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Knee Joint Biomechanics and Neuromuscular Control During Gait Before and After Total Knee Arthroplasty are Sex-specific

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Abstract

The future of total knee arthroplasty (TKA) surgery will involve planning that incorporates more patientspecific characteristics. Despite known biological, morphological, and functional differences between men and women, there has been little investigation into knee joint biomechanical and neuromuscular differences between men and women with osteoarthritis, and none that have examined sex-specific biomechanical and neuromuscular responses to TKA surgery. The objective of this study was to examine sex-associated differences in knee kinematics, kinetics and neuromuscular patterns during gait before and after TKA. Fifty-two patients with end-stage knee OA (28 women, 24 men) underwent gait and neuromuscular analysis within the week prior to and one year after surgery. A number of sex-specific differences were identified which suggest a different manifestation of end-stage knee OA between the sexes.

Keywords: total knee arthroplasty; sex; gait; biomechanics; electromyography; knee osteoarthritis

Total knee arthroplasty (TKA) surgery has been shown to improve functional outcomes for individuals with end stage knee osteoarthritis (OA). Typically, postoperative assessments have shown improvements in walking velocity, peak magnitudes of joint loading, joint angles, and neuromuscular activation during gait moving toward more asymptomatic values <u>1</u>. and <u>2</u>. However, some patterns of loading, motion, and neuromuscular control over the gait cycle remain altered <u>2</u>. and <u>3</u>.

The future of TKA surgery likely involves the incorporation of patient-specific joint characteristics to improve longevity, functional outcome, and satisfaction. Recent studies have highlighted knee joint and femoral morphologic differences by ethnicity [4] and sex [5]. Joint anatomy and morphology may contribute to joint function; however, understanding actual differences in joint dynamics between demographic groups may also be important because specific joint loading and muscle activation patterns during walking have been shown to be associated with postoperative implant micromotion measured with Radiostereometric Analysis <u>6., 7.</u> and <u>8.</u>

Women are afflicted with knee OA two to three times more than men [9], and there are established functional differences between men and women, such as in strength [10], lower extremity alignment [11], and even in muscle activation patterns and movement patterns during walking and particular exercises 12., 13., 14. and 15.. The objective of this study was to examine the sex-associated differences in knee kinematics, knee kinetics and knee neuromuscular patterns during gait before and after TKA surgery. We hypothesized that similar to previous study of men and women earlier in the knee OA disease process [15], women would display gait and neuromuscular patterns preoperatively that are more severe than men, and that the persistence of abnormal gait patterns post-TKA would be more pronounced for women than men.

Materials and Methods

Patients

Patients with severe knee OA were recruited from a wait list for primary total knee arthroplasty (TKA) surgery from 2003 to 2011. All patients visited the Dynamics of Human Motion laboratory for gait analysis testing within the week prior to their surgery, and at approximately one year postoperatively. Patients were included in the study if they were able to walk unassisted along a six-meter walkway in the laboratory, and were excluded if they had any neuromuscular disease, cardiovascular disorders or other lower limb surgeries within the year prior to gait testing that would affect their gait or put them at risk. Consent was obtained from all patients in accordance to the Capital Health Research Ethics Board. All patients had standard anterior–posterior radiographs taken within 12 months prior to baseline gait testing, which were graded for OA severity by one orthopedic surgeon (M.J.D.) using the Kellgren Lawrence (K.L.) global rating [16]. All patients had KL scores of three or four, indicative of severe osteoarthritic joint changes, and all had either predominant medial compartment involvement or were equally affected in both compartments based on Scott's joint space narrowing rating [17].

One experienced, high volume, fellowship trained TKA surgeon (M.J.D.) performed all surgical procedures. Several knee implant systems were included in this study and were from previous studies at our institution 2., 3. and 18.; however all were posterior-stabilized designs with similar bearing surfaces. Systems included the NexGen Posterior Stabilized Complete Knee System (Zimmer, Warsaw, Indiana) (two subsets of the NexGen knees were used: one with the traditional cemented titanium base plate and one with the uncemented Trabecular Metal tibial base plate). A few cases utilized the Triathlon posterior-stabilized system (Stryker Orthopedics, Kalamazoo, MI), which would have a slightly different bearing surface curvature than the NexGen system. There were similar distributions of implant systems between the sexes.

All surgeries were performed with intramedullary alignment of the femur and extramedullary alignment of the tibia. The distal femoral cut was set for five-degree valgus and the tibial cut was set for neutral (0 degree). Anterior and posterior cruciate ligaments were resected in all cases and patellae were resurfaced using an inset patellar button. The measured resection technique was used to obtain a balanced flexion and extension gap. All knees were considered balanced at the end of the case with full extension and a minimum of 110 degrees of flexion. Patellar tracking was balanced in all cases and no lateral retinacular releases were required. Patients were immobilized for the first postoperative day and then started on a standardized physiotherapy regime including immediate and full weight bearing, continuous passive motion machine application on a daily basis and routine quadriceps strengthening.

Gait Analysis

Patients walked at their self-selected speeds along a 6-meter walkway in the Dynamics of Human Motion laboratory at Dalhousie University. Three-dimensional motion of the lower extremity of the affected side and external ground reaction forces and moments were captured during gait with a synchronized Optotrak 3020 motion capture system (Northern Digital Inc., Waterloo) and an AMTI force platform (Advanced Mechanical Technology Inc., Watertown MA). Motion data were captured at 100 Hz, and force platform data at 2000 Hz and down-sampled to match the motion data.

A series of three-marker triads of infrared light emitting diodes were placed on each of the foot, shank, thigh and pelvis and tracked during the walking trials. Individual markers were placed based on standardized protocols to define anatomical and joint coordinate systems [19]. The three-dimensional joint angles during walking were computed for one complete gait cycle using the joint coordinate system and a least squares optimization method 20. and 21. Custom software written in Matlab was used to

calculate net external joint moments using an inverse dynamics procedure. Moments were normalized to body mass and represented about the anatomical axes of the joint coordinate system [21].

A synchronized electromyography (EMG) system was used to capture the activation patterns of seven periarticular knee muscles at the same time during the walking trials using a standardized collection and analysis protocol [22]. Muscles included the medial and lateral gastrocnemius (MG, LG), the medial and lateral hamstrings (MH, LH), and three quadriceps muscles, the vastus medialis (VM), the vastus lateralis (VL), and the rectus femoris (RF). Electrodes were placed using previously defined and standardized protocols [23]. The raw EMG signals were pre-amplified and processed in a standardized fashion [23]. Following the gait trials, a series of maximum voluntary isometric contractions (MVIC) were performed for EMG amplitude normalization [24]. Angle, moment and EMG data were normalized to one complete gait cycle (0–100%) and the average of five good trials of data for each patient was used.

Principal Component and Statistical Analysis

Principal component analysis (PCA), a multivariate statistical pattern recognition and data reduction technique, has been used in previous gait studies to identify discriminatory features of gait and EMG waveforms 2., 3., 25. and 26.. Detailed descriptions of the technique as applied to gait biomechanics and electromyography data have been outlined previously 23. and 25.. Principal components (PCs) were described for knee flexion, adduction and rotation angles as well as 3D knee moments. PC models were created for each EMG muscle group [23].

Two-factor ANOVA models were used to examine sex, visit (pre- and post-TKA) and interaction effects for each set of PCscores for the angle and moment waveform data. Three-factor (sex, visit, and muscle) ANOVA models were used to examine main and interaction effects for the electromyography PCscores. Only statistically significant (P < 0.05) sex effects or interaction effects that involved the factor sex were interpreted in the current study. Tukey's honestly significant different criterion was used to determine significant pairwise comparisons.

Results

Patients

Fifty-two patients with severe medial compartment knee OA were recruited (28 women) (Table 1). Men had significantly higher body mass and height pre- and post-TKA (P < 0.05). There were, however, no differences in age or BMI between men and women pre- and post-TKA (P < 0.05). There were also no differences in change in mass or BMI in either men or women preoperatively to postoperatively (P > 0.05) (Table 1). Twenty women received the NexGen system (7 with trabecular metal tibial base) (Zimmer, Warsaw, Indiana), one received the Wright Medical Advance, and 7 received the Triathlon posterior-stabilized system (Stryker Orthopedics, Kalamazoo, MI). Fifteen men received the NexGen system (6 with trabecular metal tibial base), and 9 received the Triathlon system. All implant systems included had similar bearing surfaces.

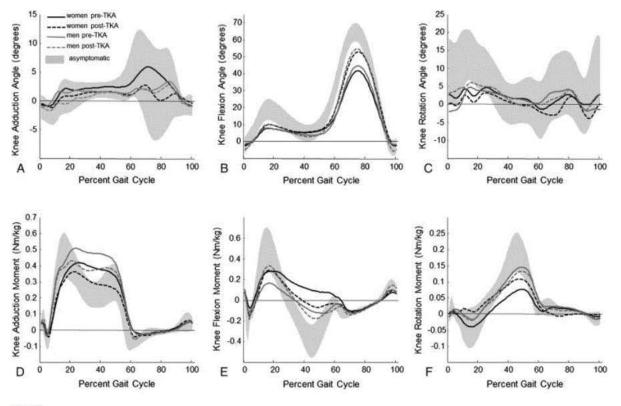
Table 1.

Patient Demographics by Sex, Including *P*-Value for Student's T-Test Statistical Comparison (Bold = Statistically Significant at α = 0.05).

Variable	Women, Mean (stdev)	Men, Mean (stdev)	P-Value
Number of subjects	28	24	n/a
Age (years, pre-TKA)	64.3 (6.5)	65.1 (7.8)	0.68
Mass (kg, pre-TKA)	84.5 (17.0)	97.8 (15.1)	0.005
Mass (kg, post-TKA)	84.6 (17.4)	98.7 (15.3)	0.003
Change in mass (kg, post-pre <mark>)</mark>	0.18 (6.0)	0.89 (4.0)	0.63
Height (m)	1.6 (0.06)	1.75 (0.09)	< 0.0001
BMI (kg/m², pre-TKA)	33.1 (6.4)	32.0 (4.6)	0.50
BMI (kg/m², post-TKA)	33.1 (6.5)	32.1 (4.4)	0.51
Change in BMI (kg/m², post-pre)	0.04 (2.4)	0.08 (1.6)	0.94
Gait testing (days, post-TKA)	414 (67)	382 (66)	0.09
Average gait speed (m/sec, pre-TKA)	0.89 (0.23)	0.85 (0.2)	0.46
Average gait speed (m/sec, post-TKA)	1.05 (0.17)	1.05 (0.22)	0.89
Change in speed (m/sec, post-pre-TKA)	0.11 (0.25)	0.20 (0.18)	0.14
Knee extension strength (Nm/kg, pre-TKA)	55.4 (20.3)	91.3 (28.9)	< 0.0001
Knee extension strength (Nm/kg, post-TKA)	74.9 (25.3)	109.7 (37.1)	< 0.0001
Change in extension strength (Nm/kg)	19.6 (23.9)	17.3 (32.8)	<mark>0.78</mark>
Knee flexion strength (Nm/kg, pre-TKA)	26.0 (11.8)	54.2 (23.6)	< 0.0001
Knee flexion strength (Nm/kg, post-TKA)	35.6 (13.6)	62.4 (34.8)	0.001
Change in flexion strength (Nm/kg)	9.9 (14.1)	7.2 (23.2)	0.62
Plantarflexion strength (Nm/kg, pre-TKA)	47.1 (16.5)	73.0 (21.3)	< 0.0001
Plantarflexion strength (Nm/kg, post-TKA)	49.6 (21.6)	83.4 (25.5)	< 0.0001

Variable	Women, Mean (stdev)	Men, Mean (stdev)	P-Value
Change in plantarflexion strength (Nm/kg)	4.0 (20.6)	8.6 (19.9)	0.49

Self-selected gait speed increased for both men and women post-TKA compared to pre-TKA (P < 0.0001). However, there were no significant differences in gait speed between men and women either pre- or post-TKA. There was a significant improvement in knee extension, knee flexion and plantarflexion strength post-TKA (P < 0.0001, 0.002, and 0.04 respectively). Knee extension, flexion and plantarflexion strength (normalized to body mass) were higher for men than for women at both time points (all $P \le 0.001$); however the change in strength pre- to post-TKA was not significantly different between men and women. The ensemble-average gait waveforms for men and women for both conditions are included in Fig. 1 and Fig. 2.





Ensemble average waveforms. Three-dimensional knee angle (A–C) and knee net resultant moment (E– F) mean patterns during gait by sex (black = women, gray = men) and visit (solid = pre-TKA, dash = post-TKA). A one standard deviation shaded gray band in the background represents the distribution of each measure from a group of 60 asymptomatic individuals for Ref. [24].

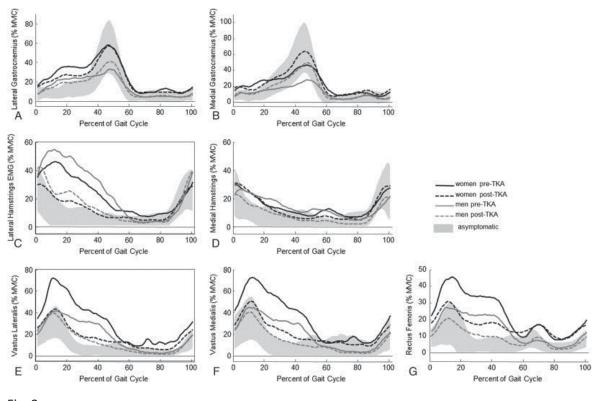


Fig. 2.

Ensemble average waveforms. Electromyography patterns (amplitude normalized to percent maximum voluntary isometric contraction) during gait for the gastrocnemius (A, B), hamstrings (C, D) and quadriceps (E–G) muscles by sex (black = women, gray = men) and visit (solid = pre-TKA, dash = post-TKA). A one standard deviation shaded gray band in the background represents the distribution of each measure from a group of 60 asymptomatic individuals for Ref. [27].

Principal Component Models

The first three principal components (PCs) for the adduction, flexion and rotation angles and moments at the knee cumulatively explained 90% to 93% of the variability in waveform data (<u>Table 2</u>). For the electromyography data, 84% to 88% of the waveform variability was cumulatively explained with the first three PCs (<u>Table 4</u>). General descriptions of each PC are provided in <u>Table 2</u> and <u>Table 4</u> for the kinematics/kinetics and electromyographic models respectively. For 6 key PCs that showed significant sex differences, the patterns and the waveforms associated with high (95th percentile) and low (5th percentile) PC scores are found in <u>Fig. 3</u> and <u>Fig. 4</u> to assist with interpretation.

Table 2.

Principal Component Variability and Descriptions of Knee Kinematic and Kinetic PCs.

Variable	PC	% Variation Explained	High PCscore Description
Knee adduction angle	1	65.5	Overall high angular magnitude during stance phase
	2	17.7	Difference early (lower) to late (higher) stance
	3	7.6	Difference foot strike (lower) to midstance (higher)
Knee flexion angle	1	68.1	Overall high angular magnitude during entire gait cycle
	2	12.7	Difference late stance extension to mid-swing peak flexion
	3	12.5	Phase shift: later peak flexion in swing
Knee rotation angle	1	54.6	Overall high angular magnitude during stance phase
	2	28.6	Difference early (more external) to late stance (higher internal)
	3	7.3	Magnitude in midstance (approximately 20% gait cycle)
Knee adduction	1	73.9	Overall high magnitude during stance phase
moment	2	13.9	Difference early stance to mid-late stance peaks
	3	3.4	Difference mid-stance and 1st and 2nd peaks
Knee flexion	1	69.0	Overall high magnitude during stance phase
moment	2	18.1	Difference early stance to late stance
	3	4.6	Phase shift: later peak moments during stance
Knee rotation	1	69	Overall high magnitude during stance phase
moment	2	19.8	Difference early (more external) to late stance (higher internal)

Variable	PC % Variation Explained		High PCscore Description		
	3	3.9	Low early (10% gait cycle) and late stance moment		

Table 3.

Two-Factor ANOVA Results for Knee Kinematic and Kinetic PC scores (Bold = Statistically Significant at α = 0.05).

Variable	PC	P-Value Sex	<i>P</i> -Value Visit	P-Value Interaction
Knee adduction angle	1	0.21	0.02	0.97
	2	0.46	0.37	0.07
	3	0.76	0.67	0.87
Knee flexion angle	1	0.59	0.0001	0.73
	2	0.03	0.04	0.48
	3	0.92	0.91	0.42
Knee rotation angle	1	0.48	0.80	0.15
	2	0.84	0.15	0.06
	3	0.03	0.79	0.64
Knee adduction moment	1	0.002	0.012	0.89
	2	0.19	0.15	0.62
	3	0.11	0.003	0.32
Knee flexion moment	1	0.001	0.24	0.07
	2	0.08	0.0005	0.20
	3	0.45	0.85	0.45
Knee rotation moment	1	0.03	0.14	0.03
	2	0.0009	0.15	0.52
	3	0.003	0.17	0.26

Table 4.

Principal Component Variability and Descriptions of Electromyography Measures.

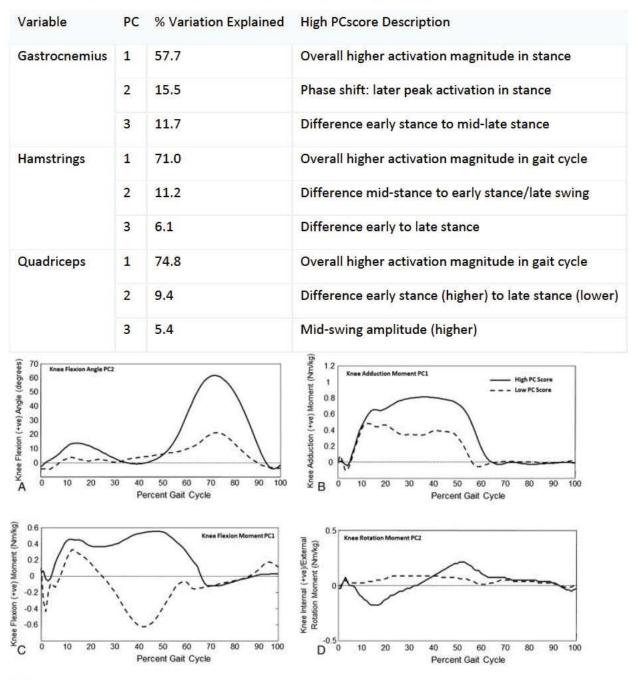


Fig. 3.

Knee angle and moment principal components. Example waveforms with high (95th percentile) and low (5th percentile) PCscores for some example PCs with statistically significant sex effects are shown. (A) PC2 of the flexion angle represented the range of motion from late stance to swing; women had lower scores than men, so less range of flexion from late stance to peak flexion mid-swing than men. (B) PC1 of the adduction moment represented the overall magnitude of the moment in stance; men had higher

scores than women indicating higher overall adduction moments than women. (C) PC1 of the knee flexion moment represented the overall magnitude of the moment in stance; women had higher and more constant overall flexion moments during stance than men. (D) PC2 of the rotation moment captured a difference in rotation moment magnitude from early to late stance; women had lower scores than men and therefore more constant rotation moments during stance than men.

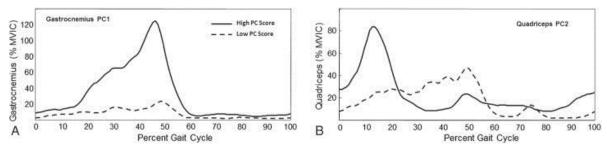


Fig. 4.

Electromyography principal components. Example waveforms with high (95th percentile) and low (5th percentile) PCscores for PCs with statistically significant sex effects are shown. (A) PC1 of the gastrocnemius EMG represented the overall magnitude of activation during stance; women had higher scores than men, meaning that women had higher overall gastrocnemius activity than men throughout stance. (B) PC2 of the quadriceps represented the difference in quadriceps activity from early to midlate stance; men had lower PC2 scores than women and therefore more constant quadriceps activation throughout stance.

Knee Angle Differences

A significant sex effect was found in the knee flexion angle PC2 (Fig. 3A), with women having a lower range of flexion/extension angular motion between late stance and mid-swing than men (Fig. 1B) (P = 0.03). There was a significant sex effect in PC3 of the rotation angle (P = 0.03), with women having lower scores, and therefore lower mid-stance (approximately 20% of gait cycle when knee is in peak stance phase flexion) internal rotation angles than men (Fig. 1C). There was a trend toward a sex by visit interaction in PC2 of the rotation angle (P = 0.06). Men had higher PC2 scores postoperatively than preoperatively, characterized by an altered pattern of a difference between more external rotation in early stance and more internal rotation in late stance postoperatively compared to more constant rotation angles preoperatively throughout stance (Fig. 1C). Women had similar preoperative and postoperative scores, with neither different than prescores and postscores of men. There was also a trend toward a sex by visit (pre/post) interaction in PC2 of the knee adduction angle (P = 0.07), with men having higher PC2 scores postoperatively than preoperatively indicative of a pattern change to greater difference in early stance adduction (lower) to late stance adduction (higher) postoperatively compared to more constant adduction angles through stance preoperatively. Women had similar preoperative and postoperative scores, and similar scores to men postoperatively.

Knee Moment Differences

There was a significant sex effect in PC1 of the knee adduction moment (<u>Table 3</u>; <u>Fig. 3</u>B), with men having higher PC1 scores and therefore higher overall knee adduction moments during stance than women (<u>Fig. 1</u>D). A significant sex effect was also found in PC1 of the knee flexion moment, with women

having higher and more constant overall flexion moments during stance than men (P = 0.001) (Fig. 3C). PC1 of the knee flexion moment also had a trend toward a sex by visit interaction (P = 0.07), such that the higher flexion moments found in women were decreased more postoperatively than the lower preoperative flexion moments in men (Fig. 1E). A trend toward a significant sex effect was found in PC2 of the knee flexion moment (P = 0.08), with women having lower scores and therefore a more constant knee flexion moment during stance than men (Fig. 1E).

There was a significant sex by visit interaction in PC1 of the rotation moment, with women having a lower overall internal rotation moment (or more external rotation moment) magnitudes preoperatively, due to the higher external moment magnitude in early stance and lower internal moment in late stance than men preoperatively, and both men and women postoperatively (P = 0.03) (Fig. 1F). Significant sex effects were found for PC2 and PC3 of the knee rotation moment as well (P = 0.0009 and P = 0.003 respectively). Women had more constant rotation moments than men throughout stance (lower PC2 scores; Figs. 1F, 3D) and more external rotation moment in early (approximately 10% of the gait cycle) and late stance (60%) than men (higher PC3 scores, Fig. 1F).

Neuromuscular Differences

Statistically significant findings are found in Table 5. A significant sex effect was found in PC1 of the gastrocnemius (P < 0.0001), with women having higher overall gastrocnemius activation amplitudes than men throughout stance (Figs. 2A, B and 4A). There was a significant sex by visit interaction in PC1 (overall activation amplitude) of the quadriceps muscles (P = 0.05). Women had higher PC1 scores than men preoperatively and postoperatively, meaning that women had higher quadriceps activity in stance than men, and women's PC1 scores decreased postoperatively relative to preoperatively, whereas men's scores did not. There was a significant sex effect in PC2 of the quadriceps activation (P = 0.003) (Fig. 4B), with women having higher PC2 scores than men meaning that women had less prolonged stance phase quadriceps activity than men. There was a significant visit by sex interaction in PC3 of the quadriceps (P = 0.03). PC3 was dominated by mid-swing activation amplitude, and women preoperatively had higher PC3 scores (higher quadriceps activity mid-swing) than postoperatively, and than men preoperatively and postoperatively. There was a significant sex by muscle interaction in PC2 of the hamstrings (P = 0.02). Men had higher postoperative lateral hamstring PC2 scores than preoperatively medial hamstring activity preoperatively. There was no difference in women's scores between hamstrings muscles.

Table 5.

Three-Factor ANOVA Results for Electromyography PC Scores (V = Visit, S = Sex, M = Muscle);	
(Bold = Statistically Significant at α = 0.05).	

Variable	PC	<i>P</i> -Value Sex	P-Value Visit	<i>P</i> -Value Muscle	<i>P</i> -Value Interaction (V * S, V * M, M * S, V * S * M)
Gastrocnemius	1	< 0.0001	0.25	0.40	0.21, 0.04 , 0.75, 0.79
	2	0.59	0.21	0.33	0.78, 0.04 , 0.67, 0.75
	3	0.68	< 0.0001	0.02	0.95, 0.29, 0.61, 0.68

Variable	PC	P-Value Sex	P-Value Visit	P-Value Muscle	<i>P</i> -Value Interaction (V * S, V * M, M * S, V * S * M)
Hamstrings	1	0.25	< 0.0001	< 0.0001	0.25, 0.001 , 0.08, 0.83
	2	0.12	0.03	0.19	0.46, 0.64, 0.02 , 0.30
3	3	0.26	0.91	0.33	0.93, 0.06, 0.40, 0.97
Quadriceps	1	< 0.0001	< 0.0001	0.0005	0.05 , 0.56, 0.78, 0.71
	2	0.003	< 0.0001	0.03	0.41, 0.71, 0.81, 0.59
	3	0.016	0.52	< 0.0001	0.03 , 0.52, 0.93, 0.98

Discussion

Our previous work has demonstrated differences in both biomechanics and electromyographic patterns between pre-and post TKA surgery, illustrating that some patterns do not return to asymptomatic <u>2</u>. and <u>3</u>. We have also examined sex-specific biomechanical differences during gait with and without moderate levels of knee OA [15]. However, little is known whether there are sex-specific biomechanical and neuromuscular differences with end-stage knee OA, and also in response to TKA treatment.

Some characteristics of women's gait patterns such as lower range of knee flexion angle (PC2), more constant stance phase knee flexion and rotation moments (PC2), and higher quadriceps activity during stance (PC1), could be considered 'more severe' in the sense that these patterns are typical of more severe stages of knee osteoarthritis <u>25.</u>, <u>26.</u>, <u>28.</u> and <u>29.</u>. Still, the higher overall knee adduction moments during stance (PC1), the lower overall knee flexion moments during stance (PC1), and the lower activation of the gastrocnemius muscles during stance (PC1) that characterized men's gait patterns could also be considered 'more severe'. Since some risk factors for OA have been shown to be sex-specific, such as increased varus alignment in men <u>[30]</u> and decreased muscle strength for women <u>[10]</u>, it is reasonable that the disease might manifest itself differently between the two sexes.

The only knee joint kinematic difference between the sexes was in the sagittal plane knee angle range (knee flexion angle PC2). Both preoperatively and postoperatively women had lower knee joint flexion angle range from late stance to mid-swing during gait compared to men, a characteristic of their gait patterns that were further from asymptomatic than men (Figs. 1B and 3A), and consistent with a more severe knee OA gait pattern [28]. This finding implies that women with severe knee OA walk with a more constant knee flexion angle (i.e. 'stiffer' knee) during gait than men with severe knee OA, and although range of motion during gait improves for both sexes pre- to post-TKA, women still lag men postoperatively in this feature. Because men and women did not walk at significantly different self-selected speeds in this study either pre- or post-TKA, this difference cannot be attributed to a velocity difference. In previous work by our group it was similarly shown that women with moderate levels of knee OA had lower stance phase range of motion than men [15].

There were several knee joint kinetic differences between men and women during gait both pre- and post-TKA. During the stance phase of gait, men had lower overall net external flexion moments

preoperatively than women and both groups postoperatively (PC1, Figs. 1E and 3C), but greater difference between peak flexion moment in early stance and peak extension moment in late stance than women (PC2, Fig. 1E). The lower flexion moment displayed by men preoperatively is consistent with a more severe knee OA gait pattern, i.e. further from asymptomatic values than women [28]. However, TKA surgery in general seems to restore this low stance phase flexion moment in men to higher values more consistent with asymptomatic gait patterns post-surgery (Fig. 1E). This result is different from previous findings on a population with moderate knee OA, where it was shown that women with moderate knee OA had significantly lower flexion moments than men with moderate knee OA (and asymptomatic men and women) [15]. However, an earlier study on a non-surgical, but severe knee OA population found a similar result, with men having lower peak stance phase flexion moments than women [31]. Net external flexion moments are often interpreted as a 'quadriceps avoidance' gait pattern in the sense that the individuals may be avoiding creating a large external flexion moment if they have insufficient knee extensor strength or activation to balance the moment internally. This argument does not account for the potential use of quadriceps/hamstrings co-contraction around the knee joint [32], and indeed, men's EMG patterns of the quadriceps muscles during early to mid-stance do not suggest a quadriceps avoidance pattern (Fig. 2E, F, G). Men do, however, display large lateral hamstring activity at this phase of the gait cycle (Fig. 2C), indicating that quadriceps/hamstrings cocontraction could be contributing to the reduced external flexion moment.

In addition to the overall net external flexion moment difference between the sexes (PC1), we also identified a trend toward a difference (P = 0.08) between the sexes in terms of their early stance flexion moment to late stance extension moment (PC2) difference. Women did not display the typical biphasic early flexion and late extension peaks but had a more constant flexion moment during stance than men both preoperatively and postoperatively. This difference was dominated by less late stance extension moment in women compared to men (Fig. 1E), suggesting that women extend during push off and tended to keep the knee more flexed at toe-off than men, a complimentary finding to that of PC2 of the flexion angle discussed above, showing that women had less range of knee joint motion from late stance to mid-swing. This aspect of the flexion moment pattern would be considered 'more severe' in the sense that it is further from asymptomatic patterns [28]. While TKA improved this difference between early stance flexion moment and late stance extension moment in both men and women toward more asymptomatic levels, women continued to lag men post-TKA with respect to this feature.

In the frontal plane, men had higher overall knee adduction moments than women both preoperatively and postoperatively (PC1; Figs. 1D and 3B). Greater levels of varus knee deformity and varus thrust in men with knee OA have been reported by others [33], and varus thrust has been associated with higher knee adduction moment magnitudes during stance [34]. Higher peak and impulse of the knee adduction moment has been associated with higher odds for OA structural progression 35. and 36. Although overall magnitudes of the adduction moment were decreased for both sexes postoperatively, men continued to have higher adduction moments displayed by men because as our previous work has found a significant association between high overall knee adduction moments (PC1) preoperatively and the amount of micromotion (i.e. loosening) of the implant measured with Radiostereometric Analysis (RSA) postoperatively [6]. Previous work by our group showed no significant difference in the overall magnitude of the adduction moment between men and women with moderate levels of knee OA [15], therefore this is another example of a discrepancy between the sexes that manifests in more severe

stages of the disease. The previous work also showed that women with moderate levels of knee OA had more constant adduction moments (lack of frontal plane unloading) during stance than men, a pattern that has also been associated with moderate knee OA presence compared to asymptomatic individuals [19]. In our severe population, neither men nor women showed significant unloading in the frontal plane during stance (Fig. 1D); however postoperatively both men and women had higher PC3 scores of the adduction moment, indicating a mid-stance unloading phase after surgery.

A number of significant differences between men and women in the transverse plane were noted. Women's internal/external rotation angle patterns during gait both preoperatively and postoperatively were characterized by lower internal rotation angles than men at approximately 20% of the gait cycle when the knee is reaching peak stance phase flexion (PC3) (Fig. 1C). While there is considerable variability among even asymptomatic individuals in transverse plane angular gait motion (Fig. 1C), the higher internal rotation angles displayed by men at 20% of the gait cycle are more similar to asymptomatic magnitudes than those of women. This sex-specific difference was evident both pre- and post-TKA, again suggesting that TKA leads to different biomechanical response between the sexes despite similar surgical decisions.

Preoperatively women had lower overall rotation moments (i.e. less internal rotation moment) than post-TKA (PC1), and lower than men pre- and post-TKA (Fig. 1F). Women also had less difference between early stance external rotation moment and late stance internal rotation moment (PC2, Fig. 3D) than men. This more constant rotational loading, in combination with the finding of more constant sagittal plane loading, suggests that women adopt a gait pattern with severe knee OA that continuously loads the joint in one direction more so than men. This pattern tends to persist after TKA intervention, with yet unknown consequences. Constant loading may reflect a 'stiffer' joint in the sense that there is a lack of joint unloading (usually coupled with knee flexion), which can signal a lack of confidence for joint use. This may be due to differences in soft tissue surrounding the joint, muscular control (differences of which are shown in this study), or even an improperly sized or placed implant.

Preoperatively, women had significantly higher overall quadriceps activity than men during stance and higher than both groups postoperatively (PC1, Fig. 4D) which can in part be explained by lower muscle strength. Consistent with other studies, men had higher isometric knee extension and flexion and plantarflexion strength values than women in this study (<u>Table 1</u>). Also, the decrease postoperatively in women can be explained by the larger increase in knee extensor strength in women (35%) compared to men (19%). The burst in activity early in stance was close to 80% of MVIC for the two vasti muscles preoperatively and then 40%–50% postoperatively in women or similar to the values for men (Fig. 2E, F, G). Women also showed greater difference between their early stance and later-stance quadriceps activation levels, likely dominated by their very high early stance magnitudes preoperatively. This high activity of the quadriceps muscles in stance is consistent with severe knee OA [29], and has been shown to be a discriminator of moderate knee OA gait patterns relative to asymptomatic [26]. The differential effect of the TKA intervention cannot all be explained by strength improvements postoperatively as both men and women had improvements in their mid-stance magnitudes toward asymptomatic values This finding is significant because prolonged patterns (PC2) of quadriceps activity (vastus medialis in particular) during stance preoperatively was associated with implant migration measured postoperatively with Radiostereometric Analysis [8].

Women had higher overall activation levels of the gastrocnemius activity during stance than men preand post-TKA. This, in combination with higher quadriceps activity, may represent a higher level of coactivity in early to mid-stance, possibly to improve joint stability. High gastrocnemius and quadriceps coactivity on the medial side in early stance has been shown previously in individuals with knee OA and medial joint instability [37]. Previous work has shown that women tend to be more lax in the knee than men [27], and Landry et al [38] have shown that female adolescents adopt a pattern of increased gastrocnemius activity in early to mid-stance during a running and cross-cutting maneuver. Prolonged lateral gastrocnemius activity during stance preoperatively has also been shown to relate to implant migration post-TKA [8], and while this pattern improved for both groups (decrease PC3 scores), the more prolonged preoperative pattern adopted by women may be indicative of an unfavorable pattern in terms of TKA outcome.

While three-dimensional patterns of knee joint loading during gait have been shown in the past to move toward asymptomatic patterns post-TKA [2], the current results suggest that preoperative patterns and, at times, pattern changes post-TKA, are sex-specific (Fig. 1). Similarly, it has been shown that EMG patterns also move toward asymptomatic patterns post-TKA [3]. While irregular EMG patterns improve toward asymptomatic levels for both men and women post-TKA in this study, women tended to continue to lag their male counterparts post-TKA in this regard and display more prolonged activity of the quadriceps and gastrocnemius muscles throughout stance.

There is a paucity of data on three-dimensional joint dynamic differences and neuromuscular control between men and women at late stages of knee osteoarthritis. Our results indicate that the effect of TKA on knee joint kinematics, kinetics and neuromuscular activation patterns during gait is sex-specific. These findings have implications for sex-specific surgical decision-making, implant design and positioning and potentially post-TKA rehabilitation efforts.

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