Asymptomatic and Symptomatic Individuals with the Same Radiographic Evidence of Knee Osteoarthritis Walk With Different Knee Moments and Muscle Activity

Janie L. Astephen Wilson, William D. Stanish, Cheryl L. Hubley-Kozey

Abstract

There is an established discordance between the structural joint damage and clinical symptoms of knee osteoarthritis; however, there has been little investigation into the differences in joint level biomechanics and muscle activation patterns during gait between symptomatic and asymptomatic individuals with the same radiographic evidence of osteoarthritis. The objective of this study was to examine three-dimensional knee joint biomechanics and muscle activation differences during gait between asymptomatic and symptomatic individuals with radiographic knee osteoarthritis. A total of 54 asymptomatic and 59 symptomatic individuals with a Kellgren–Lawrence osteoarthritis radiographic grade of 2 underwent a comprehensive gait analysis to examine differences in the magnitude and patterns of the knee flexion angle, three-dimensional net resultant moments, and electromyography of the quadriceps, hamstrings, and gastrocnemii during over ground walking between the two groups. The symptomatic group walked with significantly higher overall magnitudes and less mid-stance unloading of the net resultant knee adduction moment, lower peak flexion moments, and higher lateral hamstrings and quadriceps activity during stance than the Asymptomatic group ($p < 0.05$, sex-adjusted analysis), with a trend ($p = 0.07$) toward greater transverse plane range of moment over stance. The differences found suggest a “stiffer” frontal and sagittal plane pattern with symptomatic individuals, but with more muscle activity and a trend toward more torsional loading in the transverse plane, which may have implications for shear loading of the joint. This is the first evidence of differences in three-dimensional knee joint biomechanics and muscle activation between asymptomatic and symptomatic individuals with the same radiographic grade.

Introduction

Knee osteoarthritis (OA) structural joint damage and clinical symptoms are not always well correlated,[1, 2] and tend to be more correlated for higher grades of radiographic knee OA severity.[3] This has led to the distinction between OA “disease” and “illness,”[4] with the disease component linked to joint tissue damage, and the illness related to the pain and symptoms experienced by the patient. Individuals with clinical presentations of pain and symptoms do not always have radiographic evidence of disease, and many asymptomatic individuals can have even severe structural OA changes to their knee joints.[5] This makes it challenging to identify populations early in the disease or illness process, thus examining differences in characteristics between those with similar structural damage but different presentation for symptoms may provide evidence for early detection or intervention protocols.

Instrumented gait analysis is an established method for evaluating the functional implications of knee osteoarthritis, and there have been numerous cross-sectional investigations that have examined joint-level kinematic, kinetic, and at times muscular changes during walking associated with knee OA,[6-10] as well as changes between pre-defined severity levels of OA, including both radiographic,[11-13] and more clinical definitions of severity.[14-16] There has also been a recent surge in investigations of the interaction between gait mechanics and the progression of knee OA longitudinally over time, again using

radiographic[17-19] as well as clinical[20] definitions of OA progression. What is difficult to ascertain from this literature is the contribution of the potentially discordant effects of radiographic and symptomatic aspects of knee OA in the observed changes in gait mechanics. “Radiographic progression” may be confounded by simultaneous symptomatic progression, and “clinical progression to total joint replacement surgery” as defined by Hatfield et al.[20] involves both radiographic and symptomatic aspects of the disease.

Some previous investigations have provided insight into the role of radiographic and symptomatic knee OA on gait mechanics. Cross-sectional studies have shown that increased structural severity (regardless of symptom level or presence) has been associated with higher knee adduction moments.[12, 21, 22] Pain, as reflected by the WOMAC osteoarthritis index, has been associated with slower walking speeds and more prolonged activity of the lateral gastrocnemius and medial hamstring during gait.[22] However, pain relief investigations have also associated pain reduction with higher knee joint compressive forces during gait,[23] as well as higher knee adduction and flexion moments.[24] Thorp et al. [2007][25] conducted the only study that examined differences between the presence and absence of symptoms in those with similar radiographic OA evidence on frontal plane knee joint moments during walking, providing a model to examine the role of radiographic and symptomatic knee OA separately. Their study showed that the overall peak knee adduction moment occurring during mid-stance and the knee adduction moment impulse was higher in the symptomatic group with a Kellgren Lawrence (KL)[26] radiographic grade of 2 compared to an asymptomatic group with the same KL grade. Interestingly, they found no difference in the knee adduction moment between their two asymptomatic groups, one with and without radiographic evidence of knee OA. Their findings provide evidence that the presence or absence of symptoms, despite similar radiographic OA evidence damage is linked to changes in knee adduction moment characteristics that have been implicated in both structural progression[17-19] and more recently clinical progression.[20]

Recent evidence, however, shows that joint level kinetics other than solely the knee adduction moment and muscle activation features are discriminatory among OA severity levels based on radiographic[13, 22] or combined radiographic and clinical severity,[8, 15, 16] and more recently for predicting OA progression.[19, 20, 27] What is missing from existing literature is a clear understanding of the differences in three-dimensional loading and muscle activity during gait based purely on symptomatic state, without the confounding effects of differences in radiographic disease. This information is important because understanding the differences in gait mechanics between individuals with and without symptomatic OA will provide direction for the development and testing of interventions aimed at symptomatic improvement and delayed clinical progression of OA. Therefore, to add to our understanding of the characteristics of gait that are unique to OA symptoms, this study examined differences in the three-dimensional knee joint kinematic, kinetic and muscle activation differences during walking between a group of individuals with symptomatic knee OA and a KL grade of 2 (symptomatic), and a group of asymptomatic individuals also with a KL grade of 2 (asymptomatic). We hypothesized that the symptomatic group would walk with a “stiffer” gait pattern, less knee joint range of motion, more constant loading patterns, and higher and more prolonged muscle activation (i.e., a pattern more consistent with recent gait progression models).

METHODS

Participants

This was an observational case-control study with two participant groups (level of evidence = III). Participants were selected that had a Kellgren–Lawrence (KL) grade of 2[26] based on a standardized AP radiograph within two months of gait testing (intra-rater reliability (WDS) = 0.91), from a larger group of asymptomatic participants (*N* = 68, herein referred to as asymptomatic) and a symptomatic group diagnosed clinically with medial compartment knee OA (*N* = 163, herein referred to as Symptomatic) by an orthopedic surgeon according to the American College of Rheumatology criteria.[28] Participants were considered symptomatic based on their clinical diagnosis which included established self-reported pain and symptoms.[28] Asymptomatic participants were recruited through university and hospital postings and had no history of knee pain. Symptomatic participants were recruited from the Orthopedic and Sports Medicine Clinic of Nova Scotia and the Orthopaedic Assessment Clinic at the QEII Health Sciences Center. All participants self-reported the ability to walk a city block, jog 5 m, and walk upstairs in a reciprocal manner. Exclusion criteria for this study included history of cardiovascular disease, any neuromuscular disease, other forms of arthritis, gout, or history of surgery to the lower limb,[9] as well as a radiographic KL score of anything other than 2. All participants had dominant medial compartment OA involvement, based on radiographic evidence of a medial joint space narrowing score greater than or equal to lateral joint space narrowing score.[29] We did not control for patellofemoral OA in this study, and the most symptomatic knee for the symptomatic group and a randomly assigned knee for the Asymptomatic group were included in the current analysis. This resulted in 54 asymptomatic participants with a KL grade of 2, and 59 symptomatic participants with a KL grade of 2. All participants signed a written consent form in accordance with the institutional ethics review.

Gait Analysis

Kinematics and Kinetics

All participants underwent gait testing in one visit to the Dynamics of Human Motion laboratory at Dalhousie University. After a brief warm-up period, participants completed at least five over ground walking trials, along a 6-m walkway at a comfortable, self-selected walking speed, which we have shown to have high day to day repeatability.[30] Three-dimensional motion of the most symptomatic (symptomatic group) or a randomly selected (asymptomatic group) lower extremity limb was captured during the walking trials with a two camera bank Optotrak™ 3020 motion capture system at 100 Hz (Northern Digital Inc., Waterloo, ON, Canada). Four three-marker triads of infrared light-emitting diodes were placed on the sacrum, lateral thigh, lateral shank, and foot segments. Individual diodes were placed on the greater trochanter, lateral epicondyle, lateral malleolus, and shoulder. Eight virtual markers were identified on anatomical points during quiet standing, including the right and left anterior superior iliac spines, medial epicondyle, fibular head, tibial tuberosity, medial malleolus, second metatarsal, and calcaneus. External ground reaction forces were recorded at 2,000 Hz from an AMTI force platform embedded within the walkway (Advanced Mechanical Technology Inc., Watertown, MA), synchronized, and down-sampled to match the motion capture data.

Custom Matlab (The Mathworks Inc., Natick, MA) code was used to model the three-dimensional knee joint angles and net resultant moments during gait according to the joint coordinate system[31] and using a previously described inverse dynamics procedure.[14] Joint moments were normalized to body mass (Nm/kg). Five trials of joint angles and moments were averaged for each participant and then time-normalized to one complete gait cycle from initial (0%) to second (100%) foot contact with the ground, or 101 data points each.

Electromyography

Surface electromyography (EMG) was used to capture muscle activation patterns during the gait trials, with an eight-channel system (AMT-8 EMG, Bortec Inc., Calgary, AB) synchronized with the motion capture system. EMG collection and processing followed a standard protocol that has between day reliability for those with knee OA.[9, 32] Standard preparation of skin was performed (shaving and cleaning with alcohol + water) and the silver/silver chloride pellet surface electrodes (10 mm diameter, 20 mm inter-electrode distance) were attached in a bipolar configuration over seven muscle sites, the rectus femoris (RF), vastus lateralis (VL), vastus medialis (VM), lateral (LH) and medial hamstrings, lateral and medial gastrocnemius (LG and MG). Attachment locations were initially based on standard anatomical landmarks.[9] Isolated movements aimed at activating the different muscles were performed to validate locations and electrode attachment.[33] A reference electrode was mounted on the shaft of tibia. Raw EMG signals were sampled at 2,000 Hz after they were pre-amplified (500×) and further amplified (band-pass 10–1,000 Hz; common mode rejection ratio of 115 dB (at 60 Hz); input impedance of 10 GΩ). Gains were adjusted based on a second set of isolated movements performed by the participants to ensure the collection of a good quality signal and to asses crosstalk.[33] A bias trial was performed with participants lying relaxed and supine. A series of eight exercises previously described in detail[9] were performed after the walking trials to elicit maximum voluntary isometric contraction (MVIC) including three knee extension, three knee flexion and one plantar flexion exercise on a Cybex dynamometer (Lumex, NY) and one resisted standing heel rise exercise. Each exercise was performed twice, with verbal encouragement and a minimum of 1 min rest between exercises. The average torque over a 1-s steady state value was used as a measure of knee extension (at 45°), knee flexion (at 55°), and plantarflexion strength.[9] EMG signals were band pass filtered between 20 and 500 Hz,[34] corrected for gain and bias, full wave rectified and low pass filtered using a second order non-recursive Butterworth low pass filter with a cut off frequency of 6 Hz.[35] For each individual, EMG waveforms of at least five trials were amplitude normalized to MVIC and time normalized to 100% of the gait cycle and then ensemble averaged to yield the final waveforms for each of the seven muscles.

Statistical Methods

Dominant amplitude and temporal pattern features of the knee flexion angle, the three-dimensional net results moments at the knee, and EMG waveform (each muscle group separately; quadriceps, gastrocnemii, hamstrings) were extracted using principal component analysis (PCA) as previously described.[6, 9] Data for each angle and moment were arranged in separate data matrices ($X_{113 \times 101}$), where 113 represents the total number of subjects, and 101 each percent of the gait cycle. EMG data were arranged in data matrices ($X_{339 \times 101}$) for the three quadriceps muscles and two ($X_{226 \times 101}$) matrices for the hamstrings and gastrocnemii, respectively. PCA was then applied to each of these original data matrices to extract principal components (PCs), which are major patterns of amplitude and temporal variability among the participants.[6, 9, 36] Principal component scores (PC scores) were calculated for each participant and each PC. PC scores represented the extent to which the participant's waveform data reflected the pattern depicted by the PC. PCs were interpreted based on their pattern over the gait cycle, the variation explained, as well as examination of extremes (5th and 95th percentiles) of the PC score distribution.[9, 15] We chose to examine group differences in the first two PCs of the knee flexion angle and the three-dimensional net resultant knee moments, and the first two of each muscle group, representing just the dominant features of magnitude and pattern variability in each. All features have shown high day-to-day reliability.[30, 32] We also examined differences in some discrete scores,

including the first and second peak, mid-stance value and impulse of the knee adduction moment during stance, and the RMS of the EMG waveforms, to provide context for literature findings and dimensional units. PC and discrete scores were examined for normality, and analysis of variance adjusted for sex was used to examine statistically significant differences between asymptomatic and symptomatic groups with KL scores of 2 ($\alpha = 0.05$, sex-adjusted). We additionally compared WOMAC osteoarthritis index total and subscale scores,[37] mass, age, hip to waist ratios, BMI, stride characteristics, and muscle strength between groups using the same statistical testing methods.

RESULTS

The symptomatic group was marginally older (56.7 vs. 53.2 years), had a higher male to female ratio, a 2.3 kg/m^2 higher mean BMI (29.9 vs. 27.6 kg/m^2), with a greater waist to hip circumference ratio than the asymptomatic group (Table 1). Additionally, the symptomatic group walked with slightly slower average self-selected walking speeds (1.27 vs. 1.35 m/s), longer stride and stance times, and had lower mass normalized knee extension, flexion. and plantarflexion strength. As expected, they also had significantly higher total, pain, stiffness. and function WOMAC scores[37] (Table 1).

Table 1. Participant Demographics Summary

	Asymptomatic	**Symptomatic**	***p*-Value**
Sample size	54	59	
Sex distribution (female:male)	37:17	20:39	
Age (years)	53.2 (8.2)	56.7 (8.4)	0.026
Body mass (kg)	77.9 (16.1)	89.2 (16.6)	<0.001
Height (m)	1.68 (0.10)	1.73 (0.09)	0.009
BMI (kg/m^2)	27.6 (5.2)	29.9 (4.7)	0.016
Waist circumference (m)	0.89 (0.13)	0.97 (0.11)	0.017
Hip circumference (m)	1.05 (0.10)	1.05 (0.08)	0.91
Waist to hip ratio	0.85 (0.08)	0.92 (0.09)	0.001
Average walking speed (m/s)	1.35 (0.16)	1.27 (0.21)	0.021
Stride length (m)	1.43 (0.14)	1.41 (0.16)	0.33
Stride time (s)	1.07 (0.08)	1.12 (0.12)	0.003
Stance time (s)	0.68 (0.06)	0.72 (0.08)	0.003

	Asymptomatic	Symptomatic	*p*-Value
Stance percent	63.6 (1.8)	64.1 (2.0)	0.18
WOMAC total (/96)	1.74 (4.46)	30.12 (16.98)	<0.001
WOMAC pain sum (/20)	0.22 (0.69)	6.37 (3.77)	<0.001
WOMAC stiffness sum (/8)	0.37 (0.81)	3.27 (1.73)	<0.001
WOMAC function sum (/68)	1.15 (3.46)	20.45 (12.22)	<0.001
Knee extension strength (Nm/kg)	1.66 (0.52)	1.35 (0.46)	0.002
Knee flexion strength (Nm/kg)	0.71 (0.27)	0.59 (0.23)	0.021
Plantarflexion strength (Nm/kg)	1.21 (0.41)	1.05 (0.44)	0.05

Data are presented as mean (standard deviation) where appropriate. *p*-values correspond to Student's *t*-test for comparison of asymptomatic and symptomatic groups for variable of interest

Mean three-dimensional knee joint flexion angles and net resultant moments during gait are provided in Figure 1, and mean MVIC normalized EMG waveforms during gait are provided in Figure 2. The first two PCs of the knee flexion angle during gait represented the overall magnitude and the range of flexion/extension motion throughout the gait cycle. There were no statistically significant group differences in the knee flexion angle during gait. PC1 of the knee adduction moment represented the overall magnitude of the moment during stance, and PC2 represented the difference between the first peak of the adduction moment and its mid to late stance value. Statistically significant group differences were found for PC1 and PC2 (Table 2 and Fig. 1c), as well as impulse, mid-stance minimum and late stance peak (Table 3). The symptomatic group had significantly higher PC1 scores, and, therefore, higher overall magnitude of the knee adduction moment during stance, consistent with the higher knee adduction moment impulse (Table 3). The symptomatic group also had significantly lower PC2 scores of the knee adduction moment, or a more constant knee adduction moment during stance, and reflecting both the higher mid-stance and late stance values of the moment (Table 3).

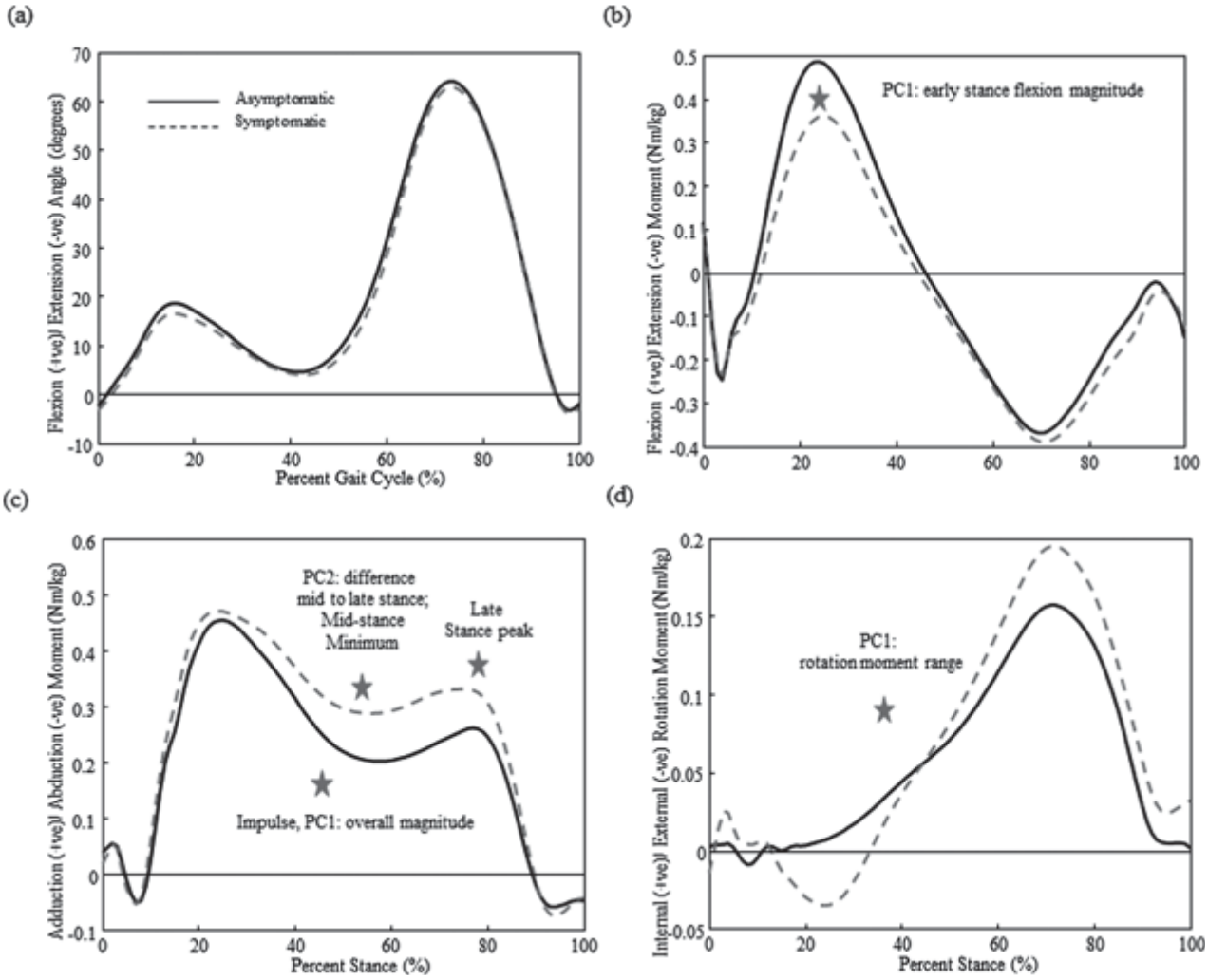

Figure 1.

Mean group waveforms of the knee flexion angles and three-dimensional knee moments during gait. Mean group waveforms of the asymptomatic (solid lines) and symptomatic (dashed lines) groups with KL grades of 2 are shown for the (a) knee flexion angle over entire gait cycle; (b) the net resultant external knee flexion/extension moment during stance; (c) the net resultant external knee adduction moment during stance; and (d) the net resultant external internal/external rotation moment during stance. Stars indicate statistically significant sex-adjusted differences between groups ($p < 0.05$, with trend ($p = 0.07$) also indicated for PC2 of rotation moment).

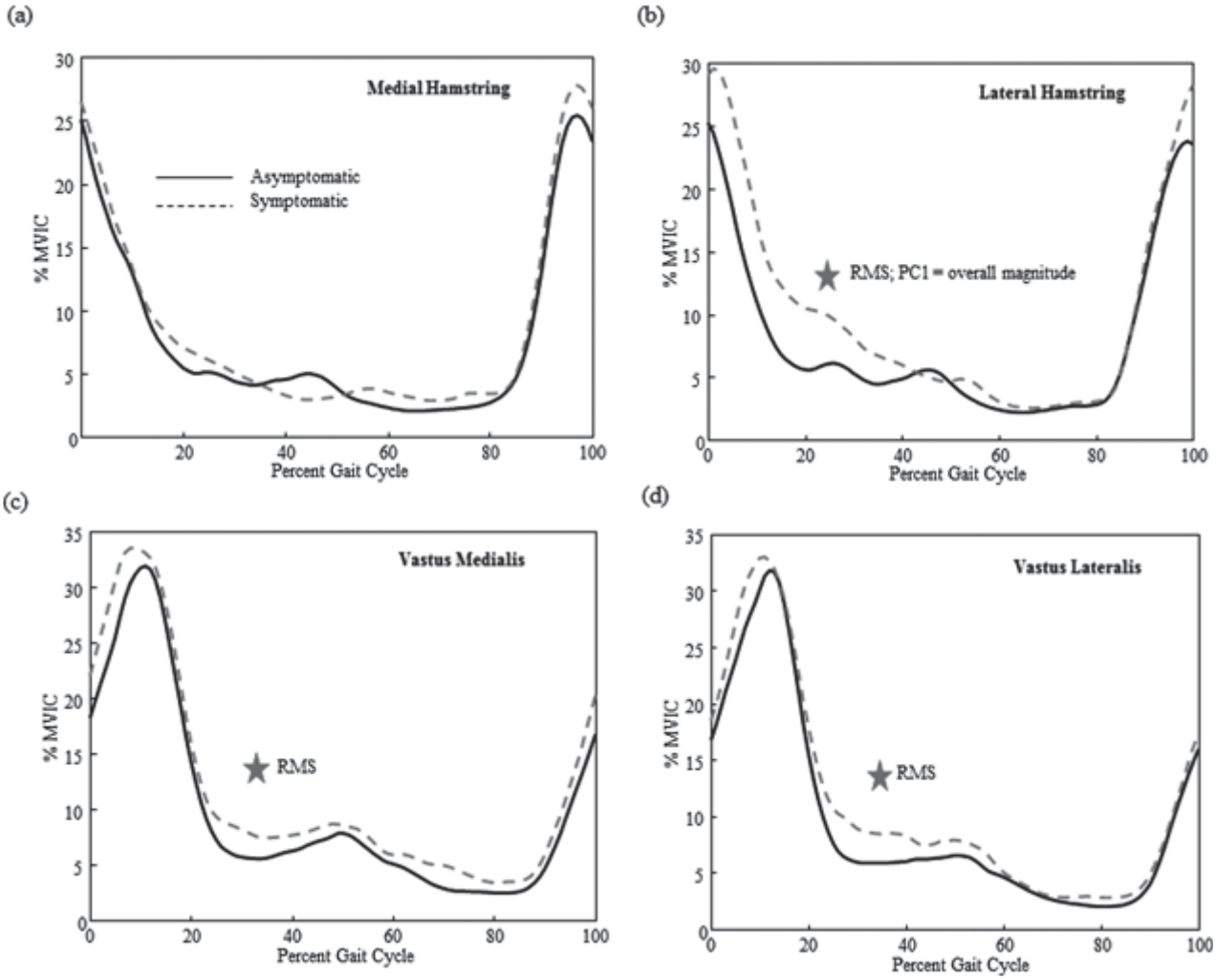

Figure 2.

Mean group waveforms of electromyography during gait. Mean group waveforms of the maximum voluntary isometric contraction (MVIC) normalized processed EMG signals are shown for the asymptomatic (solid lines) and symptomatic (dashed lines) groups with KL grades of 2 for the (a) medial hamstrings; (b) lateral hamstrings; (c) vastus medialis; and (d) vastus lateralis. Stars indicate statistically significant sex-adjusted difference in activation between groups ($p < 0.05$). Note that three asymptomatic participants and two symptomatic were unable to perform the MVIC exercises to normalize the EMG data, and, therefore, were not included in the analysis. Additionally there were missing EMG data for medial gastrocnemius (1 asymptomatic), lateral gastrocnemius (1 asymptomatic), and vastus medialis (3 symptomatic). Therefore, EMG analysis for the gastrocnemii included 50 radiographic and 57 symptomatic participants, analysis for the vastus medialis included 51 radiographic and 54 symptomatic participants, and analysis for the vastus lateralis, rectus femoris, and lateral and medial hamstrings included 51 asymptomatic and 57 symptomatic OA participants.

Table 2. Principal Component Statistical Results

Variable	PC	Variability Explained (%)	Asymptomatic PC Score	Symptomatic PC Score	*p*-Value	Interpretation
Adduction moment	1	61.5	−0.27 (0.78)	0.24 (0.97)	0.009	Overall stance magnitude, symptomatic higher
Adduction moment	2	18.5	0.12 (0.45)	−0.11 (0.53)	0.002	Difference first to second peak, symptomatic less difference
Flexion moment	1	47.1	0.29 (1.04)	−0.27 (1.3)	0.001	Overall early stance flexion magnitude, symptomatic lower
Rotation moment	1	58.0	−0.13 (0.42)	0.12 (0.4)	0.07	Difference early stance external and late stance internal rotation moment, symptomatic less difference
Lateral hamstrings	1	82.3	102.3 (52)	127.8 (66.2)	0.01	Symptomatic higher overall activation magnitude

Statistical comparison of knee angle, moments, and electromyography magnitudes and patterns over the gait cycle, captured using principal component analysis. Interpretation of principal components and *p*-values with statistically significant sex-adjusted ($p < 0.05$) differences in PC scores between asymptomatic and symptomatic groups are provided. PC score data are presented as group mean (standard deviation) for those PCs showing statistically significant ($p < 0.05$) or a trend ($p = 0.07$) toward significant group differences.

Table 3. Discrete Metrics Statistical Results

Variable	Metric	Asymptomatic	Symptomatic	*p*-Value
Knee adduction moment (Nm/kg)	Early stance peak (0–50% stance)	0.48 (0.16)	0.51 (0.15)	0.58
Knee adduction moment (Nm/kg)	Late stance peak (70–100% stance)	0.27 (0.11)	0.35 (0.13)	0.005
Knee adduction moment (Nm/kg)	Mid-stance minimum (35–65% stance)	0.18 (0.08)	0.27 (0.13)	<0.001

Variable	Metric	Asymptomatic	Symptomatic	*p*-Value
Knee adduction moment (Nm × s/kg)	Impulse (area under stance curve)	0.14 (0.05)	0.18 (0.7)	0.002
Lateral Gastrocnemius EMG	Gait cycle RMS (%MVIC)	22.0 (11.0)	20.9 (9.3)	0.64
Medial gastrocnemius EMG	Gait cycle RMS (%MVIC)	25.8 (11.7)	24.9 (9.0)	0.47
Vastus lateralis EMG	Gait cycle RMS (%MVIC)	13.6 (5.8)	15.0 (8.6)	0.05
Vastus medialis EMG	Gait cycle RMS (%MVIC)	13.8 (7.2)	15.9 (11.0)	0.02
Rectus femoris EMG	Gait cycle RMS (%MVIC)	8.1 (3.7)	9.4 (6.9)	0.007
Lateral hamstring EMG	Gait cycle RMS (%MVIC)	11.0 (5.9)	14.0 (7.4)	0.01
Medial hamstring EMG	Gait cycle RMS (%MVIC)	11.3 (6.3)	12.4 (6.2)	0.20

Discrete metrics were extracted from the angle, moment and EMG waveforms. Mean (standard deviation) values of these metrics are presented for the asymptomatic and moderate OA groups, along with *p*-values for a sex-adjusted analysis of variance.

The symptomatic group walked with statistically significantly lower peak flexion moments (PC1) during stance (Tables 2 and 3 and Fig. 1b), but not with statistically significantly different late stance extension moments (PC2). The symptomatic group also walked with a trend toward ($p = 0.07$) a greater difference between early stance external rotation moment and later stance internal rotation moment (PC1; Table 2 and Fig. 1d), but not with statistically significant differences in the mid-stance value of the rotation moment (PC2).

PC1 for each muscle group represented the overall magnitude of MVIC normalized activation over the gait cycle. The symptomatic group had a significantly greater overall magnitude (PC1) of the lateral hamstrings muscle (Table 2), but no statistically significant differences in PC1 of other muscles. There were no statistically significant differences in PC2 for any muscle, which represented a prolonged activity of the muscle throughout mid to late stance (gastrocnemius), or mid-stance muscle activity (quadriceps, hamstrings). In addition, the symptomatic group also walked with higher RMS activation of the lateral hamstrings, and the three quadriceps muscles over the gait cycle (vastus lateralis, vastus medialis, rectus femoris) (Table 3 and Fig. 2b–d) and from Figure 2c and d, the mid-stance phase was where the amplitude differences were evident.

DISCUSSION

We identified frontal, sagittal, and muscle activation differences during gait between asymptomatic and symptomatic individuals with the same radiographic severity (KL grade 2), and a trend toward a difference in transverse plane loading during stance. The symptomatic group were expectedly characterized by greater clinical symptoms, slightly higher body mass and BMI, and less knee muscle

strength (Table 1), and (slightly) slower walking speeds, consistent with our previous work.[9, 15] The small age (3.5 years) and BMI (2.3 kg/m^2) differences would unlikely influence our results, as both groups would be classified as overweight based on their mean BMI, and the mean age of both groups was mid-50s and not elderly. We discovered a significantly greater ratio of men to women in our symptomatic group compared to asymptomatic, and proceeded to use sex-adjusted analysis of variance to compare biomechanical and muscle activation variables between groups differences because we have previously reported biomechanical differences during gait between men and women.[38, 39] The walking velocity difference between groups was approximately 5%, and although we are aware that walking velocity and joint level mechanics can be related (e.g., Landry et al. [2007][14]), reduced walking speed is an integrated effect of OA symptoms and controlling walking speed using an ANCOVA model would not be appropriate as this effect is not simply an erroneous sampling issue such as the difference in sex distribution between the groups.[40]

The significantly higher overall magnitudes of the knee adduction moment during stance (PC1, impulse), and less mid to late-stance "unloading" (PC2) (Fig. 1c) suggest an inability of the Symptomatic individuals to relieve the joint of frontal plane loading during single leg stance, compared to asymptomatic individuals. This is interesting and somewhat contrary to experimental pain models that have shown reductions in the knee adduction moment with pain onset.[41] However, only peak values for healthy participants and not patterns of frontal plane moments were considered previously. The higher mid-stance and impulse of the knee adduction moment in the symptomatic group was consistent with the previous study by Thorp[25] with similar participant groups, so providing further support for these features being related to symptoms. We have recently linked similar features of the knee adduction moment waveform at baseline to later clinical progression to total knee arthroplasty,[20] and, therefore, this result further supports that these frontal plane features during gait may be associated with symptomatic knee OA and clinical progression. Similarly in the sagittal plane, the lower overall flexion moment in early stance (PC1, peak value), further supports a "stiffer" joint with symptomatic individuals, with the higher activation magnitudes of the quadriceps muscles and the lateral hamstrings muscles (Fig. 2) indicative of higher co-activation, particularly in early to mid-stance phase of gait. Thus, joint stiffening may be a guarding mechanism in response to pain or potentially lack of perceived stability of the joint (not assessed in the current methods). While all three muscle groups tested (Table 1) had lower muscle strength for the symptomatic group, the overall amplitude (PC1) was higher for the lateral hamstrings only and the RMS amplitudes were higher for the three quadriceps and the lateral hamstring only, suggesting that the amplitude differences were not uniform among muscles. Therefore, in part, the activation amplitudes may reflect the differences in muscle strength between the groups, but the lack of systematic increase would suggest this co-activation response may be associated with active joint stiffening, which is a reflection of the lack of unloading captured from the knee adduction and flexion moment features. The lack of mid-stance unloading and reduced peak flexion moment may also be related to the speed differences between the groups; however, the overall magnitude of the moment has been shown to be independent of speed differences.[14] It is unclear from the current study design whether these changes pre-date the onset of symptoms or are a result of the symptoms, and it is, therefore, possible that this joint stiffening gait pattern may have contributed to the onset of symptoms and OA illness. In any case, this "stiffer" joint is likely less able to dissipate the repetitive loading, which may in turn contribute to further joint damage consistent with OA pain pathways.[42-44]

There was a trend toward the symptomatic group having a greater dynamic range of the rotation moment during stance than the asymptomatic group (PC1, $p = 0.07$; Fig. 1d), which could be interpreted as a less stiff joint in the transverse plane with the symptomatic group compared to asymptomatic. It is possible that this greater range of torsional loading on the joint results in shear stresses on the free nerve endings that are involved in nociceptive pathways,[45] and, therefore, the lack of this shear loading in the asymptomatic group may be pain protective. The lingering interesting question would be why the symptomatic group would adopt this change, and it may reflect compensation due to the stiffening in the frontal and sagittal planes described above. The muscle activation differences perhaps explain the differences in dynamic moments among planes. It is also possible that this greater range of transverse plane loading is involved in joint damage specific to OA pain pathways.

The differences identified in the activation magnitudes of the lateral hamstrings and quadriceps muscles during gait between the groups are consistent with differences reported in our previous work[9, 13] comparing those with moderate levels of clinically diagnosed knee OA and an age-matched asymptomatic cohort with unknown levels radiographic disease involvement. Our current findings suggest that these increases in lateral hamstring muscle activation with the symptomatic group during stance likely reflect a compensation to unload a painful medial compartment of the knee joint ("guarding"), whereas quadriceps and hamstrings co-activation may contribute to the onset of symptoms based on potential increases in joint loading. Recent modeling work by Brandon et al.[46] suggests that lateral muscle activation during gait does not in fact "unload" the medial compartment of the knee joint in terms of actual joint compressive and shear contact forces, but does represent a strategy to increase knee joint stiffness, without large increases to contact forces within the knee joint. Furthermore, the increase in both the lateral hamstring and quadriceps muscles in early stance with the symptomatic group could in part be responsible for the early reduction in the knee flexion moment due to antagonist co-activation. Collectively these findings support a protective mechanism against pain. Given that the symptomatic group had lower normalized flexor and extensor strength than the asymptomatic group (Table 1), it is possible that some of the difference in activation magnitude normalized to maximum voluntary isometric contraction reflect this difference in strength values. However, the higher lateral versus medial hamstring during early stance in the symptomatic group suggests a rotational coupling not consistent with the asymptomatic group. This differential requires further investigation as the asymptomatic pattern is consistent with a more balanced external–internal rotation moment in the transverse plane.

We examined both principal components as well as a few commonly extracted discrete gait metrics in this paper to interpret the particular contribution of knee OA symptoms to previously identified joint and muscle-level biomechanical changes with more generally defined knee OA. The added value of PC approach is the ability to objectively identify not only magnitude, but also uncorrelated pattern differences that have been associated with clinical OA progression in previous research[20] that can be difficult to define using discrete metrics.[47] The interpretation of the current findings are limited to the cross-sectional observation of the data, and longitudinal examinations of gait biomechanics in conjunction to isolated symptomatic OA progression can provide further evidence for the role of these factors in disease progression. Whether the differences identified here have contributed to the symptomatic/pain pathways of the disease, or represent a compensation to reduce pain in the joint cannot be determined from this cross-sectional design. Despite this, some interesting biomechanical and muscle activation differences were observed that may be attributed to the symptomatic state of

participants, and, therefore, likely more implicated in a biomechanical response to pain and symptoms than radiographic disease. In general, symptomatic participants walked with a “stiffer” joint in the frontal and sagittal planes, but this stiffness may have a trade-off with a trend toward more torsional loading in the transverse plane. Longitudinal follow-up is allowing us to establish whether these adaptations can further progress joint damage or clinical progression, and, therefore, whether or not management strategies should aim to improve these metrics. For instance, our recent work[46] links an aspect of these adaptations, the inability to unload the knee joint in the frontal plane during stance, to clinical progression and the need for total knee arthroplasty surgery. Further longitudinal investigation that includes the electromyography information, as well as a comparison of radiographic versus symptomatic progression will allow us to examine this further.

We were unfortunately unable to identify a cohort of asymptomatic individuals with no/small radiographic evidence of knee OA in this study (only 8 of 68 asymptomatic participants had KL grade of 0 or 1), and, therefore, were unable to provide a control group for examination of biomechanical factors related to radiographic OA severity in the absence of symptoms. However, the objective of the current study was to identify biomechanical changes that may be associated with symptomatic OA, and Thorp et al.[25] found that asymptomatic individuals with KL grades of 0 and 1 walked with similar net resultant knee adduction moments as the asymptomatic individuals with KL grades of 2. Our study involved only participants, both asymptomatic and symptomatic, with a KL grade of 2, or established radiographic evidence of knee OA. The implications of these findings to individuals without a KL grade of 2 are, therefore, unclear. Our study was also limited to the biomechanics and imaging of one lower extremity knee joint per participant. We could, therefore, not make any conclusions on gait asymmetry due to symptomatic OA. As well, lack of radiographic information from the contralateral knee joint or the patellofemoral joint means that any heterogeneity among participants in radiographic involvement at these sites which could affect gait mechanics of the ipsilateral knee were not accounted for in the current study. Additionally, the symptomatic group included in this study was defined based on self-reported pain and symptoms within a clinical diagnosis of osteoarthritis according to the American College of Rheumatology criteria.[28] The origin of pain and symptoms within each individual is, therefore, unclear and may be heterogeneous in nature. We are aware that joint effusion can specifically have an effect on joint-level biomechanics and muscle activity, particularly being associated with prolonged activation of the quadriceps and hamstrings muscles and lower knee extension moments[48]; however, we had no specific information on synovitis in our participant cohort in this study.

Overall, this work supports that biomechanical metrics are manifested differently with radiographic changes versus radiographic changes plus symptoms. Clinical implications of this work are that these markers provide potential targets for changing gait patterns and the changes needed are not just systematic changes to frontal plane joint moments. The identified features should be examined in longitudinal investigations of OA clinical progression to understand their role in the development and manifestation of clinical symptoms. If validated in longitudinal models, future work should explore the development and validation of symptomatic OA management strategies that reduce the “stiff” knee gait biomechanical changes identified, which could include physiotherapy strategies and/or gait retraining.

In conclusion, biomechanical and muscular activation differences exist between asymptomatic and symptomatic individuals with the same radiographic grade, suggesting that some identified features of joint level mechanics and muscle may reflect the symptomatic disease more than structural joint-level

changes. Collectively, the moment and muscle activation patterns shown that with the presence of symptoms, there is a “stiff” knee gait pattern, and attempts to manage and monitor outcome based on biomechanical metrics should, therefore, consider the potentially different reflections of the radiographic and symptomatic disease on chosen outcome metrics.

AUTHORS’ CONTRIBUTIONS

All authors have read and agree with the content presented in the manuscript. Janie Astephen Wilson contributed to the conception and design, collection, analysis, and interpretation of data, drafting of article, and final approval of manuscript, statistical expertise, provision of study materials, and obtaining funding. Cheryl Hubley-Kozey contributed to the conception and design, collection, analysis, and interpretation of data, drafting of article and final approval of manuscript, provision of study materials, and obtaining funding. William Stanish contributed to the study design, provision of participants, diagnosis, interpretation of data, preparation, and final approval of manuscript.

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