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ARE UNILATERAL AND BILATERAL KNEE OSTEOARTHRITIS PATIENTS UNIQUE SUBSETS OF KNEE OSTEOARTHRITIS? A BIOMECHANICAL PERSPECTIVE

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Author Contributions

- Dr. Messier had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the analysis.
- Conception and design: *Messier, Beavers, Herman, Hunter, DeVita*
- Analysis and interpretation of the data: *Messier, Beavers, Herman, Hunter, DeVita*
- Drafting of the article: *Messier, Beavers, Herman, Hunter, DeVita*
- Critical revision of the article for important intellectual content: *Messier, Beavers, Herman, Hunter, DeVita*
- Final approval of the article: *Messier, Beavers, Herman, Hunter, DeVita*

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Abstract

Objective—To compare the gait of adults with unilateral and bilateral symptomatic and radiographic knee osteoarthritis (OA) to determine whether these subgroups can be treated similarly in the clinic and when recruiting for randomized clinical trials, and to use these data to generate future hypotheses regarding gait in these subsets of knee OA patients.

Methods—Cross-sectional investigation of patients with unilateral and bilateral knee OA on gait mechanics using 136 older adults (age ≥ 55 yrs.; 27 $kg.m^{-2} \geq BMI \leq 41$ $kg.m^{-2}$; 82% female) with radiographic knee OA. Comparisons were made between the most affected side of the bilateral group (Bi) and the affected side of the unilateral group (Uni), and between symmetry indices of each group.

Results—There were no significant differences in any temporal, kinematic, or kinetic measures between the Uni and Bi cohorts. Comparison of symmetry indices between groups also revealed no significant differences.

Conclusion—The similarity in lower extremity mechanics between unilateral and bilateral knee OA patients is sufficiently robust to consider both subsets as a single cohort. We hypothesize that biomechanical adaptations to knee OA are at least partially systemic in origin and not based solely on the physiological characteristics of an affected knee joint.

Arthritis is the leading cause of disability in adults over the age of 55 years (1). By 2030, a projected 67 million Americans aged ≥ 18 years will have doctor-diagnosed arthritis with osteoarthritis (OA) being its most common form (2). The knee is the most common weight-bearing joint affected by OA with a prevalence estimated at 250 million people worldwide (3, 4). Knee OA patients often alter their gait to alleviate knee pain, presumably by attenuating knee joint loads (5). Common alterations include decreased stride length and walking speed, decreased knee flexion and knee range of motion, increased cadence, and adaptations in ankle and hip joint moments (6–10).

Many biomechanical studies of knee OA confine their analysis to a single limb (11–14); however, few studies have examined whether this is representative of both limbs, and if unilateral and bilateral disease result in similar gait alterations. Marmon et al. (15) found similar functional ability and perceived functional ability between unilateral and bilateral knee OA groups. In contrast, Creaby et al. (6) indicated that knee flexion during stance, and the external knee flexion moment were different between unilateral and bilateral knee OA. Unilateral OA patients presented with asymmetric gait whereas symmetry characterized bilateral OA gait. Adding further to the discussion, recent data indicates that 80% of unilateral knee OA patients develop bilateral disease within 12 years (16), making it unclear in cases where only one knee is symptomatic whether both sides should be treated.

From clinical trials and biomechanics research perspectives, most studies in which gait is an outcome assume that the differences between unilateral and bilateral knee OA are trivial and these groups can be considered as one. However, if gait characteristics are dissimilar between groups this may increase between subject variability and reduce the ability to detect an intervention's effect on gait or a statistically significant result.

Hence, whether treating knee OA patients in a clinic or recruiting them for participation in a clinical or basic research trial, knowledge of whether unilateral and bilateral OA patients exhibit similar gait mechanics appears important. Additionally, the limited number of relevant studies and the conflicting outcomes requires further investigation. Our purpose was to compare the gait of older adults with unilateral and bilateral mild to moderate symptomatic and structural knee OA with the intent to use our data to generate future hypotheses regarding gait in these subsets of knee OA patients.

METHODS

Study Sample

Participants were a subsample (n = 136) from the Intensive Diet and Exercise for Arthritis (IDEA) cohort (n=454); 68 with unilateral knee OA (Uni) and 68 with bilateral knee OA (Bi). Eligible persons were ambulatory, community-dwelling who were 55 years of age or older with: 1) mild to moderate radiographic medial and/or lateral tibiofemoral OA or tibiofemoral plus patellofemoral OA with Kellgren and Lawrence (K-L) grade 2 or 3 in one or both knees (17); 2) $27 \text{ kg.m}^{-2} \leq \text{BMI} \leq 41 \text{ kg.m}^{-2}$; and 3) current sedentary lifestyle defined as less than 30 minutes of formal exercise per week within the past 6 months. Eligibility and screening measurements are detailed elsewhere (18). Briefly, we excluded significant co-morbidities such as symptomatic or severe coronary artery disease, severe hypertension, active cancer (excluding skin cancer), significant cognitive impairment, or previous acute knee injury. IDEA was conducted at Wake Forest University and Wake Forest School of Medicine between July 2006 and April 2011, the final date of follow-up. It was approved by the Human Subjects Committee of Wake Forest Health Sciences. Informed consent was obtained in writing from all participants.

For our subsample, unilateral participants had painful symptoms combined with radiographic evidence of knee OA in the ipsilateral knee and no radiographic evidence of OA (K-L grade of 0 or 1) or symptoms in the contralateral knee. Participants with bilateral knee OA (K-L grade of 2 or 3 on both knees) also had painful bilateral symptoms; the most painful side was considered the most affected side. These cohorts were matched on age, gender, K-L grade, knee pain, presence of OA in other joints, and BMI.

Measurements and Procedures

Gait Analysis—Prior to testing, participants' freely chosen walking speeds were assessed using a Lafayette Model 63501 photoelectric control system interfaced with a digital timer. Photocells were positioned 7.3 m apart on a 22.5 m elevated walkway. Participants traversed the course 6 times, and freely chosen walking speed was calculated as the mean of the 6 trials. This speed (± 3.5%) was used in all subsequent gait evaluations.

Three-dimensional motion analysis used a 6-camera system (Motion Analysis Corporation, Santa Rosa, CA) set at a camera speed of 60 Hz with a 37-reflective marker set arranged in a Cleveland Clinic full-body configuration. Raw kinematic coordinate data were smoothed using a Butterworth low-pass digital filter with a cut-off frequency of 6 Hz. Kinetic data were collected using an AMTI model OR6-5-1 force platform (AMTI, Newton, MA) at a sampling rate of 480 Hz and synchronized with the kinematic data to allow calculation of *internal* joint moments and powers, and joint-reaction forces using an inverse dynamics model. Results were input to calculate tibiofemoral compressive, anteroposterior shear, and patellofemoral compressive forces using a musculoskeletal model developed by DeVita and Hortobagyi (19) and is comprehensively detailed, including its limitations, elsewhere (20). Briefly, our musculoskeletal torque-driven model has two basic components: (a) joint moments and joint-reaction forces are calculated from kinematic, physiological, and force-plate data; (b) forces in the gastrocnemius, hamstring, and quadriceps muscles and lateral support tissues in the knee are determined and applied along with joint-reaction forces to the tibia to determine knee-joint forces. Our estimates for muscle and joint forces are similar to those of other predictive models (21–25) and to measured forces from instrumented knee joint prostheses (26, 27). To control for footwear effects, each participant wore the identical make and model of athletic shoes during testing.

Gait Symmetry Index—Inter-limb comparison of gait variables was evaluated using a symmetry index (SI) modified from one defined by Herzog et al. (28):

$$\mathrm{SI}\,(\%)=[\,|\mathrm{x_a}-\mathrm{x_u}|/.5\,(|\mathrm{x_a}|+|\mathrm{x_u}|)]\times 100 \quad (1)$$

where:

SI = symmetry index (%)

x_a = affected or most affected knee

x_u = unaffected or less affected knee

Prefect symmetry is indicated when SI = 0. Acceptable asymmetry is indicated by a SI ≤ 10% or less than a 10% difference between sides (28). This modified equation determines asymmetry independent of side. The absolute value functions identify the magnitude of asymmetry regardless of the relationship between most and least affected sides.

X-rays—Bilateral, semi-flexed, posteroanterior, weight-bearing knee x-rays were used to identify tibiofemoral arthritis and sunrise views to identify patellofemoral OA. Kellgren-Lawrence (K-L) grade (0–4) was used to quantify severity of tibiofemoral OA (17).

Pain and Function—The Western Ontario McMasters Universities Osteoarthritis Index (WOMAC) pain and function subscales were used to measure self-reported pain and function (29, 30). Participants indicate on a scale from 0 (none) to 4 (extreme) the degree of pain experienced performing daily living activities in the last 48 hours due to knee OA. Total scores for the 5 items range from 0–20; higher scores indicate greater pain. The function subscale was made up of 17 items. Individual scores for each question were totaled to a summary score ranging from 0–68, with higher scores indicating poorer function.

Confidence in Performing Activities—The Activities-specific Balance Confidence (ABC) scale (31) is an 11-point scale and consists of whole numbers (0–100) for each item. It was used to indicate participants' level of confidence in doing mobility activities without losing their balance or becoming unsteady. Higher numbers indicate better confidence in maintaining balance and steadiness.

Statistical Analysis

All statistical analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC). Baseline characteristics were summarized separately for the Uni and Bi groups and for the overall IDEA study using means and standard deviations or percentages. All participants with unilateral knee OA were matched to a gender-race-age-BMI participant among bilateral OA participants. If a match could not be found with a BMI within 2.0 kg/m^2 or an age within 5 years the participant was excluded. We conducted an analysis of variance to compare the means of all variables between the matched Uni and Bi cohorts. Comparisons were deemed significantly different for all p-values less than 0.05. Comparisons included the most affected knee (i.e., most pain) in the Bi cohort to the affected knee in the Uni group, and between symmetry indices of each group. Gait kinematic and kinetic figures were created by scaling participants' gait cycles to a relative scale (% cycle), linearly interpolating values at predefined % cycle points, averaging per participant over the three trials per leg separately for the affected and unaffected sides for the Uni group and the most and less affected sides for the Bi group, and averaging across all participants, with error clouds representing 95% confidence intervals.

RESULTS

Mean values and standard deviations for selected descriptive characteristics for the Uni and Bi cohorts and the total IDEA sample are summarized in Table 1. Participants were similar in age, BMI, average walking speed, pain, function, ABC score, and gender and race distribution.

Temporal, kinematic, and kinetic variables were compared between the most affected side in the Bi group and the affected side in the Uni group. There were no significant differences in any temporal or kinematic measures between the Uni and Bi cohorts. Comparison of symmetry indices between groups also revealed no significant differences (Table 2).

There were no significant between-group differences in any lower extremity kinetic variables (Table 3). Hip, knee, and ankle peak moments and powers were similar between groups. SI values above the 0–10% range were common and similar between the Uni and Bi groups. Peak knee extension moment and peak knee power absorption had the highest SI values ranging between 48% and 64%, suggesting that substantial asymmetry within both groups was present. Figure 1 represents a comparison of the mean angular position, sagittal plane moment, and power curves for the most and least affected sides for the BI group and the affected and unaffected sides of the Uni group with SI values noted.

DISCUSSION

It is well established that knee osteoarthritic gait differs from healthy gait (7–9, 32, 33). Since knee OA can affect one or both knees, there are clinically relevant and study design questions that are based on whether gait changes as a function of the number of diseased knees. Since most unilateral knee OA patients develop bilateral disease, should both knees be treated clinically? For OA researchers involved in studies in which gait mechanics are outcome measures, is it appropriate to treat unilateral and bilateral OA patients as a single cohort (34)?

Studies providing insight into these questions have varied conclusions; one suggesting that unilateral and bilateral knee OA patients are functionally similar (15), while another reporting that knee mechanics differ between the groups (6). Our results support the former; of the 23 comparisons between temporal, kinematic, and kinetic gait variables and their corresponding symmetry indices, a total of 46 comparisons, none were significantly different. Hence, unilateral and bilateral knee OA patients, matched on BMI, age, gender, KL score, pain, ABC score, and the presence of OA in other joints, have statistically similar gait characteristics. The results are generalizable to overweight and obese patients with mild to moderate radiographic knee OA.

A concern with non-significant results is that they may be interpreted as a Type II statistical error and merely indicative of an absence of appropriate evidence. However, our large sample size and relatively high statistical power would argue against this position. For example the p-value for knee compressive forces was 0.65 and the 95% confidence intervals (CI) for the Uni and Bi groups were 2,379–2769 N and 2,398–2,898 N respectively, a 95% overlap. The respective CI values for knee positive power were p=0.64 and 45–59 W and 47–61 W for the Uni and Bi groups, an 81% overlap. Most other variables had similarly large overlapping 95% CIs. These results provide statistical evidence that we correctly identified true non-significant differences.

A clinically relevant threshold for symmetrical gait is unknown. Based on differences in performance and strength variables, Lathrop-Lambach et al. (35) suggested a 10% difference between sides as acceptable. Using this definition of symmetry, there is evidence that asymmetry is the “rule rather than the exception” in both healthy and osteoarthritic gait. Specifically, Herzog et al. (28) examined the ground reaction forces during healthy gait in young adult males (N = 33) and females (N = 29) and found unexpectedly large upper and lower limits in SI values leading them to conclude that healthy human gait is asymmetrical. In our osteoarthritic cohort, temporal-spatial, hip, knee, and ankle range of motion, and vertical ground reaction data were symmetrical in both the Uni and Bi groups, yet joint moments and powers showed considerable asymmetries, ranging from 13% to 64% (Table 3). Taken together, these studies suggest that striving to correct “abnormal gait” due to osteoarthritis or other musculoskeletal or neuromuscular diseases by making it more symmetrical may not be prudent in many cases.

Creaby et al.’s (6) suggestion that both knees should be treated in people with unilateral knee OA even when only one is painful appears logical in light of recent data indicating that

80% of unilateral knee OA patients develop bilateral disease within 12 years (16). The absence of biomechanical and symmetry differences in our data supports this recommendation, with the caveat that cross-sectional analyses provide little indication on how groups react to a longitudinal intervention. We also suggest that both unilateral and bilateral knee OA patients who are overweight or obese and have mild to moderate disease (KL = 2 or 3) can be included as a single cohort in most randomized clinical trials.

The knee external adduction moment (equivalent in magnitude to our internal abduction moment) is a valuable surrogate measure of medial compartment loading because it is predictive of OA progression (36) and severity (37). Hunt et al. (38) examined gait symmetry in 100 men and women with moderate to severe knee OA and found increased knee external adduction moments in the affected limb. Briem and Snyder-Mackler (39) found relative symmetry in external knee frontal plane moments in people with varus aligned knees, but asymmetry in the external hip adduction moments, with 25% lower peak values on the involved side. We found similar SI values between groups in our knee frontal plane and hip internal abduction moments. The disparity among studies could be due to differences in inclusion criteria for disease severity (mild to moderate vs. moderate to severe) and frontal plane knee alignment (all alignments included vs. varus aligned only).

Herzog et al. (28) noted that the SI may not be a reliable measure for variables that are close to zero. Small differences between sides could result in inflated SI values. We addressed this issue by modifying Herzog's formula by using absolute values to calculate SI independent of side (i.e., all SIs were positive). This eliminated two possibilities, (1) that small positive and negative values for opposite sides produces a large SI, and (2) that positive SI values for some subjects are averaged with negative values for other subjects resulting in a mean SI close to zero indicating little asymmetry in the group when there may be considerable asymmetry independent of side. Nonetheless, a value very close to zero for one side only would still result in a large SI. We also used a cutoff of 10% to indicate symmetry, however, this was based on performance and strength data (35). To our knowledge, there is no gold standard for what is considered symmetrical gait.

Our purpose was to compare the gait of older adults with unilateral and bilateral mild to moderate symptomatic and structural knee OA with the intent to use our data to generate future hypotheses regarding gait in these subsets of knee OA patients. The similarity in lower extremity mechanics between unilateral and bilateral knee OA patients was sufficiently robust to consider both subsets as a single cohort. This similarity leads us to hypothesize that biomechanical adaptations to knee OA are at least partially systemic in origin and not based solely on the physiological characteristics of an affected knee joint. Specifically, we propose that cortical or subcortical alterations may occur as a result of the diseased joint, the downstream effect being similar biomechanical gait adaptations between limbs, even when only one knee is symptomatic.

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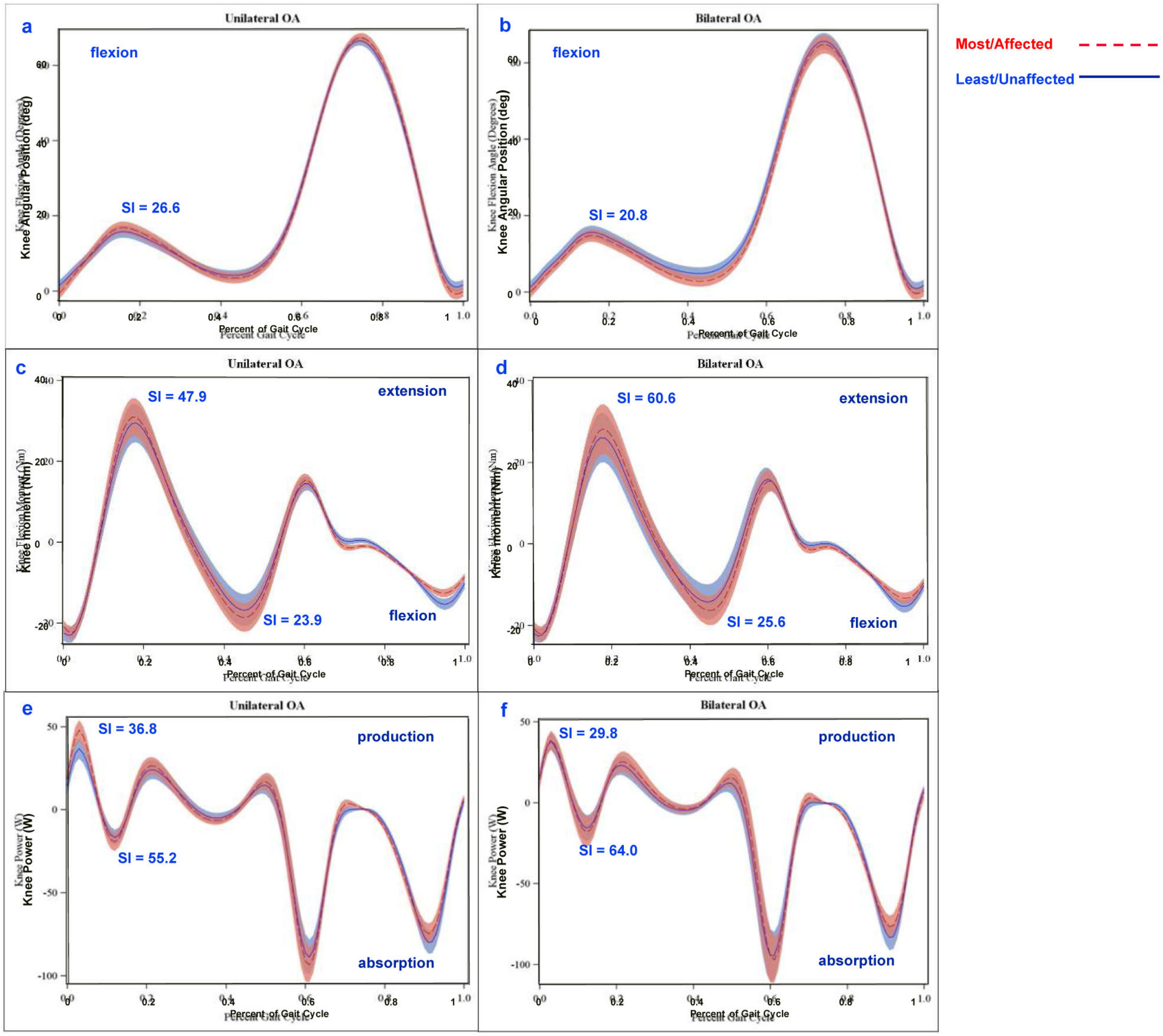

Figure 1.

Mean (95% CI) sagittal plane **(a, b)** knee angular position, **(c, d)** knee moment, and **(e, f)** knee power versus percent of gait cycle (heel strike = 0%; heel strike of the same foot =100%) for the unilateral (Uni) and Bilateral (Bi) groups on the most/affected and least/ unaffected sides. Mean symmetry indices (SI) for peak knee flexion during stance, peak extension moment, and peak power production and absorption are also noted.

Table 1

Descriptive statistics (Mean ± SD) of Unilateral and Bilateral cohorts, and the entire IDEA population. BMI = body mass index; WOMAC = Western Ontario McMasters Universities Osteoarthritis Index; ABC = Activities-specific Balance Confidence scale.

	Unilateral (n = 68)	**Bilateral (n = 68)**	**All IDEA (n = 454)**
Age (years)	64.0 ± 5.6	64.3 ± 5.3	65.6 ± 6.2
Gender (% female)	82	82	72
Race (% white)	85	85	83
BMI (kg.m^{-2})	33.3 ± 3.8	33.2 ± 3.7	33.6 ± 3.7
Mean walking speed (m.s^{-1})	1.22 ± 0.18	1.20 ± 0.21	1.20 ± 0.18
WOMAC pain (0–20 scale)	6.7 ± 3.5	6.8 ± 3.3	6.5 ± 3.1
WOMAC function (0–68 scale)	24.5 ± 12.4	25.7 ± 10.8	24.2 ± 10.9
ABC (0–100 scale)	79.6 ± 17.5	76.6 ± 19.5	78.1 ± 18.5

Table 2

Comparison of mean (95%CI) peak kinematic and temporal variables and symmetry index in the affected leg (most pain) in the unilateral OA group and the most affected leg of the bilateral OA group and the symmetry index for each group.

Variable	Unilateral Affected	Bilateral Most affected	P	Symmetry Index (%) Unilateral	Symmetry Index (%) Bilateral	P
Hip ROM (°)	43.3 (41.8, 44.7)	42.4 (40.9, 43.8)	0.39	8.2 (6.1, 10.2)	8.4 (6.3, 10.4)	0.90
Knee ROM (°)	68.2 (66.2, 70.2)	66.8 (64.8, 68.8)	0.33	7.0 (3.9, 10.0)	10.3 (7.2, 13.3)	0.13
Knee Flexion ROM during stance (°)	14.8 (13.7, 16.0)	14.7 (13.5, 15.9)	0.90	26.6 (21.1, 32.1)	20.8 (15.3, 26.4)	0.15
Ankle ROM (°)	24.7 (23.8, 25.6)	25.1 (24.2, 26.0)	0.57	10.8 (8.7, 12.9)	9.9 (7.8, 12.0)	0.54
Stride length (cm)	129.2 (125.0, 133.4)	127.8 (123.6, 132.0)	0.64	1.7 (1.3, 2.1)	1.5 (1.1, 1.9)	0.57
Support time (%)	65.3 (64.8, 65.7)	65.4 (65.0, 65.9)	0.58	1.8 (1.3, 2.3)	1.9 (1.4, 2.4)	0.66
Initial Double support (%)	13.1 (12.4, 13.8)	13.5 (12.8, 14.2)	0.41	6.4 (4.9, 8.0)	7.1 (5.5, 8.6)	0.56

Table 3

Comparison of mean (95%CI) peak kinetic variables in the affected leg (most pain) in the unilateral OA group and the most affected leg of the bilateral OA group and the symmetry (between sides) index for each group.

	Unilateral affected	Bilateral most affected	P	Symmetry Index (%) (Unilateral)	Symmetry Index (%) (Bilateral)	P
Hip Extension Moment (Nm)	63.7 (55.6, 71.8)	70.6 (62.5, 78.8)	0.24	15.9 (12.1, 19.6)	13.6 (9.9, 17.4)	0.41
Hip Flexion Moment (Nm)	−60.6 (−68.4, −52.8)	−64.1 (−71.9, −56.3)	0.53	20.4 (15.4, 25.5)	19.0 (14.0, 24.1)	0.70
Hip Abduction Moment (Nm)	82.4 (77.4, 87.3)	83.4 (78.5, 88.4)	0.77	13.3 (10.8, 15.9)	11.2 (8.7, 13.7)	0.24
Knee flexion Moment (Nm)	−27.9 (−30.5, −25.3)	−28.4 (−31.0, −25.8)	0.79	23.9 (19.3, 28.6)	25.6 (21.0, 30.3)	0.61
Knee extension Moment (Nm)	30.9 (25.7, 36.1)	29.2(24.0, 34.4)	0.66	47.9 (33.7, 62.0)	60.6 (46.4, 74.8)	0.21
Knee abduction Moment (Nm)	24.6 (21.0, 27.8)	28.3 (24.9, 31.7)	0.12	34.3 (26.1, 42.4)	37.5 (29.4, 45.7)	0.58
Dorsiflexion Moment (Nm)	−13.0 (−14.5, −11.5)	−11.8 (−13.3, −10.2)	0.27	27.7 (20.3, 35.1)	33.2 (25.8, 40.6)	0.30
Plantar flexion Moment (Nm)	103.0 (97.4, 108.5)	105.6 (100.0, 111.1)	0.51	6.8 (5.3, 8.3)	7.1 (5.6, 8.6)	0.78
Vertical Ground Reaction Force (BW)	1.07 (1.06, 1.09)	1.06 (1.04, 1.07)	0.17	2.9 (2.2, 3.6)	3.3 (2.6, 4.0)	0.39
Hip Power Production (W)	89.2 (74.4, 104.0)	102.7 (87.8, 117.5)	0.21	32.0 (25.5, 38.5)	25.1 (18.6, 31.6)	0.14
Hip Power Absorption (W)	−52.0 (−59.1, −44.9)	−50.6 (−57.7, −43.6)	0.79	32.9 (25.5, 40.3)	32.4 (25.0, 39.7)	0.92
Knee Power Production (W)	51.6 (44.7, 58.5)	53.9 (47.0, 60.8)	0.64	36.8 (30.9, 42.7)	29.8 (23.9, 35.7)	0.10
Knee Power Absorption (W)	−25.2 (−31.3, −19.2)	−26.2 (−32.2, −20.2)	0.82	55.2 (44.4, 66.0)	64.0 (53.2, 74.8)	0.26
Ankle Power Production (W)	160.7 (147.0, 174.5)	162.4 (148.6, 176.1)	0.87	15.2 (11.6, 18.8)	18.6 (14.9, 22.2)	0.20
Knee compressive force (N)	2574 (2348, 2800)	2648 (2422, 2874)	0.65	13.5 (10.3, 16.7)	15.0 (11.8, 18.1)	0.52
Knee A-P shear force (N)	378 (346, 411)	357 (325, 390)	0.37	21.7 (16.6, 26.8)	23.1 (17.9, 28.2)	0.71