



Full length article

Dynamic knee joint stiffness and contralateral knee joint loading during prolonged walking in patients with unilateral knee osteoarthritis

Jonathan A. Gustafson^a, William Anderton^b, Gwendolyn A. Sowa^c, Sara R. Piva^b, Shawn Farrokhi^{d,*}^a Department of Orthopedic Surgery, Rush University Medical Center, Chicago, IL, USA^b Department of Physical Therapy, University of Pittsburgh, Pittsburgh, PA, USA^c Department of Physical Medicine and Rehabilitation, University of Pittsburgh, Pittsburgh, PA, USA^d DOD-VA Extremity Trauma and Amputation Center of Excellence, Naval Medical Center San Diego, CA, USA

ARTICLE INFO

Keywords:

Knee osteoarthritis
Stiffness
Joint contact force
Walking

ABSTRACT

Background: Long duration walking, a commonly recommended treatment option for knee osteoarthritis (OA), may lead to increased knee joint loading.**Research question:** To evaluate the effects of prolonged walking on dynamic knee joint stiffness and contralateral knee joint contact forces (KCFs) in individuals with unilateral symptomatic knee OA.**Methods:** Twenty-six older adults with knee OA completed a 45-minute bout of walking on a treadmill. Dynamic knee joint stiffness, estimated KCFs, measured ground reaction forces (GRFs), and simulated muscle forces were evaluated for both the symptomatic and asymptomatic limbs at 15-minute intervals using repeated measures, analysis of variance (ANOVA).**Results:** Dynamic knee joint stiffness during the early weight-acceptance phase of gait was significantly higher for the symptomatic limb throughout the 45-minute bout of walking. A significant increase in peak KCFs and simulated muscle forces were also observed during the weight-acceptance phase of gait for both limbs after 30 and 45 min of walking. Additionally, significantly elevated peak KCFs and muscle forces were observed during the late-stance phase of gait for the contralateral asymptomatic limb throughout the 45-minute bout of walking.**Significance:** Walking durations of 30 min or greater lead to increased knee joint loading. Additionally, the elevated dynamic knee joint stiffness observed for the symptomatic knee during the weight acceptance phase of gait appears to be unrelated to the knee joint loading profile. Finally, the greater KCFs during the late-stance phase of gait observed for the asymptomatic limb are consistent with previously demonstrated risk factors for OA development and progression.

1. Introduction

Knee osteoarthritis (OA) is a common debilitating joint disease that has been projected to affect more than 15% of the population over the age of 45 by 2032 [1]. Walking exercise is a commonly suggested conservative treatment strategy that has shown to be effective in reducing pain and improving function in patients with knee OA [2,3]. Current recommendations by clinical practice guidelines advocate for at least 30 min of moderate intensity aerobic exercise, such as walking [4,5], with further participation above the minimum recommendations being encouraged for additional health benefits [6]. Despite the general systemic benefits of walking exercise, it has been hypothesized that

prolonged walking in patients with knee OA could lead to excessive knee joint loading due to quadriceps muscle fatigue and loss of effective shock absorption [7]. In support of this premise, findings from a recent study suggests that prolonged walking of 30 min or greater may lead to undesirable increases in knee joint loading and pain in patients with unilateral knee OA [8].

Previous research suggests that increased symptoms during walking can lead to deleterious compensatory strategies that place the arthritic knee joint at risk for disease progression [9,10]. One such compensatory strategy includes increased walking knee joint stiffness, a measure of increased resistance to movement provided by the muscles and soft tissues of the knee joint, as a means of mitigating disease-associated

* Corresponding author at: DOD-VA Extremity Trauma and Amputation Center of Excellence, Naval Medical Center San Diego, 34800 Bob Wilson Dr., San Diego, CA, 92134, USA.

E-mail address: shawn.farrokhi.civ@mail.mil (S. Farrokhi).

<https://doi.org/10.1016/j.gaitpost.2018.10.032>

Received 8 January 2018; Received in revised form 26 October 2018; Accepted 30 October 2018

0966-6362/ Published by Elsevier B.V.

increases in knee joint laxity [10–13]. However, a potential deleterious effect of increased dynamic knee joint stiffness is that the amplified activity of the muscles crossing the knee joint can lead to elevated knee joint contact forces and greater risk of disease progression [10]. Similarly, compensatory strategies during gait to offload the symptomatic limb may place the contralateral limb at greater risk for overloading and disease development [14–16]. To this end, incidence of contralateral knee OA development in patients with unilateral knee OA has been reported to be as high as 34%–80% [17,18]. To date, whether prolonged walking leads to increased dynamic knee joint stiffness or overloading of the contralateral knee joint has not been experimentally evaluated in patients with unilateral knee OA.

The main objective of this exploratory study was to examine the differences in knee joint biomechanics between the symptomatic and asymptomatic limbs of individuals with unilateral, symptomatic knee OA during a prolonged, 45-minute bout of walking. We hypothesized that dynamic knee joint stiffness would be significantly greater in the symptomatic knee, as compared to the asymptomatic knee, throughout the 45-minute bout of walking. We also hypothesized that as compared to the symptomatic limb, the asymptomatic arthritic knee would experience increased knee joint contact forces (KCFs) throughout the 45-minute bout of walking due to greater magnitude of ground reaction force (GRF) and compressive muscle forces.

2. Methods

2.1. Subjects

A total of 26 older adults who met the American College of Rheumatology (ACR) classification criteria for unilateral symptomatic knee OA participated in this study (Table 1). All participants signed an informed consent approved by the institutional review board of the University of Pittsburgh prior to testing. To be included in the study, participants had to meet both of the following criteria: 1) pain in only one knee; and 2) radiographic knee OA (grade II or greater) in the symptomatic painful limb. Participants were excluded from the study if they exhibited contralateral knee pain; history of knee trauma; total joint arthroplasty; hip or spine pain; neurological disease affecting gait;

and history of two or more falls within the prior year. Participants were not excluded if evidence of radiographic knee OA was observed in their asymptomatic knee. This decision was made based on the previous evidence indicating that radiographic knee OA is an imprecise guide to the likelihood that knee pain or disability will be present [19].

2.2. Data collection

All participants were screened to ensure they were capable of maintaining a continuous 45-minute bout of walking on a treadmill at a speed of 1.3 m/s, while maintaining a previously recommended [20] moderate aerobic exercise intensity of 40–60% of heart rate reserve monitored through a heart rate monitor. Walking speed was kept constant to ensure that all participants covered the same distance, while minimizing the influence of variable gait speed on knee joint contact forces. On the day of testing, participants were fitted with clusters of reflective markers (modified Cleveland Clinic Gait Marker Set) on their lower extremities. Virtual markers were calibrated at the hip joint center using a previously published functional method [21] and at the knee and ankle joint centers by anatomical digitization (The MotionMonitor, Chicago, IL, USA). After a short acclimation time on the treadmill (1–3 minutes), participants performed a single bout of walking on an instrumented, split-belt treadmill (Bertec Corp., Columbus, OH, USA) for a total of 45 min. All participants were attached to a ceiling mounted safety harness to avoid accidental falls and injury. Thirty seconds of passive marker trajectory data sampled at 100 Hz (Vicon motion Systems Ltd., Oxford, UK) along with ground reaction forces sampled at 1000 Hz were collected at baseline and during the 15th, 30th, and 45th minute of walking.

2.3. Dynamic joint stiffness calculation

Dynamic knee joint stiffness was quantified as previously described [22,23] as the change in sagittal plane knee joint angle in response to the applied joint moment over the period starting with the peak knee flexion moment to the peak knee flexion angle or the peak knee extension moment (whichever occurred first), during the weight-acceptance phase of gait. Dynamic knee joint stiffness was analyzed over this

Table 1
Summary of participant characteristics.

Age (years)	63.6 ± 7.8		
Female, n (%)	19 (73.1%)		
Height (cm)	168.1 ± 8.6		
Weight (kg)	77.4 ± 14.7		
Body Mass Index (kg/m ²)	27.3 ± 3.8		
Symptomatic Limb Radiographic Osteoarthritis: severity, n (%) ^a	Medial Compartment	Lateral Compartment	Patellofemoral Compartment
Grade 0	1 (4%)	14 (54%)	4 (15%)
Grade 1	1 (4%)	5 (19%)	10 (38%)
Grade 2	13 (50%)	0 (0%)	7 (27%)
Grade 3	9 (35%)	1 (4%)	1 (4%)
Grade 4	2 (8%)	6 (23%)	4 (15%)
Asymptomatic Limb Radiographic Osteoarthritis: severity, n (%)	Medial Compartment	Lateral Compartment	Patellofemoral Compartment
Grade 0	6 (23%)	17 (65%)	9 (35%)
Grade 1	3 (12%)	8 (31%)	7 (27%)
Grade 2	15 (58%)	1 (4%)	6 (23%)
Grade 3	1 (4%)	0 (0%)	1 (4%)
Grade 4	1 (4%)	0 (0%)	3 (12%)
Knee Injury and Osteoarthritis Outcome Score (KOOS) ^b			
Pain (Range: 0 – 100)	65.7 ± 17.0		
Symptoms (Range: 0 – 100)	64.4 ± 16.4		
Function in Daily Living (Range: 0 – 100)	73.1 ± 17.6		
Function in Sport and Recreation (Range: 0 – 100)	46.7 ± 25.6		
Knee Related Quality of Life (Range: 0 – 100)	53.4 ± 19.0		

^a Values are mean ± standard deviations unless indicated otherwise.

^a All patients had to have at least a grade 2 evidence of radiographic knee OA in their symptomatic limb to be included in the study.

^b KOOS scoring: 100 indicates no problems and 0 indicates extreme problems.

linear region by fitting a linear regression line to the data points created by plotting the sagittal plane knee joint moment on the Y-axis and the knee flexion angle on the X-axis. Dynamic knee joint stiffness was determined as the slope of the best fit line, with a larger positive slope indicating greater dynamic knee joint stiffness.

2.4. Knee contact force calculation

A 3-dimensional, muscle-actuated, computational musculoskeletal model was adapted from the Lower Limb Model [24] in OpenSim [25] to simulate subject-specific knee joint contact forces (KCFs). The adapted model contained 23° of freedom (DOF) and 96 Hill-type muscles and was scaled to match each participant's height and weight. Virtual markers representing the centroids of the modified Cleveland Clinic marker sets were used as the final marker set applied to the adjusted model. The knee in the model was represented as a 1 DOF hinge joint allowing anterior-posterior translation of the tibiofemoral joint as a function of flexion/extension knee joint motion. Subject-specific models were anthropometrically scaled from the adapted model until the total root mean square (RMS) error between the predicted marker location and actual marker location was less than 0.01 m.

Model joint angles were calculated using an inverse kinematics tool which involved minimizing the weighted square errors of the predicted marker location to the actual marker location. A computed muscle control algorithm [25] calculated muscle excitations and forces from inverse kinematic results by resolving the equations of motion for the unknown muscle forces. Finally, the KCFs were predicted as the sum of the muscle forces and the joint reaction forces calculated from inverse dynamics equations. The KCFs were subsequently decomposed into orthogonal components for each child segment in the parent frame (distal to proximal), with the vertical KCF component reported as the measure of knee joint loading during gait. The KCFs and total muscle forces were predicted for 5 consecutive steps during the stance phase of gait and were averaged and normalized to the participant's body weight (BW) for reporting purposes.

2.5. Statistical analysis

In order to determine whether dynamic knee stiffness, KCF, GRF, and simulated muscle force differed between limbs (symptomatic vs. asymptomatic) or throughout the bout of walking (baseline, 15, 30, 45 min), a 2 × 4 (limb × walking time) analysis of variance (ANOVA) with repeated measures was performed. For all factorial ANOVA tests, significant main effects were reported only if there were no significant interactions. For all significant main effects, individual differences were compared using independent sample t-tests with adjustments for multiple comparisons using Bonferroni corrections. In addition, a post-hoc analysis using Pearson's correlation coefficient (r) was used to assess the relationship between baseline knee joint stiffness and KCF for each limb. A P < 0.05 was considered statistically significant and all statistical analyses were performed using SPSS statistical software (SPSS, Inc., Chicago, IL, USA).

3. Results

The ANOVA results for dynamic knee joint stiffness (Fig. 1) revealed a significant limb effect ($F_{1,25} = 5.70, P = 0.025$), with the symptomatic knee exhibiting greater average knee joint stiffness compared to the asymptomatic limb (mean difference = 13%). However, there were no significant walking time effects ($F_{3,75} = 0.34, P = 0.80$) nor a limb × walking time interaction ($F_{3,75} = 0.27, P = 0.84$).

The KCF, GRF and simulated muscle force curves typically exhibited two peaks during the stance phase of gait, which were consistent for all time points and for both limbs (Fig. 2). The first peak occurred during the weight-acceptance phase of gait, with the second peak occurring during the late stance phase of gait. The ANOVA results for the first

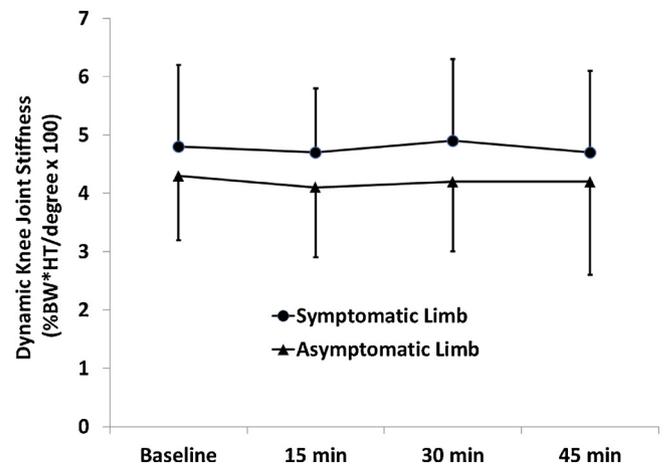


Fig. 1. Comparison of dynamic knee joint stiffness between the symptomatic and asymptomatic limbs during the 45-minute bout of walking. A significant limb main effect was detected, indicating a difference between limbs across all time points. Standard deviation bars are indicated by vertical lines at each marker.

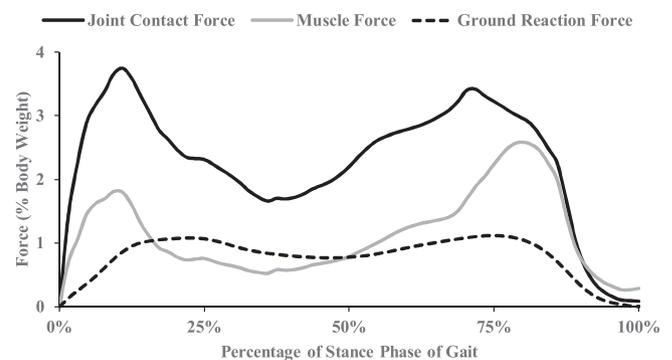


Fig. 2. Representative curves of the joint contact force, muscle force, and ground reaction force profile during the stance phase of gait for a single participant. Two peaks occur at the weight acceptance and during the late stance phases of the gait cycle.

peak in KCF (Table 2) revealed a significant walking time effect ($F_{3,75} = 5.52, P = 0.002$) but no significant limb effect ($F_{1,25} = 0.38, P = 0.54$) or limb × walking time interaction ($F_{3,75} = 0.15, P = 0.93$). When averaged across the two limbs, post-hoc analysis revealed that as compared to baseline, the first peak KCF was greater after 30 min (mean difference = 18% BW; $P = 0.04$) and 45 min of walking (mean difference = 25% BW; $P = 0.01$). Interestingly, baseline dynamic knee joint stiffness and KCF during the weight acceptance phase of gait were not linearly associated for the symptomatic ($r = 0.12, P = 0.57$) or asymptomatic ($r = -0.06, P = 0.77$) limbs. The ANOVA results for the second peak in KCF (Table 2) revealed a significant limb effect ($F_{1,25} = 7.58, P = 0.01$), with the asymptomatic knee exhibiting significantly greater peak KCF as compared to the symptomatic limb (mean difference = 41% BW). However, there were no significant walking time effects ($F_{3,75} = 1.59, P = 0.20$) or a limb × walking time interaction ($F_{3,75} = 0.76, P = 0.52$).

The ANOVA results for the first peak muscle force (Table 3) revealed a significant walking time effect ($F_{3,75} = 8.28, P < 0.01$) but no significant limb effect ($F_{1,25} = 0.14, P = 0.71$) nor limb × walking time interaction ($F_{3,75} = 0.09, P = 0.92$). When averaged across the two limbs, post-hoc analysis revealed that the first peak muscle force was greater after 30 min (mean difference = 20% BW; $P < 0.01$) and 45 min of walking (mean difference = 26% BW; $P < 0.01$) as compared to baseline. The ANOVA results for the second peak muscle force revealed a significant limb effect ($F_{1,25} = 12.88, P < 0.01$), but no

Table 2

Comparison of the change in first and second peak knee joint contact force between the symptomatic and asymptomatic limbs during the bout of walking.

Knee Contact Force (1 st Peak)	Baseline	15 min	30 min	45 min
Symptomatic Limb (xbody weight)	2.70 (0.57)	2.78 (0.55)	2.89 (0.62)	2.97 (0.70)
Asymptomatic Limb (xbody weight)	2.82 (0.65)	2.90 (0.72)	2.99 (0.71)	3.06 (0.77)
Combined (xbody weight)	2.76 (0.61)	2.84 (0.64)	2.94 (0.67) ^a	3.02 (0.74) ^a
Knee Contact Force (2nd Peak)	Baseline	15 min	30 min	45 min
Symptomatic Limb (xbody weight)	2.78 (1.09)	2.77 (1.03)	2.67 (1.00)	2.70 (0.97)
Asymptomatic Limb (xbody weight) ^b	3.26 (0.98)	3.16 (1.01)	3.03 (1.01)	3.11 (1.06)
Combined (xbody weight)	3.02 (1.04)	2.97 (1.02)	2.85 (1.01)	2.91 (1.02)

^a Significant time main effect indicating a difference between time points relative to baseline.

^b Significant limb main effect indicating a difference between limbs across all time points.

walking time effect ($F_{3,75} = 0.84, P = 0.41$) nor a limb x walking time interaction ($F_{3,75} = 0.06, P = 0.99$). When comparing limbs, the asymptomatic knee exhibited significantly greater second peak muscle force compared to the symptomatic limb (mean difference = 59% BW; $P < 0.01$).

The ANOVA results for the first peak in GRF (Table 4) revealed a significant limb effect ($F_{1,25} = 6.97, P = 0.01$) and walking time effect ($F_{3,75} = 17.74, P < 0.01$), but no limb x walking time interaction ($F_{3,75} = 0.32, P = 0.814$). When comparing limbs, the GRF for the asymptomatic knee was significantly higher than the symptomatic limb (mean difference = 3% BW; $P = 0.01$). When averaged across the two limbs, post-hoc analysis revealed that the first peak GRF was significantly greater after 15 min (mean difference = 2% BW; $P < 0.01$), 30 min (mean difference = 3% BW; $P < 0.01$) and 45 min (mean difference = 4% BW; $P < 0.01$) as compared to baseline. No significant changes were observed for the second peak GRF.

4. Discussion

The findings of the current study indicate that individuals with unilateral knee OA demonstrate significantly greater dynamic joint stiffness during gait in their symptomatic knees as compared to their asymptomatic knee joints. Although statistically significant, this finding should be interpreted cautiously as the magnitude of inter-limb differences (13%) were much smaller than those previously reported between individuals with knee OA and healthy controls (25%–80%) [10,13]. The smaller magnitude of observed differences in dynamic joint stiffness in our study as compared to previous reports may be in part due to heterogeneity of joint disease severity and pain in the symptomatic knees and/or presence of radiographic OA in the asymptomatic knees of our cohort. Additionally, the results of our post-hoc analyses failed to demonstrate a relationship between baseline dynamic knee joint stiffness and KCF for either limb. This finding supports the results from a prior study which found no relationship between dynamic knee joint stiffness and markers of joint loading such as the rate of loading or the peak knee adduction moment in individuals with knee

OA [13]. Future longitudinal studies are needed to assess whether between limb differences in dynamic knee joint stiffness have potential clinical implications related to symptomology or rates of disease progression in patients with knee OA.

The findings from the current study also support the hypothesis that as compared to the symptomatic knee, the asymptomatic arthritic knee will experience increased knee joint loading during prolonged walking. More specifically, the magnitude of the second peak KCF was on average 41% of body weight greater with every step for the contralateral asymptomatic limb. This is an interesting finding as a previous study reported that individuals with healthy knees or symmetric bilateral OA exhibit symmetry of KCFs between their right and left limbs [26]. The reduced second peak KCF of the symptomatic limb in subjects with knee OA found in the current study supports prior reports suggesting these force reductions as a compensatory mechanism to reduce pain by decreasing the forward propelling forces produced by muscles around the knee [26]. For instance, the forces produced by the gastrocnemius muscle have been deemed as the primary contributors to the second peak KCF during gait [27]. Given that the second peak KCF coincides with the forward propulsion of the center of mass, the observed increase in the second peak KCF on the contralateral, asymptomatic limb may indicate an attempt to compensate for the reduced propulsive forces generated by the symptomatic limb to maintain a higher overall gait speed.

The observed increases in first peak KCF for both symptomatic and asymptomatic limbs with prolonged walking may also have important clinical implications in terms of appropriate exercise prescription. More specifically, significant increases in first peak KCF of 18% and 25% of body weight were observed after 30 and 45 min of walking, respectively. The increased KCFs observed in our study were for the most part driven by increased muscle forces (20–26% body weight) and, to a much lesser extent, by the increased GRFs (2–4% body weight). In support of this concept, prior studies have suggested that muscles crossing the knee joint (mainly the quadriceps) can contribute substantially to the first peak KCF during gait (up to several times body weight) in both individuals with healthy and arthritic knees [26–28].

Table 3

Comparison of the change in first and second peak knee muscle force between the symptomatic and asymptomatic limbs during the bout of walking.

Knee Muscle Force (1 st Peak)	Baseline	15 min	30 min	45 min
Symptomatic Limb (xbody weight)	2.65 (0.49)	2.73 (0.45)	2.84 (0.55)	2.92 (0.58)
Asymptomatic Limb (xbody weight)	2.70 (0.54)	2.79 (0.60)	2.90 (0.57)	2.94 (0.61)
Combined (xbody weight)	2.68 (0.52)	2.76 (0.53)	2.87 (0.56) ^a	2.93 (0.60) ^a
Knee Muscle Force (2nd Peak)	Baseline	15 min	30 min	45 min
Symptomatic Limb (xbody weight)	3.47 (1.33)	3.48 (1.27)	3.30 (1.24)	3.36 (1.29)
Asymptomatic Limb (xbody weight) ^b	4.09 (1.30)	4.04 (1.16)	3.88 (1.20)	3.95 (1.14)
Combined (xbody weight)	3.78 (1.32)	3.76 (1.22)	3.59 (1.22)	3.66 (1.22)

^a Significant time main effect indicating a difference between time points relative to baseline.

^b Significant limb main effect indicating a difference between limbs across all time points.

Table 4

Comparison of the change in first and second peak vertical ground reaction force between the symptomatic and asymptomatic limbs during the bout of walking.

Vertical Ground Reaction Force (1st Peak)	Baseline	15 min	30 min	45 min
Symptomatic Limb (xbody weight)	1.09 (0.08)	1.12 (0.09)	1.13 (0.08)	1.13 (0.08)
Asymptomatic Limb (xbody weight) ^b	1.12 (0.08)	1.14 (0.09)	1.15 (0.09)	1.16 (0.09)
Combined (xbody weight)	1.11 (0.08)	1.13 (0.09) ^a	1.14 (0.09) ^a	1.15 (0.09) ^a
Vertical Ground Reaction Force (2nd Peak)	Baseline	15 min	30 min	45 min
Symptomatic Limb (xbody weight)	1.04 (0.07)	1.04 (0.08)	1.04 (0.07)	1.05 (0.08)
Asymptomatic Limb (xbody weight)	1.05 (0.09)	1.05 (0.09)	1.06 (0.09)	1.05 (0.09)
Combined (xbody weight)	1.05 (0.08)	1.05 (0.09)	1.05 (0.08)	1.05 (0.09)

^a Significant time main effect indicating a difference between time points relative to baseline.^b Significant limb main effect indicating a difference between limbs across all time points.

Additionally, muscles that do not cross the knee joint (e.g., gluteus maximus and soleus) could also have significant influence on the KCFs through their contributions to the ground reaction forces [27]. Given the important contribution of muscles to KCFs, design of an appropriate exercise prescription should consider the strength and endurance of muscles contributing to knee joint loading during gait. For example, a previous study has suggested that completing the same volume of walking exercise with rest breaks to avoid muscle fatigue can limit the deleterious exercise-associated knee joint loading and pain during prolonged walking [8].

The findings of this study must be interpreted considering several limitations. Given the within subject design of the study, it is difficult to make definitive inferences regarding whether the inter-limb differences in second peak KCF are elevated for the asymptomatic limb or reduced for the symptomatic limb. However, the magnitudes of the first and second peak KCF reported in the current study agree with a prior study using similar techniques [26] and are within the ranges previously reported for KCF using instrumented knee arthroplasty during level walking [29,30]. Additionally, we did not consider compartmental loading in our OpenSim model, despite prior studies showing that loading on the medial compartment is greater than loading on the lateral compartment during overground walking [29,30]. However, this study was primarily interested in changes in net compartmental joint loads due to prolonged walking, particularly as there were no subject recruitment restrictions based on compartment-specific presence of OA. Lastly, the lower extremity model [24] utilized for this study did not account for any changes in muscle activation during prolonged walking. As we did not directly measure muscle activation in our patients, the default muscle model was used. To this end, it has been previously shown that patients with knee OA exhibit significantly greater muscular co-contraction as compared to age matched OA-free control subjects [28]. Therefore, the generic muscle model used in the current study may be underestimating the actual muscular contraction forces. However, given the within subject design of our study, any change due to walking time, regardless of the muscle model chosen, will still be reflected in the model and is relevant.

In summary, individuals with unilateral knee OA demonstrate greater dynamic knee joint stiffness in their symptomatic painful limb during gait that appears to be unrelated to the loading profile of the knee joint. In addition, prolonged walking times of greater than 30 min are associated with an 18–25% of body weight greater first peak in KCF for both limbs, suggesting a significant increase in articular cartilage loading that may be undesirable. Finally, significantly elevated peak KCFs of as high as 41% BW were observed during the late-stance phase of gait for the contralateral asymptomatic limb, which are consistent with previously demonstrated risk factors for OA development and progression.

Declarations of interest

None.

Conflict of interest statement

There are no conflicts to disclose for this study from the authors.

Acknowledgements

The project described was supported by the University of Pittsburgh Medical Center Rehabilitation Institute, Pittsburgh Claude D. Pepper Older Americans Independence Center through (Grant number P30 AG024827) and the National Institutes of Health (Grant numbers UL1 RR024153, UL1 TR000005 and K12 HD055931).

References

- [1] A. Turkiewicz, I.F. Petersson, J. Björk, G. Hawker, L.E. Dahlberg, L.S. Lohmander, et al., Current and future impact of osteoarthritis on health care: a population-based study with projections to year 2032, *Osteoarthr. Cartil.* 22 (2014) 1826–1832.
- [2] W.H. Ettinger Jr., R. Burns, S.P. Messier, W. Applegate, W.J. Rejeski, T. Morgan, et al., A randomized trial comparing aerobic exercise and resistance exercise with a health education program in older adults with knee osteoarthritis. The Fitness Arthritis and Seniors Trial (FAST), *JAMA* 277 (1997) 25–31.
- [3] P.A. Kovar, J.P. Allegrante, C.R. MacKenzie, M.G. Peterson, B. Gutin, M.E. Charlson, Supervised fitness walking in patients with osteoarthritis of the knee. A randomized, controlled trial, *Ann. Intern. Med.* 116 (1992) 529–534.
- [4] American Geriatrics Society Panel on E, Osteoarthritis. Exercise prescription for older adults with osteoarthritis pain: consensus practice recommendations. A supplement to the AGS Clinical Practice Guidelines on the management of chronic pain in older adults, *J. Am. Geriatr.* Soc. 49 (2001) 808–823.
- [5] L. Loew, L. Brosseau, G.A. Wells, P. Tugwell, G.P. Kenny, R. Reid, et al., Ottawa panel evidence-based clinical practice guidelines for aerobic walking programs in the management of osteoarthritis, *Arch. Phys. Med. Rehabil.* 93 (2012) 1269–1285.
- [6] M.E. Nelson, W.J. Rejeski, S.N. Blair, P.W. Duncan, J.O. Judge, A.C. King, et al., Physical activity and public health in older adults: recommendation from the American College of Sports Medicine and the American Heart Association, *Med. Sci. Sports Exerc.* 39 (2007) 1435–1445.
- [7] I. Syed, B. Davis, Obesity and osteoarthritis of the knee: hypotheses concerning the relationship between ground reaction forces and quadriceps fatigue in long-duration walking, *Med. Hypotheses* 54 (2000) 182–185.
- [8] S. Farrokhi, P. Jayabalan, J.A. Gustafson, B.A. Klatt, G.A. Sowa, S.R. Piva, The influence of continuous versus interval walking exercise on knee joint loading and pain in patients with knee osteoarthritis, *Gait Posture* 56 (2017) 129–133.
- [9] M.W. Creaby, K.L. Bennell, M.A. Hunt, Gait differs between unilateral and bilateral knee osteoarthritis, *Arch. Phys. Med. Rehabil.* 93 (2012) 822–827.
- [10] J.A. Zeni Jr., J.S. Higginson, Dynamic knee joint stiffness in subjects with a progressive increase in severity of knee osteoarthritis, *Clin Biomech.* 24 (2009) 366–371.
- [11] M.D. Lewek, K.S. Rudolph, L. Snyder-Mackler, Control of frontal plane knee laxity during gait in patients with medial compartment knee osteoarthritis, *Osteoarthr. Cartil.* 12 (2004) 745–751.
- [12] J.A. Gustafson, S. Gorman, G.K. Fitzgerald, S. Farrokhi, Alterations in walking knee joint stiffness in individuals with knee osteoarthritis and self-reported knee instability, *Gait Posture* 43 (2016) 210–215.
- [13] S.J. Dixon, R.S. Hinman, M.W. Creaby, G. Kemp, K.M. Crossley, Knee joint stiffness during walking in knee osteoarthritis, *Arthritis Care Res.* 62 (2010) 38–44.
- [14] A.J. Metcalfe, M.L. Andersson, R. Goodfellow, C.A. Thorstensson, Is knee osteoarthritis a symmetrical disease? Analysis of a 12 year prospective cohort study, *BMC Musculoskelet Disord.* 13 (2012) 153.
- [15] R.K. Jones, G.J. Chapman, A.H. Findlow, L. Forsythe, M.J. Parkes, J. Sultan, et al., A new approach to prevention of knee osteoarthritis: reducing medial load in the contralateral knee, *J. Rheumatol.* 40 (2013) 309–315.
- [16] A. Metcalfe, C. Stewart, N. Postans, A. Dodds, C.A. Holt, A. Roberts, The effect of osteoarthritis of the knee on the biomechanics of other joints in the lower limbs,

- Bone Jt. J. 95 (2013) 348–353.
- [17] T.D. Spector, D.J. Hart, D.V. Doyle, Incidence and progression of osteoarthritis in women with unilateral knee disease in the general population: the effect of obesity, *Ann. Rheum. Dis.* 53 (1994) 565–568.
- [18] R.K. Jones, G.J. Chapman, A.H. Findlow, L. Forsythe, M.J. Parkes, J. Sultan, et al., A new approach to prevention of knee osteoarthritis: reducing medial load in the contralateral knee, *J. Rheumatol.* 40 (2013) 309–315.
- [19] J. Bedson, P.R. Croft, The discordance between clinical and radiographic knee osteoarthritis: a systematic search and summary of the literature, *BMC Musculoskelet. Disord.* 9 (2008) 116.
- [20] Exercise prescription for older adults with osteoarthritis pain: consensus practice recommendations. A supplement to the AGS Clinical Practice Guidelines on the management of chronic pain in older adults, *J. Am. Geriatr. Soc.* 49 (2001) 808–823.
- [21] A. Leardini, A. Cappozzo, F. Catani, S. Toksvig-Larsen, A. Petitto, V. Sforza, et al., Validation of a functional method for the estimation of hip joint centre location, *J. Biomech.* 32 (1999) 99–103.
- [22] S.J. Dixon, R.S. Hinman, M.W. Creaby, G. Kemp, K.M. Crossley, Knee joint stiffness during walking in knee osteoarthritis, *Arthritis Care Res.* 62 (2010) 38–44.
- [23] J.A. Zeni, J.S. Higginson, Dynamic knee joint stiffness in subjects with a progressive increase in severity of knee osteoarthritis, *Clin Biomech.* 24 (2009) 366–371.
- [24] E.M. Arnold, S.R. Ward, R.L. Lieber, S.L. Delp, A model of the lower limb for analysis of human movement, *Ann. Biomed. Eng.* 38 (2010) 269–279.
- [25] S.L. Delp, F.C. Anderson, A.S. Arnold, P. Loan, A. Habib, C.T. John, et al., OpenSim: open-source software to create and analyze dynamic simulations of movement, *IEEE Trans. Biomed. Eng.* 54 (2007) 1940–1950.
- [26] C. Richards, J. Higginson, Knee contact force in subjects with symmetrical OA grades: differences between OA severities, *J. Biomech.* 43 (2010) 2595–2600.
- [27] K. Sasaki, R.R. Neptune, Individual muscle contributions to the axial knee joint contact force during normal walking, *J. Biomech.* 43 (2010) 2780–2784.
- [28] K.W. Nha, A. Dorj, J. Feng, J.H. Shin, J.I. Kim, J.H. Kwon, et al., Application of computational lower extremity model to investigate different muscle activities and joint force patterns in knee osteoarthritis patients during walking, *Comput. Math. Methods Med.* 2013 (2013) 9. Article ID 314280.
- [29] D. Zhao, S.A. Banks, K.H. Mitchell, D.D. D'Lima, C.W. Colwell Jr., B.J. Fregly, Correlation between the knee adduction torque and medial contact force for a variety of gait patterns, *J. Orthop. Res.* 25 (2007) 789–797.
- [30] A. Mundermann, C.O. Dyrby, D.D. D'Lima, C.W. Colwell Jr., T.P. Andriacchi, In vivo knee loading characteristics during activities of daily living as measured by an instrumented total knee replacement, *J. Orthop. Res.* 26 (2008) 1167–1172.