)	37 (39.8)	34 (36.6)	
2	67 (24.3)	27 (30.0)	24 (25.8)	16 (17.2)	
3+	33 (12.0)	14 (15.6)	11 (11.8)	8 (8.6)	
Psychosocial factors					
Post-secondary education, n (%).	155/274 (56.6)	49/92 (53.3)	54/91 (59.3)	52/91 (57.1)	0.7
PHQ-8 depressive symptoms (0–24), mean (SD)	6.8 (5.7)/276	8.7 (6.4)/91	6.5 (5.6)	5.1 (4.5)/92	<0.001
Lubben social networking score (0–30), mean (SD)	17.8 (5.2)/270	17.4 (5.0)/90	18.6 (4.5)/90	17.5 (5.9)/90	0.29
Gignac arthritis coping score (0–20), mean (SD)	13.1 (3.9)/242	11.6 (4.0)/77	13.3 (3.5)/85	14.7 (3.4)/80	<0.001
Pain catastrophizing score (0–52), mean (SD)	18.0 (13.1)/276	21.8 (13.7)/92	17.6 (12.8)/92	14.6 (11.9)/92	<0.001
Knee OA symptom severity					
WOMAC pain (0–100), mean (SD)	57.0 (16.5)	62.0 (14.5)	56.5 (17.5)	53.0 (16.0)	0.0009
KOOS physical function short form (0–100), mean (SD)	52.9 (16.2)/270	58.3 (15.0)/90	52.2 (17.4)	48.1 (14.65)/87	<0.0001
Six-minute walk test					
Six minute walk distance (m), mean (SD)	323.1 (104.7)	205.5 (60.1)	331.5 (26.3)	431.0 (55.0)	<0.0001

WOMAC Western Ontario and McMaster Universities OA Index (higher score indicates worse pain); KOOS-PS Knee injury and OA Outcome Score physical function short form (higher score indicates worse disability); PHQ-8 Eight-item Patient Health Questionnaire Depression Scale.

Sample size provided at top of each column with denominators included when <100 % response.

P-value as indicated, calculated using Chi-square or Wilcoxon rank sum tests, as appropriate.

deviation 8.5) and 182 (65.5%) were female. Mean BMI was 32.2 kg/m² (SD 6.1). Mean WOMAC pain was 57.0/100 (SD 16.5) and mean KOOS-PS was 52.9/100 (SD 16.2). Most participants had both musculoskeletal and non-musculoskeletal comorbidities. Mean 6MWT distance was 323.1 (SD 104.7) meters.

3.2. Participant characteristics by tertile of six-minute walk test distance

When examined by tertile of 6MWT distance, participants in the lowest tertile (shortest distance) were more likely to be older ($p = 0.003$), more likely to be female ($p = 0.03$), have higher BMI ($p = 0.01$), more depressive symptoms ($p < 0.001$), lower (worse) scores for perceived arthritis coping efficacy ($p < 0.001$), higher (worse) pain catastrophizing scores ($p < 0.001$), have lower back pain ($p = 0.04$), and higher (worse) scores for WOMAC pain ($p < 0.001$) and KOOS-PS ($p < 0.0001$) than those in the middle and uppermost tertiles (Table 1).

3.3. Association between knee OA-related symptoms and other patient-level factors with 6MWT distance

The results of multivariable linear regression modeling (adjusted beta coefficients with 95 % confidence intervals [CI]) are shown in Tables 2 and 3. In model 1, which included only knee OA symptom severity, greater knee pain ($\beta -1.3$ per unit increase in WOMAC, 95 % CI -2.3, -0.3) and greater functional impairment ($\beta -1.5$ per unit increase in KOOS-PS, 95 % CI -2.5, -0.5) were associated with shorter 6MWT distance. R^2 of this model was 0.14 (Table 2). In model 2 which included all exposures of interest, greater knee pain ($\beta -1.2$ per unit increase in WOMAC pain, 95 % CI -2.1, -0.2), greater functional impairment ($\beta -1.1$ per unit increase in KOOS-PS, 95 % CI -2.0, -0.1), older age ($\beta -4.0$, 95 % CI -5.4, -2.5), female sex ($\beta -43.0$, 95 % CI -67.3, -18.7), and presence of obesity ($\beta -44.4$, 95 % CI -68.2, -20.5) were associated with shorter 6MWT distance. Greater arthritis coping efficacy ($\beta 5.2$ per unit increase in score, 95 % CI 1.4, 9.0) was associated with longer

Table 2

Multivariable linear regression analysis of the association between knee OA-specific patient factors and six-minute walk test distance.

Independent Variables	Dependent Variable: Six-Minute Walk Test Distance			
	Adjusted Beta-Estimate	95 % Confidence Interval		P value
WOMAC pain (0–100), per unit	-1.3	-2.3	-0.3	0.009
KOOS-PS (0–100), per unit	-1.5	-2.5	-0.5	0.003
	Model $R^2 = 0.14$			

WOMAC: Western Ontario and McMaster Universities OA Index (higher score indicates worse pain); KOOS-PS: Knee injury and OA Outcome Score physical function short form (higher score indicates worse disability).

6MWT distance. No statistically significant associations were found for number of troublesome joints, presence of low back pain, depressive symptoms, pain catastrophizing or post-secondary education with 6MWT distance. The model R^2 was 0.37. (Table 3).

4. Discussion

In this cross-sectional study of individuals with symptomatic knee OA awaiting TKA, we evaluated the associations between knee OA symptom severity and other patient factors that could affect walking ability with 6MWT distance. We found that while 6MWT distance declines with greater OA symptom severity, it is also influenced by age, sex, BMI, non-musculoskeletal comorbidity burden and perceived arthritis coping efficacy. This study underscores that additional biomedical and psychosocial factors beyond OA symptom severity influence 6MWT performance in individuals with knee OA, helping clinicians and researchers who use 6MWT to evaluate walking ability in people with knee OA to interpret test results.

Table 3
Multivariable linear regression analysis of the association between patient factors and six-minute walk distance.

Independent Variables	Dependent Variable: Six-Minute Walk Distance			
	Adjusted Beta-Estimate	95 % Confidence Interval		P value
Age, per year	-4.0	-5.4	-2.5	<0.0001
Female sex (ref = male)	-43.0	-67.3	-18.7	0.0006
Post-secondary education (ref = no)	19.9	-3.4	43.1	0.09
WOMAC pain (0–100), per unit	-1.2	-2.1	-0.2	0.02
KOOS-PS (0–100), per unit	-1.1	-2.0	-0.1	0.03
Number of troublesome joints, per category increase ^a	1.6	-7.6	10.7	0.74
Presence of lower back pain (ref = no)	-6.6	-30.2	17.0	0.58
Obesity (ref = no) ^b	-44.4	-68.2	-20.5	0.0003
Non-musculoskeletal comorbidities, per category increase ^c	-12.6	-22.1	-3.2	0.009
PHQ-8 (depressive symptoms), per unit increase	-2.3	-5.4	0.7	0.14
Gignac arthritis coping efficacy, per unit increase	5.2	1.4	9.0	0.007
	Model R ² = 0.37			

WOMAC: Western Ontario and McMaster Universities OA Index (higher score indicates worse pain); KOOS-PS: Knee injury and OA Outcome Score physical function short form (higher score indicates worse disability); PHQ-8 Eight-item Patient Health Questionnaire Depression Scale.

^a Number of lower extremity troublesome joints was categorized as 0–1, 2, and 3 or more joints and did not include the lower back.

^b Obesity was defined as a BMI ≥ 30 kg/m².

^c Number of non-musculoskeletal comorbidities was categorized as 0, 1, 2, and 3 or more conditions.

The model including only OA-related pain and patient-reported functional impairment had an R² of 0.14 which increased to 0.37 when additional biomedical and psychosocial factors were included. The modest association between our patient-reported outcome measures (WOMAC and KOOS) and our outcome is consistent with our understanding of PROMs as providing information on an individual's perceived ability to perform activities while performance-based measures like the 6MWT objectively assess capacity to perform specific activities [16,19–23]. The improvement in the R² after inclusion of additional biopsychosocial factors supports the notion that walking is multidimensional behaviour. Collectively, this highlights the need for clinicians and researchers to consider the broader patient context when using the 6MWT to evaluate walking ability in people with knee OA.

Neither the presence of low back pain nor the number of troublesome lower-extremity joints demonstrated independent associations with 6MWT performance, despite the high prevalence of multisite joint involvement and lower back pain in this sample (Table 1). Previous studies have shown that involvement of additional lower extremity joints adds to the burden of OA symptoms [35,36]. The lack of association in our study may reflect the greater influence of factors beyond musculoskeletal symptoms alone. 6MWT may also not fully reflect the impact of musculoskeletal-related mobility limitations; given that the 6MWT is administered on a flat, unobstructed surface [2], it likely does not entirely represent the agility, balance, and coordination required for walking in the community. Negotiating uneven terrain, stairs, inclines, and crowded environments are common sources of mobility restriction not represented in the 6MWT and better assessments of real-world mobility restrictions would be useful in this population [16].

The associations we observed between 6MWT performance and age, sex and obesity align with prior literature and could be attributed to differences in body composition or muscle mass and aerobic capacity between age groups, sexes and those with differing BMI [11,43]. Similarly, our finding that the number of non-musculoskeletal comorbidities was associated with 6MWT distance is in keeping with prior research establishing the 6MWT as a reflection of cardiorespiratory fitness [2, 44–46]. Notably however, we found no difference in the prevalence of specific cardiorespiratory comorbidities across tertiles of 6MWT distance, which might have been expected [2,44–46]. It is possible that since participants had been scheduled for surgery, individuals with significant non-musculoskeletal comorbidities, such as advanced cardiorespiratory disease, diabetic neuropathy, or prior stroke, were excluded and as a result, we may have underestimated the contribution of these comorbidities to 6MWT performance and, conversely, overestimated the influence of OA. Our study has also demonstrated the additive influences of psychosocial factors such as OA coping on 6MWT

performance. These are known to compound OA symptoms by affecting motivation, pain perception and engagement with physical activity in general [47,48]. Given that the R² for our multivariable model was only 0.37, unmeasured factors account for additional unexplained variability in 6MWT distance beyond what our model captured. These may include additional psychosocial factors such as motivation, sleep and fatigue [49]. The relationship between additional psychosocial constructs and how they relate to walking limitation in people with knee OA merits further study.

This study has several notable strengths. First, the study leveraged a well-characterized cohort from the BEST-Knee prospective study [19, 26], which included comprehensive biomedical, psychological, and functional data. This cohort was also clinically relevant as the mean 6MWT distance was substantially lower than values reported for healthy adults of a similar age [42,43], fitting with a symptomatic knee OA population. Thus, the study participants may be representative of those enrolled into OA clinical trials. Importantly, we included under-studied psychological variables such as arthritis coping efficacy in our analyses, contributing novel insights into how psychological resilience may influence performance-based measures like the 6MWT.

Our study also has some limitations. Participants were scheduled for TKA and thus presumably had more advanced knee OA. This may have introduced spectrum bias, limiting the generalizability of our findings to populations with earlier or less severe knee OA. However, participants represented the full range of WOMAC pain and KOOS-PS scores, which suggests variability in perceived symptoms and function even within this pre-surgical cohort. Participation in the 6MWT was voluntary which may have introduced selection bias. Additionally, test-day factors are difficult to account for as the assessment was only administered once prior to TKA in contrast to other similar studies where participants performed it multiple times and a best-test was selected for analyses [11, 50].

In conclusion, multiple factors influence 6MWT distance beyond OA symptoms in people with knee OA. Clinicians using the 6MWT to assess physical function in people with knee OA should consider the broader health and psychosocial profile of each individual, and how these factors may be contributing to an observed change or lack thereof in 6MWT performance.

Author contributions

Conception and design: SM, GH, LK. Analysis and interpretation of the data: SM, GH, LK. Drafting of the article: SM, GH, LK. Critical revision of the article: SM, PN, IS, GH, LK. Final approval of the article: SM, PN, IS, GH, LK.

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Declaration of interest statement

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