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Gait and neuromuscular pattern changes are associated with differences in knee osteoarthritis severity levels

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Abstract

Knee osteoarthritis (OA) is a multifactoral, progressive disease process of the musculoskeletal system. Mechanical factors have been implicated in the progression of knee OA, but the role of altered joint mechanics and neuromuscular control strategies in progressive mechanisms of the disease have not been fully explored. Previous biomechanical studies of knee OA have characterized changes in joint kinematics and kinetics with the disease, but it has been difficult to determine if these biomechanical changes are involved in the development of disease, are in response to degenerative changes in the joint, or are compensatory mechanisms in response to these degenerative changes or other related factors as joint pain. The goal of this study was to explore the association between biomechanical changes and knee OA severity in an effort to understand the changing role of biomechanical factors in the progression of knee OA. A three-group cross-sectional model was used that included asymptomatic subjects, subjects clinically diagnosed with moderate knee OA and severe knee OA subjects just prior to total joint replacement surgery. Principal component analysis and discriminant analysis were used to determine the combinations of electromyography, kinematic and kinetic waveform pattern changes at the knee, hip and ankle joints during gait that optimally separated the three levels of severity. Different biomechanical mechanisms were important in discriminating between severity levels. Changes in knee and hip kinetic patterns and rectus femoris activation were important in separating the asymptomatic and moderate OA gait patterns. In contrast, changes in knee kinematics, hip and ankle kinetics and medial gastrocnemius activity were important in discriminating between the moderate and severe OA gait patterns.

Keywords: Knee osteoarthritis; Severity; Gait analysis; Electromyography

1. Introduction

Knee osteoarthritis (OA) is a metabolically active, dynamic process that includes both destruction and repair mechanisms that can be triggered by mechanical insults (Felson et al., 2000). Modern gait analysis offers a unique means of providing insight into mechanisms of knee OA progression by measuring the biomechanical response of the musculoskeletal system to the disease, and electromyography (EMG) is a valuable tool for understanding concomitant changes in neuromuscular response. While mechanical factors have been implicated in the progression of knee OA (Andriacchi et al., 2004), the mechanistic role of biomechanical factors are still not well understood (Brandt, 1998). This is largely attributable to the lack of comprehensive biomechanical studies that consider simultaneous changes in neuromuscular function and joint dynamics in all joints of the lower extremity, and to the poor treatment and characterization of disease severity in biomechanical studies. Longitudinal studies would be ideal for developing predictive models of knee OA disease

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progression, but properly designed cross-sectional studies of different levels of knee OA severity can also provide important insight into the changing role of biomechanical factors throughout the progression of the disease.

Gait analysis has been used to identify mechanical factors that may be important at different levels of knee OA disease advancement. Kinetic factors such as joint loading have been suggested to be potentially important in the early phases of the disease process (Radin and Paul, 1972; Arokoski et al., 2000), and changes in the knee and hip adduction moments have been recently associated with early to moderate levels of knee OA (Mundermann et al., 2005; Chang et al., 2005). Kinematic gait factors, such as joint ranges of motion, have been associated with more advanced stages of the disease (Messier et al., 1992; Deluzio and Astephen, 2007; Al Zahrani and Bakheit, 2002). However, the single-OA group design of many of these studies and the poor characterization of disease severity has made it difficult to determine if these biomechanical changes are involved in the development of disease, are in response to degenerative changes in the joint, or are compensatory mechanisms in response to these degenerative changes or other related factors such as joint pain. There have been a few studies that have captured biomechanical changes between two different levels of knee OA radiographic severity (Hurwitz et al., 2002; Sharma et al., 1998), and a few short-term longitudinal progression studies of knee OA (Miyazaki et al., 2002; Chang et al., 2005), but these studies have focused specifically on changes in the frontal plane kinetics of the knee and hip joints.

Classification of knee OA disease severity is difficult because of the complexity and multitude of associated symptoms with the disease. Clinical severity represents a combination of both symptomatic and radiographic disease, yet most biomechanical studies have solely used radiographic classifiers to define severity (Sharma et al., 1998; Mundermann et al., 2005; Chang et al., 2005; Miyazaki et al., 2002). Because there is surprisingly little relationship between structural disease severity and symptoms (Hannan et al., 2000; Dieppe, 2005), clinical severity classification should reflect both radiographic and symptomatic markers of the disease. In the present study, the biomechanical patterns of three clinical levels of knee OA severity were compared: asymptomatic, moderate knee OA and severe knee OA. Distinction between moderate and severe levels was based on a clinical criterion that assumed that individuals indicated for total joint replacement represented a distinctly different level of clinical severity than those who were not. A multivariate analysis approach (Deluzio and Astephen, 2007) was used to identify the most important combinations of biomechanical factors that distinguished between the three severity groups. From previous literature, it was hypothesized that changes in joint moments that represent the loading patterns on the joints would be most important in discriminating moderate knee OA gait patterns from asymptomatic and that kinematic variables would be more important in defining the severe OA group.

2. Methods

2.1. Subjects

This study included 60 asymptomatic subjects, 60 with moderate knee OA and 61 with severe knee OA. The asymptomatic subjects were recruited through postings on the University bulletin board and posters at local hospitals. Subjects were included if they were over 35 years old, able to walk a city block, jog 5 m and walk upstairs in a reciprocal manner and had no history of knee pain or surgical interventions to either lower limb. Patient categorization into either the moderate or severe knee OA group was based on a clinical criterion of indication for total joint replacement surgery, a division that resulted in a good level of separation between groups in terms of demographics and WOMAC health outcome measures (Table 1). Moderate OA subjects were diagnosed with a clinical assessment that included radiographs and a physical exam and were *not* candidates for knee replacement surgery. The severe OA subjects were scheduled to receive total knee replacement surgery immediately after gait testing. Exclusion criteria included any major surgery or trauma to the lower limb, neuromuscular disorders, other forms of arthritis, gout or history of stroke and cardiovascular disease. Informed consent was obtained from all subjects in accordance with the Institutional Ethics Boards.

2.2. Gait analysis

Three-dimensional kinematics of the lower limb and external ground reaction forces were recorded with a synchronized Optotrak 3020 motion capture (Northern Digital, Inc.), and force platform (AMTI, Watertown, MA) system. Three-marker triads of infrared light emitting diodes were placed on the pelvis, thigh, leg and foot segments. Individual markers on the greater trochanter, lateral epicondyle, lateral malleolus and shoulder were identified during quiet standing. These and eight virtual markers were used to define anatomical coordinate systems in each of the four segments (Landry et al., 2007), and their kinematics were computed for a complete gait cycle using a least squares optimization routine (Challis, 1995). Intersegmental joint moments were calculated with inverse dynamics (Braune and Fischer, 1987). Joint angles and net external joint moments normalized to body mass were reported about the non-orthogonal axes described by Grood and Suntay (1983). Gait measures were defined with 101 data points, one for each percentage of the gait cycle.

2.3. Electromyography

Electromyography from seven muscles surrounding the knee was collected during the gait trials, including vastus lateralis (VL), vastus medialis (VM), rectus femoris (RF), biceps femoris (lateral hamstrings, LH), semimembranosus (medial hamstrings, MH) and lateral (LG) and medial (MG) gastrocnemius. Bi-polar electrode type, placement, amplification and filtering have been described previously (Hubley-Kozey et al., 2006). Raw EMG signals were preamplified ($500\times$) then further amplified (bandpass 10–1000 Hz, CMRR = 115 dB (at 60 Hz), input impedance $\sim$10 GΩ). Subjects performed a series of maximal voluntary isometric contractions (MVICs) on a Cybex^{TM} (Lumex, NY) dynamometer (Burden et al., 2003). A 0.1 s moving window algorithm identified the maximum EMG amplitude from each muscle MVIC, and this value was used to scale the EMG amplitudes during the gait trials (Vezina and Hubley-Kozey, 1998).

2.4. Statistical methods

2.4.1. Principal component analysis of gait and EMG waveforms

Principal component analysis (PCA) is a multivariate statistical technique that has been shown to be an effective tool in the reduction

Table 1
Subject demographic, stride characteristic and WOMAC score comparisons between the three subject groups

Parameter	Group A mean (±S.D.)	Group M mean (S.D.)	Group S mean (S.D.)	Multiple comparisons		
				M vs. A	S vs. A	S vs. M
BMI (kg/m^2)	25.45 (±4.04)	30.98 (±5.17)	32.05 (±5.48)	<0.0001	<0.0001	0.270
Weight (kg)	73.5 (±14.19)	93.61 (±17.81)	91.08 (±15.92)	<0.0001	<0.0001	0.410
Age	50.27 (±10.09)	58.32 (±9.31)	64.49 (±7.75)	<0.0001	<0.0001	<0.0001
Speed (m/s)	1.36 (±0.19)	1.25 (±0.22)	0.92 (±0.24)	0.002	<0.0001	<0.0001
Stride length (m)	1.44 (±0.13)	1.39 (±0.16)	1.16 (±0.19)	0.073	<0.0001	<0.0001
Stride time (s)	1.06 (±0.09)	1.13 (±0.12)	1.29 (±0.19)	<0.0001	<0.0001	<0.0001
Stance time (s)	0.67 (±.07)	0.73 (±0.09)	0.85 (±0.14)	<0.0001	<0.0001	<0.0001
Stance (%)	62.8 (±1.59)	64.23 (±1.90)	65.64 (±2.26)	<0.0001	<0.0001	<0.0001
WOMAC pain	0.44 (±1.41)	7.53 (3.94)	10.62 (±5.82)	<0.0001	<0.0001	0.001
WOMAC stiffness	0.31 (±1.02)	3.65 (±1.66)	4.47 (±1.76)	<0.0001	<0.0001	0.017
WOMAC function	1.67 (±5.01)	23.19 (±13.07)	34.37 (±17.8)	<0.0001	<0.0001	<0.0001
WOMAC total	2.27 (±6.9)	34.37 (±17.8)	50.89 (±17.7)	<0.0001	<0.0001	<0.0001

Gender	Group A distribution	Group M distribution	Group S distribution
Female	37 (62%)	20 (33%)	33 (54 %)
Male	23 (38%)	20 (33%)	28 (46 %)

There were significant group differences in all parameters using one-way ANOVA statistical analyses ($P<0.0001$). Multiple comparison P-values between subject groups for each parameter are shown. Gender distribution among the subject groups is included at the bottom of the table.
A, asymptomatic; M, moderate OA; S, severe OA.

and interpretation of gait waveform data (Deluzio and Astephen, 2007). Waveform PCA was applied to the flexion/extension angle, the net external flexion/extension moments, ab/adduction moments and internal/external rotation moment waveforms at the hip, knee and ankle joints separately (12 gait measures in total), and to the EMG waveforms for the three muscle sets, the quadriceps (VL, VM, RF), the hamstrings (LH, MH), and the gastrocnemius (LG, MG). Gait data were arranged in 12 separate 181×101 data matrices (181 subjects $\times$ 101 time points per gait cycle) for the PCA procedure; EMG data were arranged in larger matrices to represent the muscle groups ($[181 \times 3$ muscles $=]543 \times 101$; $([181 \times 2$ muscles $=]362 \times 101$). In each case, the first three principal components (PCs) were extracted, representing the majority of the variation in the original data (>80%). PC scores, the contributions of each PC loading vector to each subject's waveform, were then calculated. Group differences in PC scores were assessed with one-way analysis of variance (ANOVA) models for gait measures and with two-factor (muscle set, subject group) ANOVA models for EMG measures. Tukey post hoc tests were used to examine pair-wise subject group differences in scores.

Three forward selection stepwise discrimination analyzes between all combinations of subject groups were performed with all PC scores showing significant pair-wise differences ($P<0.05$) entered as input to the model. The PCs identified by the stepwise procedure were then used in three linear discriminant models to define optimal boundaries of separation between the groups (Lachenbruch, 1975). The relative importance of each PC in multivariate group separation was quantified with the magnitudes of PC coefficients in the discriminant function. Group separation was quantified with a cross-validation misclassification error rate (Lachenbruch, 1975).

3. Results

3.1. Demographics

Subject group characteristics are summarized in Table 1. Consistent with the literature for subjects of similar age with and without knee OA, both OA groups were older and had higher body mass indices (BMI) than the asymptomatic group (Kaufman et al., 2001; Childs et al., 2004), and speed decreased incrementally from the asymptomatic to the moderate knee OA to the severe knee OA group. All WOMAC scores (Bellamy et al., 1988) significantly increased between severity levels ($P<0.0001$). Kellgren–Lawrence (KL) radiographic scores (Kellgren and Lawrence, 1957) were significantly different between the moderate (median = 2, range 1–4) and severe (median = 3, range 3–4) subject groups ($P<0.0001$).

3.2. Statistical results

The ANOVA procedures identified 16 significant PC differences between the asymptomatic and moderate OA groups, 28 between the moderate OA and severe OA groups, and 33 between the asymptomatic and severe OA groups ($P<0.01$). The stepwise discrimination procedure differentiated the asymptomatic and moderate OA groups based on five PCs (Table 2). Subject waveforms that represent high and low (95th percentile) PC scores for each PC are shown in Fig. 1. Major differences occurred in late stance, when the moderate group walked with a greater knee internal rotation moment coupled with a net hip external rotation moment, in contrast to the smaller knee moment and hip internal rotation moment associated with the asymptomatic group. In early stance, the moderate group had smaller hip external rotation and knee flexion moments. The moderate group also exhibited a higher mid-stance adduction moment and a shift to hip abduction moment in late stance, as well as a higher rectus femoris activation level for the majority of stance and late in swing.

Table 2
Asymptomatic and moderate OA discriminant analysis summary

	Measure	PC	Normalized co-efficient in LDF	Interpretation
1	Knee internal rotation moment	3	1.00	Moderate OA had higher knee internal rotation moments in late stance (peak internal rotation moment occurs later in stance with OA)
2	Quadriceps (rectus femoris)	1	0.91	Moderate OA had higher rectus femoris EMG activity throughout most of the gait cycle
3	Hip internal rotation moment	2	0.49	Moderate OA had smaller hip external rotation moment in early stance and smaller hip internal rotation moment in late stance (difference operator—OA had less change in moment throughout stance)
4	Hip adduction moment	3	0.41	Moderate OA had higher mid-stance hip adduction moment and lower adduction moment in late stance (difference operator)
5	Knee flexion moment	2	0.39	Moderate OA had smaller knee flexion moment in early stance

Five principal components were included in the linear discriminant function (LDF). The relative importance of each PC is represented by the magnitude of its co-efficient in the LDF, normalized to the maximum coefficient magnitude. An interpretation of each PC is given.

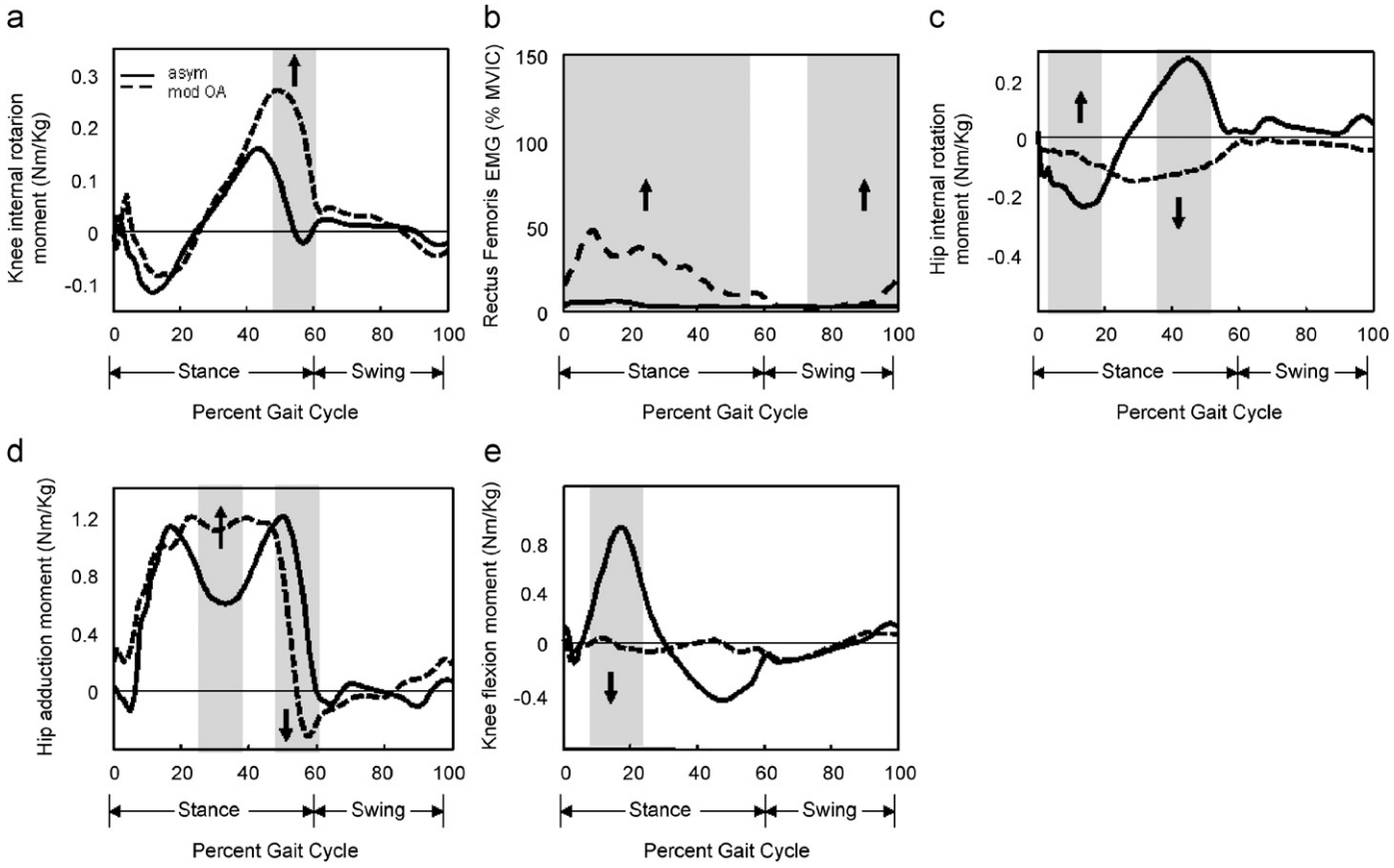

Fig. 1. Asymptomatic and moderate OA differences. The most important differences between the asymptomatic and moderate OA groups in the multivariate discrimination procedure were in the knee internal rotation moment PC3 (a), the rectus femoris activation pattern PC1 (b), the hip internal rotation moment PC2 (c), the hip adduction moment PC3 (d) and the knee flexion moment PC2 (e). Shown in the figures are example subject waveforms that represent high and low (95%) principal component scores for the indicated measure and principal component. In all cases, the waveform that represents the direction (i.e. high or low PC) which characterizes the moderate OA group is shown as a dashed line; the asymptomatic direction is indicated by a solid line.

A different set of five PCs optimally separated the moderate and severe OA groups (Table 3, Fig. 2). The hip flexion/extension moment patterns were much different, with the severe OA group displaying smaller early stance but greater mid-stance hip flexion moments than the moderate group. In early swing, the severe group showed a small hip extension moment while the moderate group produced a hip flexion moment. The severe group also had an early stance ankle external rotation moment that diminished in late stance, compared to the early stance

Table 3
Moderate OA and severe OA discriminant analysis summary

	Measure	PC	Normalized coefficient in LDF	Interpretation
1	Hip flexion moment	2	1.00	Severe OA had lower early stance and lower early swing hip flexion moment than moderate OA, and higher mid-stance hip flexion moments than moderate OA
2	Ankle internal rotation moment	2	0.97	Severe OA had lower ankle internal rotation moment in early stance and higher internal rotation moment in late stance (difference operator) than moderate OA
3	Knee flexion angle	1	0.96	Severe OA had lower overall magnitude of knee flexion angle in stance and swing than moderate OA
4	Gastrocnemius (medial)	3	0.85	Severe OA had higher medial gastroc EMG activity in early stance and in swing phase, and lower activity in late stance than moderate OA
5	Hip internal rotation moment	1	0.66	Severe OA had lower magnitude of hip internal rotation moment in stance than moderate OA

Five principal components were included in the linear discriminant function (LDF). The relative importance of each PC is represented by the magnitude of its coefficient in the LDF, normalized to the maximum coefficient magnitude. An interpretation of each PC is given.

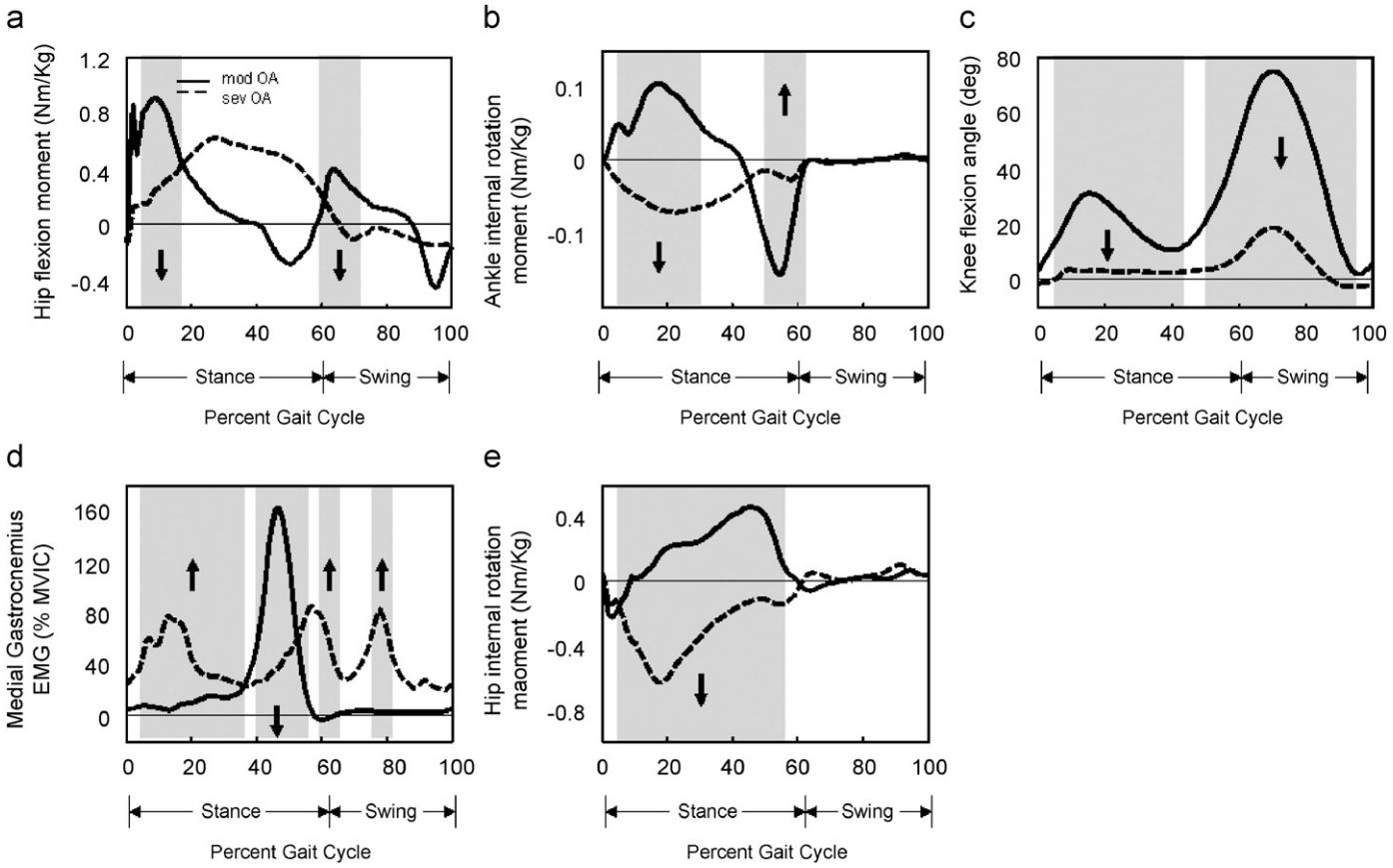

Fig. 2. Moderate OA and severe OA differences. The most important differences between the moderate OA and severe OA groups in the multivariate discrimination procedure were in the hip flexion moment PC2 (a), the ankle internal rotation moment PC2 (b), the knee flexion angle PC1 (c), the medial gastrocnemius activation pattern PC3 (d) and the hip internal rotation moment PC1 (e). Shown in the figures are example subject waveforms that represent high and low (95%) principal component scores for the indicated measure and principal component. In all cases, the waveform that represents the direction (i.e. high or low PC) which characterizes the severe OA group is shown as a dashed line; the moderate OA direction is indicated by a solid line.

internal rotation moment that switched to external rotation moment for the moderate group. The severe subjects also displayed much lower knee flexion angles throughout the gait cycle, stance phase hip external rotation moments compared to internal rotation moments for the moderate group and higher activity of the MG muscle in early stance and swing but relatively less activity in late stance.

Twelve differences between the asymptomatic and severe OA groups were important in multivariate group separation (Table 4 and Fig. 3). These differences spanned all joints and planes, and included both kinematic and kinetic measures, and several differences in EMG patterns.

In all three cases, multivariate separation with a discriminant model was significant ($P<0.0001$). Cross-validation

Table 4
Asymptomatic and severe OA discriminant analysis summary

	Measure	PC	Normalized coefficient in LDF	Interpretation
1	Knee flexion moment	2	1.00	Severe OA had lower early stance knee flexion moment
2	Hip adduction moment	3	0.94	Severe OA had higher mid-stance hip adduction moment and lower late stance moment (difference operator)
3	Knee flexion moment	1	0.81	Severe OA had higher overall magnitude of knee flexion moment during mid to late stance
4	Quadriceps (rectus femoris)	2	0.76	Severe OA had lower rectus femoris EMG activity in early stance and early swing, but higher activity in mid to late stance
5	Hamstrings (medial)	1	0.72	Severe OA had higher medial hamstring EMG activity in stance
6	Ankle flexion angle	2	0.61	Severe OA had higher early stance ankle plantarflexion angle and lower late stance to early swing dorsiflexion angle (difference operator)
7	Knee flexion angle	3	0.50	Severe OA had less knee extension in late stance and a later (delayed) peak phase flexion angle in swing
8	Hip flexion moment	1	0.39	Severe OA had higher overall magnitude of hip flexion moment in stance
9	Knee adduction moment	3	0.33	Severe OA had higher mid-stance knee adduction moment and lower late stance moment (difference operator)
10	Ankle flexion moment	2	0.30	Severe OA had greater ankle dorsiflexion moments in early stance and smaller dorsiflexion moments in late stance (difference operator)
11	Knee internal rotation moment	1	0.23	Severe OA had smaller overall magnitude of knee internal rotation moment in stance
12	Hamstrings (lateral)	1	0.08	Severe OA had greater lateral hamstring EMG activity in stance

Twelve principal components were included in the linear discriminant function (LDF). The relative importance of each PC is represented by the magnitude of its coefficient in the LDF, normalized to the maximum coefficient magnitude. An interpretation of each PC is given.

misclassification error rates were 21.7% between the asymptomatic and moderate group, 19.8% between the moderate and severe group and 6.6% between the asymptomatic and severe group. The hierarchy of the contribution of each PC to multivariate group separation was indicated by the normalized linear discriminant function coefficient included in Tables 2–4.

4. Discussion

This study investigated the biomechanical distinction among asymptomatic and two clinically different levels of knee OA severity, using a criterion that encompassed *both* radiographic changes and symptomatic severity. The goal was to identify the multivariate combinations of biomechanical variables that optimally separated the gait patterns of the three groups. The biomechanical pattern changes included in the asymptomatic–severe OA discrimination model were numerous and profound (Table 4, Fig. 3). The combinations of biomechanical factors that characterized the separation of successive severity groups, however, varied dramatically in nature. Knee and hip joint kinetic changes characterized the distinction between asymptomatic and moderate knee OA patterns. Knee kinematic and hip and ankle joint kinetic pattern changes discriminated between the moderate and severe groups. This suggested a changing role of biomechanical factors in the progression of knee OA at different stages of severity.

Mechanical loading of the joint has significant influence on the properties of articular cartilage (Arokoski et al., 2000), and knee joint loading is therefore presumably an important factor in disease progression at any level of severity. Knee kinetic changes were included in asymptomatic–moderate discrimination model, but not in the moderate–severe model. This did not suggest that knee joint loading is unimportant at later stages of the disease process, only that these changes did not add significantly to discriminating moderate to severe subjects. This result has important clinical implications because it suggests that kinetic changes at the knee joint are present early in the disease process and therefore early interventions aimed at changing the loading environment of the knee joint may be effective at early clinical levels. No kinematic changes at any joint were included in the asymptomatic–moderate model, suggesting little difference in the outward appearance of asymptomatic and moderate knee OA gait patterns. Postural and visual gait changes such as less knee flexion and slower walking speeds became important in the moderate–severe model, presumably consistent with other concomitant changes associated with the advanced disease state such as age, pain, obesity and joint stiffness. Treatments designed for individuals in later stages of the disease process should therefore take into account the effects of altered joint kinematics.

The asymptomatic–moderate model included increased mid-stance hip adduction moments during stance with the moderate group (Fig. 1d). Higher peak hip adduction moments have been associated with more radiographically severe subjects (Mundermann et al., 2005), and decreased peak hip adduction moments have been associated with decreased likelihood of knee OA disease progression (Chang et al., 2005). However, neither study commented

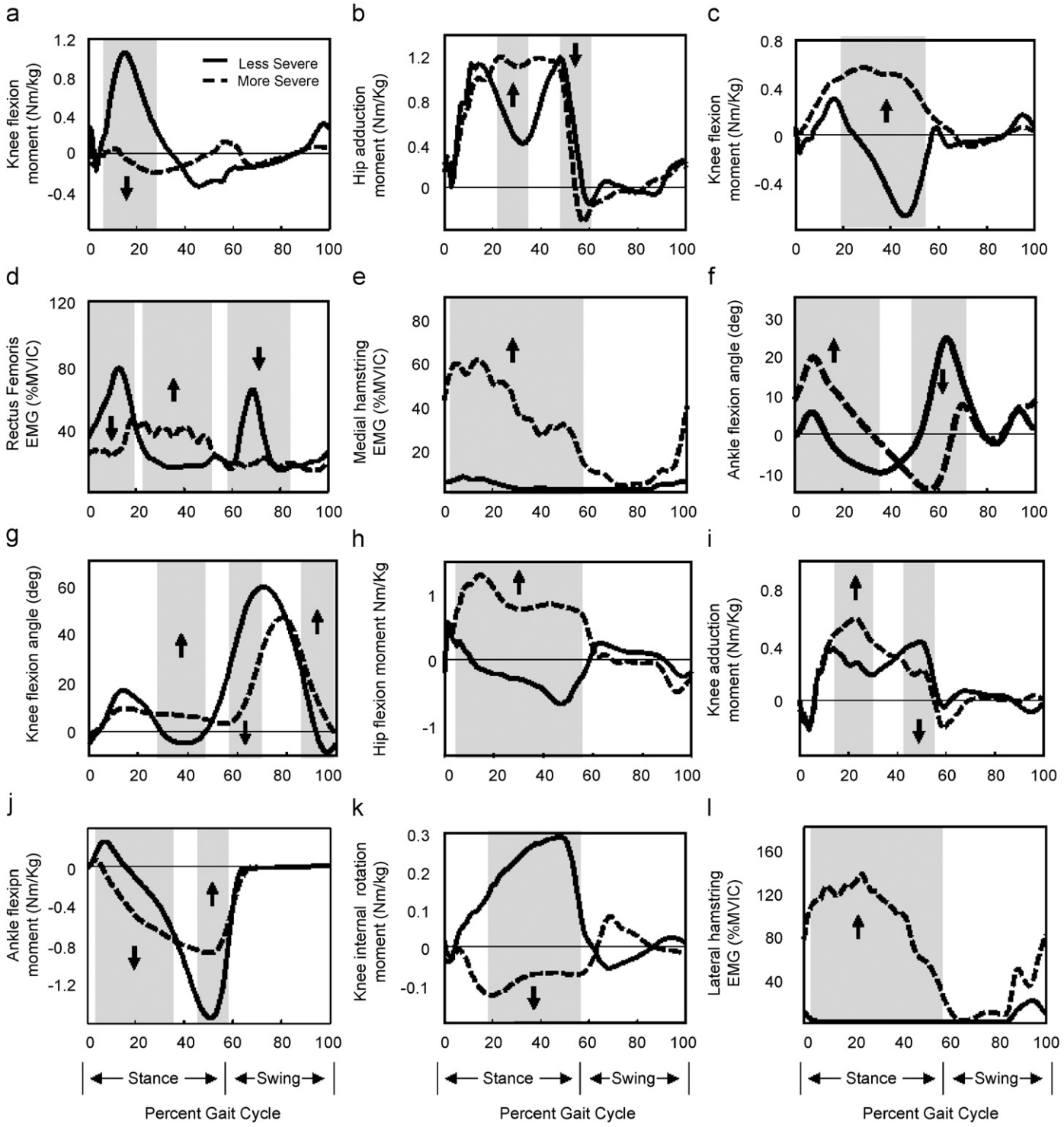

Fig. 3. Asymptomatic and severe OA differences. There were 12 important differences between the asymptomatic and severe OA groups in the multivariate discrimination procedure, including the knee flexion moment PC2 (a), the hip adduction moment PC3 (b), the knee flexion moment PC1 (c), the rectus femoris activation pattern PC2 (d), the medial hamstring activation pattern PC1 (e), the ankle flexion angle PC2 (f), the knee flexion angle PC3 (g), the hip flexion moment PC1 (h), the knee adduction moment PC3 (i), the ankle flexion moment PC2 (j), the knee internal rotation moment PC1 (k) and the lateral hamstring activation pattern PC1 (l). Shown in the figures are example subject waveforms that represent high and low (95%) principal component scores for the indicated measure and principal component. In all cases, the waveform that represents the direction (i.e. high or low PC) which characterizes the severe OA group is shown as a dashed line; the asymptomatic direction is indicated by a solid line.

specifically on the mid-stance hip adduction moments, found here to be more important than peak values in describing moderate OA gait changes, and suggesting the potential importance of *more prolonged* frontal plane loading of the hip joint during mid-stance. Other notable kinetic differences in the asymptomatic–moderate

discrimination model included transverse plane changes at the knee and hip joints. The moderate group walked with a higher late stance knee internal rotation moment, a reduced hip external rotation moment in early stance and a hip external (rather than internal) rotation moment in late stance. While transverse plane mechanics have been implicated in the progression of knee OA (Andriacchi and Mundermann, 2006), only a few studies have quantified differences in transverse plane kinetics at the knee (Gok et al., 2002; Landry et al., 2007) and none at the hip. It has been suggested that changes in transverse plane mechanics at the knee can initiate degenerative changes by placing new loads on regions of the articular cartilage that were previously conditioned for different load levels (Andriacchi and Mundermann, 2006).

Transverse plane changes were also included in the moderate–severe discrimination model. The severe group walked with altered patterns of hip and ankle internal/external rotation moments than the moderate group (Fig. 2), an important difference not identified in previous studies. Changes in the internal/external rotation moment at the hip in stance may be associated with a mechanism to alter the foot toe-out angle, which could act to reduce the knee adduction moment (Andrews et al., 1996; Hurwitz et al., 2002). Also of note was the change in MG neuromuscular pattern, which was active for most of the gait cycle in the severe OA group (Fig. 2). This contrasts with moderate OA and asymptomatic gait in which the MG is primarily used for propulsion in late stance (Hubley-Kozey et al., 2006). The continued activation of MG by the severe OA group may be a mechanism to increase stiffness in response to pain or laxity associated with decreased medial knee joint spacing (Lewek et al., 2004).

The first PCs extracted from gait waveforms are generally consistent with an overall magnitude of the gait measure throughout the gait cycle (Deluzio and Astephen, 2007), and therefore presumably associated with commonly reported peak values. The most discriminatory biomechanical features identified in this study were the second and third PCs (Table 2), which highlighted the importance of using more waveform-based gait analysis techniques. These results suggested that changes in *patterns* of gait waveforms might be as important as magnitude changes.

Some biomechanical variables that have been highly associated with knee OA, particularly the knee adduction moment (Mundermann et al., 2005; Hurwitz et al., 2002), were not identified in the discriminatory models of this study. This may in part be due to the fact that most previous studies have used radiographic classifiers for group categorization (Hurwitz et al., 2002; Mundermann et al., 2004; Lewek et al., 2004), and this study utilized a clinical criterion for group separation. As well, in a recent study we found that changes in the knee adduction moment during gait were associated with *all* individuals with knee OA, regardless of their severity (Astephen et al., 2007). Adduction moment changes may therefore be very important in characterizing knee OA gait patterns, but may not be important in the discrimination between different severity levels.

The greatest level of separation between severity groups was achieved in the asymptomatic–severe OA model (6.6% misclassification). Between "adjacent" groups (asymptomatic–moderate OA, moderate–severe OA), there was an approximate level of misclassification of 20%. Knee OA is a progressive disease that is difficult to classify, and there may have been overlap in the biomechanical patterns of subject groups. Some asymptomatic subjects may have had early radiographic signs of knee OA, and some moderate knee OA subjects may have been relatively close to severe classification.

This study was limited to three discrete clinical levels of knee OA severity. It is therefore difficult to draw conclusions about mechanisms that relate to disease progression *within* these clinical states. The moderate group in particular represented a large group of individuals with a spectrum of radiographic and symptomatic changes associated with knee OA. Future study should investigate the role of biomechanical factors in disease progression within this group to develop intervention strategies aimed at slowing disease advancement. Comprehensive longitudinal studies are also needed to make more conclusive statements on disease progression. To understand the complexity of knee OA and develop earlier and more appropriate treatment strategies for the disease will require continued study on the interrelationships between risk factors for the disease and appropriate models of disease progression. This study introduced the importance of considering the interrelationships between gait and neuromuscular factors in the study of knee OA disease progression.

Conflict of interest statement

The authors are not in any conflict of interest with regards to the work presented in this paper.

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