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Influences of Alignment and Obesity on Knee Joint Loading in Osteoarthritic Gait

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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, Pater, Beavers, Legault, Loeser, Hunter, DeVita*
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Abstract

Objective—To determine the influences of frontal plane knee alignment and obesity on knee joint loads in older, overweight and obese adults with knee osteoarthritis.

Methods—Cross-sectional investigation of alignment and obesity on knee joint loads using community dwelling older adults (age ≥ 55 yrs.; 27 $kg \cdot m^{-2} \geq BMI \leq 41$ $kg \cdot m^{-2}$; 69% female) with radiographic knee osteoarthritis that were a subset of participants (157 out of 454) enrolled in the Intensive Diet and Exercise for Arthritis (IDEA) clinical trial.

Results—A higher BMI was associated with greater ($p = 0.0006$) peak knee compressive forces [overweight, 2411 N (2182, 2639), class 1 obesity, 2772 N (2602, 2943), class 2+ obesity, 2993 N (2796, 3190)] and greater ($p = 0.004$) shear forces [overweight, 369 N (322, 415), class 1 obesity, 418 N (384, 453), class 2+ obesity, 472 N (432, 513)], independent of alignment, and varus alignment was associated ($p < 0.0001$) with greater peak external knee adduction moments, independent of BMI [valgus, 18.7 Nm (15.1, 22.4), neutral, 27.7 Nm (24.0, 31.4), varus, 37.0 Nm (34.4, 39.7)].

Conclusion—BMI and alignment were associated with different joint loading measures; alignment was more closely associated with the asymmetry or imbalance of loads across the medial and lateral knee compartments as reflected by the frontal plane external adduction moment, while BMI was associated with the magnitude of total tibio-femoral force. These data may be useful in selecting treatment options for knee osteoarthritis patients (e.g., diet to reduce compressive loads or bracing to change alignment).

Knee osteoarthritis (OA) is the leading cause of chronic disability, affecting 15% of the United States population over 65 years of age (1;2). Knee malalignment and obesity are both important biomechanical risk factors for incident knee OA, primarily due to their tendency to increase knee joint loading (3–8). Joint stress across the articular surfaces from excessive body mass and malalignment promote cartilage breakdown, osteophyte formation, subchondral bone hypertrophy, and lead to progression of knee joint destruction (4;9). However, the relationship between these risk factors and knee joint loading may not be straightforward because they may interact with one another (10).

Several studies suggest that alignment may mediate the effect that body mass or body mass index (BMI) have on disease progression (4;5;8;11). Moyer et al. (11) found that alignment and body mass produced an interaction effect: that the association between alignment and the external knee adduction moment was strongest in patients with the greatest body mass such that a one degree increase in varus alignment produced a 3.2 Nm (6% of mean value) increase in the external adduction moment in the tertile with the highest mass. While alignment accounted for 32–45% of the variance in the external knee adduction moment, body mass only accounted for 6–10%, signifying that the external knee adduction moment is more affected by differences in alignment. Additionally, only 10% of the participants had valgus alignment, hinting that joint loads were concentrated in the medial compartment of the tibiofemoral joint, thereby driving the presence of the interaction with the external knee adduction moment.

The external knee adduction moment is an important surrogate measure of medial compartment knee joint loading (11;12), primarily due to its association with disease severity and progression (5;7;13). However, no studies have examined the effect of alignment and obesity on more direct measures of knee joint loading. Studies with knee OA patients found that bone-on-bone joint forces derived from musculoskeletal models were attenuated in obese patients with knee OA after reductions in body mass (14;15) and actually increased consequent to pain medication (16). Hence, these bone-on-bone estimates of joint loads appear sensitive to both mechanical and clinical changes.

There is a great need to improve our understanding of the relationship between alignment and obesity so that interventions targeting both are better understood, thereby improving clinicians' ability to select the best treatment options. The purpose of this cross-sectional study was to investigate the interaction between alignment and BMI with knee joint loading in overweight and obese sedentary adults with knee OA. We hypothesized that there would be a significant interaction between alignment and BMI, expressed by a stronger relationship with measures of knee joint loading in people with higher BMIs.

Methods

Participants

The Intensive Diet and Exercise for Arthritis (IDEA) trial was a weight loss and exercise trial of overweight and obese sedentary older adults with grade II-III radiographic knee OA. A detailed description of the study design and resulting outcomes can be found elsewhere (15;17). Briefly, participants were ambulatory, community-dwelling persons age ≥ 55 yrs. with $27\ \text{kg}\cdot\text{m}^{-2} \geq \text{BMI} \leq 41\ \text{kg}\cdot\text{m}^{-2}$. A stratified random sample of 157 (out of 454) IDEA participants, with equal numbers from each group (Exercise, Diet, Diet+Exercise) received a full length anteroposterior (AP) x-ray at baseline to measure lower extremity alignment. Exclusion criteria included: (1) significant co-morbid disease; (2) the inability to walk; (3) previous acute knee injury; (4) knee OA other than tibiofemoral or tibiofemoral plus patellofemoral; (5) unwillingness to change eating or physical activity habits; and (5) knee injection (i.e. cortisone, hyaluronic acid, etc) or knee surgery within the past 6 months. Descriptive characteristics of the cohort are presented in Table 1.

Radiographic Analysis

Bilateral posteroanterior (PA) weight-bearing knee radiographs were used to identify tibiofemoral OA and sunrise views to identify those with patellofemoral OA. PA radiographs were obtained with the participants' knees flexed at a 15° angle using a positioning device and the x-ray beam was centered on the joint space. Tibiofemoral disease severity was determined using the Kellgren and Lawrence (K-L) grading scale that includes the formation of osteophytes, narrowing of joint cartilage, sclerosis of subchondral bone, and altered shape of bone ends with 0 = no disease; 1 = questionable; 2 = definite; 3 = moderate; and 4 = severe (18).

A full-length A-P radiograph for alignment was obtained using the Agfa ADC system (Quantum Q-Rad based imaging) approach. Participants were positioned using the methods of Sharma et al. (5) such that both lower extremities were imaged simultaneously. Both tibial tubercles were faced directly forward and the participants' feet were positioned 15 cm apart. Participants stood upright with weight equally distributed to both feet. Alignment (mechanical axis) was defined as the measure of the angle formed by the intersection of the lines connecting the centers of the femoral head and the intercondylar notch and the centers of the ankle talus and tibial spines. Alignment was categorized into three groups: a varus knee was an angle >2° in the varus direction (or a bowlegged appearance); valgus was an angle <0° in the valgus direction (or a knock-kneed appearance); and a neutral knee was defined as an angle between 0–2° in the varus direction (19). All of the measur ements were made by two physicians using the NIH ImageJ program. The intra-rater reliability of the two readers was 0.99 and the inter-rater reliability was 0.98.

Gait Analysis

Prior to testing, participants walked at their freely chosen walking speed on a 22.5 m walkway. Freely chosen walking speed was assessed using a Lafayette photoelectric control system (Model 63501-IR) with integrated digital timers and was calculated as the average time for six trials.

Participants were prepped with a 37-reflective marker set arranged in the Cleveland Clinic full-body configuration and wore a pair of laboratory running shoes (type: cushioned) to control for footwear. Successful trials were defined as placing the entire foot on the force platform during a normal walking stride while maintaining walking speed within the established range (± 3.5%). Three successful trials were collected and corresponding outcomes averaged to provide representative values for each participant. Data from the most affected side (i.e., the knee with the most pain or the dominant side if the pain was equal in both knees) were used for subsequent analysis. 3-D videography (60 Hz) was accomplished using a 6-camera motion analysis system (Motion Analysis Corporation). An AMTI (Advanced Medical Technologies, Inc.) model OR-6-5-1 force-plate (480 Hz) interfaced with a 6 channel amplifier (model SGA6-4) was integrated with the motion capture system to allow simultaneous kinetic and kinematic data collection. Kinematic data were collected, tracked, edited, and smoothed using EVaRT 4.6 software (Motion Analysis Co.) and raw coordinate data were smoothed using a 4th order low-pass Butterworth filter set at a cut-off frequency of 6 Hz. Processed data were compiled using Orthotrak 6.0 β4 clinical gait analysis software (Motion Analysis Co.) to generate lower extremity kinetic and kinematic data, and calculate joint moments and joint reaction forces. Kinematic and kinetic data were synchronized to calculate external joint moments and forces using standard inverse dynamics. The variables of interest included the peak external knee flexion and adduction moments during the first 50% of stance, knee joint forces, and ground reaction forces on the most affected side. Test-retest reliability of our gait measures ranged from intra-class correlation coefficients of 0.86 to 0.98(20).

A musculoskeletal model developed by DeVita and Hortobagyi (21) was used to calculate knee joint (tibiofemoral) compressive and AP shear forces, the compressive force between the femur and the patella, and quadriceps, hamstrings and gastrocnemius muscle forces. Our musculoskeletal torque-driven model has two basic components. The first involves calculating joint moments and joint-reaction forces from kinematic, physiological, and force-plate data. The second uses joint moments and joint-reaction forces to calculate individual muscle forces and compressive and shear forces in three steps: (1) determining the forces in the quadriceps, hamstrings and gastrocnemius muscles and lateral support tissues in the knee; (2) applying them along with joint-reaction forces onto the tibia; and (3) determining knee-joint forces. Our estimates for knee muscle and joint forces compare favorably to those of other predictive models (22–26) and are highly similar to measured forces from instrumented knee joint prostheses (27;28). Our model also incorporates the procedures of Schipplein et al. (23) to directly assess the contributions of the lateral ligaments, other supporting structures, and the quadriceps muscle to frontal plane loads. The model and its limitations are comprehensively discussed elsewhere (29).

Statistical Analysis

Initial analyses included descriptive statistics of participant demographic and clinical characteristics consisting of frequency tables and percentages for categorical variables and means and 95% confidence intervals (95% CI) for continuous variables. Statistical comparisons to compare the baseline characteristics of the x-ray subsample to the remaining IDEA participants utilized t-tests for continuous characteristics and chi-square tests for categorical characteristics. Alignment data were summarized showing the frequencies and relative frequencies of the three alignment categories as well as summary characteristics of the alignment angles within categories. Similarly, gait analysis data including forces and moments were summarized using unadjusted means and 95% CI, and the extremes within the sample. For each of the measures of knee joint loading a multivariable ANCOVA model was created using SAS v9.3 software to determine the effects that BMI and alignment had on joint loading. Three BMI groups were created: overweight (27–29.9 $kg \cdot m^{-2}$), class 1 obesity (30–34.9 $kg \cdot m^{-2}$), and class 2+ obesity (35–41.3 $kg \cdot m^{-2}$) to go along with the three alignment categories [valgus (<0.0 deg), neutral (0–2.0 deg) and varus (>2.0 deg)]. The model included both BMI and alignment categories, the interaction between the two, and adjustment variables gender and walking speed. For each model, regression assumptions were checked by analyzing residuals using univariate statistics testing for normality and visually using quantile-quantile plots and histograms. The significance level was set at a P value ≤ 0.05, and pairwise comparisons within the 3-category BMI and alignment groupings were performed using Tukey’s method. The outcome estimates and comparisons are generated from an ANCOVA model that simultaneously fits BMI category and alignment category, their interaction, gender, and gait speed. No interactions were significant (p>0.05) hence; the main effects for BMI and alignment categories are presented.

Results

There were no statistically significant differences in BMI (p=0.38), gender (p=0.34), age (p=0.95), self-reported function (p = 0.07), and walking speed (p=0.33) between the 157 individuals included in this study and the other 297 IDEA participants.

Mean alignment data measured from the full length radiographs are summarized in Table 2. The outcomes of interest from the biomechanical gait analysis are presented in Table 3.

Mean peak compressive force was 2.9 times mean body weight (BW), shear force was 0.45 BW, and patellofemoral compressive force was 0.47 BW.

Measures of alignment and BMI were included in the ANCOVA models to estimate knee joint loads (both bone-on-bone knee joint forces and joint moments) after adjusting for gender and walking speed. The BMI-alignment interaction was not statistically significant for all models; thus Table 4 presents the least squares means of the main model effects. Participants in the highest BMI category had the greatest compressive ($p = 0.0006$) and shear forces ($p = 0.004$), independent of alignment.

After adjusting for gender and walking speed, the association of alignment with the knee adduction moment was statistically significant ($p < 0.0001$) such that individuals with varus alignment had higher mean adduction moments than those with a neutral alignment, independent of BMI category (Table 4). Those with valgus alignment, on average had adduction moments that were 10 Nm less than those with a neutral alignment ($p <0.0001$). In contrast, knee force variables and the external flexion moment were not significantly related to alignment.

Discussion

Alignment and BMI were associated with different measures of joint loads in older adults with knee OA; *i)* alignment with the external knee adduction moment and *ii)* BMI with knee compressive and shear forces. However, there was no significant interaction effect after controlling for gender and walking speed; alignment did not influence the relationship between BMI and joint loads, and BMI did not influence the association between alignment and joint loads. These results may prove useful in determining the appropriate outcome measures to use in randomized clinical trials. For example, the external adduction moment would be more appropriate for a study on bracing, which seeks to alter alignment, whereas the bone-on-bone knee compressive force would be the outcome of choice for a weight loss study.

Although the results of previous studies are mixed, knee malalignment and obesity are suggested risk factors for the incidence and progression of knee OA, principally by increasing joint loading beyond normal healthy values, but with a metabolic role for obesity likely serving as a contributing factor (3–8;11). Previous work suggests that varus malalignment may mediate the effect that obesity has on OA disease progression. Moyer et al. (11) found a significant interaction of body mass with alignment on the external knee adduction moment such that people with a high body mass and varus malalignment exhibited a greater external adduction moment, a surrogate measure of medial knee joint loading. In addition to the external adduction moment used in the Moyer et al. study, we analyzed the bone-on-bone joint forces derived from musculoskeletal modeling. Furthermore, we used BMI instead of body mass because our interest was in the association of alignment with obesity. Analysis of the data using body mass instead of BMI, however, resulted in similar significant results (data not shown).

Moyer et al. (11) suggested that when evaluating the effects of an intervention that attempts to alter alignment, controlling for body mass is important because it moderates the relationship between alignment and the external knee adduction moment. In contrast, within our cohort of knee OA patients that had a wide range of frontal plane knee alignment angles, there was no significant interaction between alignment and BMI indicating that they influence different measures of joint loading; alignment is more closely associated with the symmetry or balance of loads across medial and lateral knee compartments (i.e., the external adduction moment), while BMI is associated with the magnitude of total tibio-femoral force (i.e., bone-on-bone joint forces). Both studies agree, however, that weight loss interventions do not need to control for alignment because weight has little effect on the external adduction moment.

Higher BMI was associated with greater knee joint forces. Participants in the class 2+ obesity group (BMI between 35–41 $kg \cdot m^{-2}$) had significantly greater compressive and shear forces, with a clear dose response effect (Table 4). Specifically, the class 2+ obese group exerted a peak knee compressive force per step that was 8% greater than the class 1 obesity group [$(2993\ N-2772\ N)/2772\ N \times 100 = 8\%$)] and 24% greater (582 N) than participants in the overweight group. For peak shear forces, these differences were 13% (54 N) and 28% (103 N) between class 2+ and class 1 obesity, and class 2+ and overweight, respectively. An adult takes approximately 2,000–2,500 steps per mile walked; based on our data the difference in peak compressive loads could exceed 1.2 million N and the difference in peak shear loads could exceed 206,000 N per mile walked between class 2+ obesity and overweight. Importantly, the difference in compressive loads between class 2+ and overweight (mean difference = 582 N, see Table 4) is approximately 2.5 times the group differences in body weight (difference in body weight = 230 N, see Table 2), accentuating both the detrimental mechanical effect of increased obesity on joint loads and the therapeutic benefits possible with weight loss.

The external knee adduction moment is a valuable surrogate measure of medial compartment joint loading because it is predictive of OA progression (30). Schipplein and Andriacchi (23) proposed that it is the primary determinant of medial compartment loading. Our results also indicate that malalignment influences the adduction moment, such that varus malalignment resulted in a 33% greater peak adduction moment than neutral alignment and twice the value in valgus aligned knees. Unfortunately, efforts to alter varus alignment and unload the medial compartment by reducing the length of the frontal plane knee moment arm with lateral wedges have only met with modest success (31–33).

Study Limitations

Musculoskeletal modeling provides a non-invasive prediction of the bone-on-bone forces using lower extremity joint forces and moments calculated with inverse dynamics, lower extremity kinematics from gait analysis, and anatomical and physiologic characteristics of the participants (29). Each musculoskeletal model used to estimate knee joint loads has limitations; however, they provide useful insight into factors influencing forces at the knee (24). The absence of several knee ligaments, the assumption of no co-contraction by the hip flexors, and the use of a lumped muscle model are limitations of our model. However, our estimated forces and muscle force curves are similar to those of other biomechanical models and produce acceptable and accurate data relative to these models (22;24;26;34). Our results also compare favorably with studies using instrumented prostheses that provide direct measurement of joint forces (25;27;35). Other limitations included the inability to infer causality from the results, and a hypothesis generating rather than a hypothesis driven study design.

Conclusions

Our results suggest that BMI and alignment influence different joint loading measures each linked to disease progression; alignment is more closely associated with the external knee adduction moment, an indication of the asymmetry or imbalance of loads across the medial and lateral compartments (36;37), while BMI is associated with the magnitude of total tibiofemoral force.

Although limited by the cross sectional study design, these data may be useful in selecting treatment options or interventions for knee OA patients and help determine the appropriate outcome measures. For example, bracing or lateral wedges will not likely affect total knee joint compressive loads, but may be an effective treatment to reduce the external knee adduction moment in knee OA patients whereas weight reduction, a common non-pharmacologic intervention in an obese knee OA population, may have a greater effect on knee compressive loads (29).

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Table 1

Descriptive baseline characteristics of the population (n = 157) and comparison to the other IDEA participants (n = 297) not included in this analysis.

	Alignment Cohort N = 157		**Others N = 297**	**P-value**
Variable	**N (%)**		**N (%)**	
Gender				
Female, n (%)	108 (69)		325 (72)	0.34
Race				
White, n (%)	129 (82)		377 (83)	
	Mean (SD)	Range	Mean (SD)	
BMI (kg • m^{-2})	33.4 (3.7)	27.0 – 41.3	33.6 (3.7)	0.38
Body mass (kg)	92.6 (13.9)	66.9 – 145.6	92.9 (14.7)	0.78
Age (years)	66 (6)	55 – 84	66 (6)	0.95
WOMAC function	22.9 (10.8)	0 – 48	24.2 (10.9)	0.07
Walking speed ($m \cdot s^{-1}$)	1.2 (0.2)	0.7 – 1.9	1.2 (0.2)	0.33

Table 2

Baseline alignment and body weight data per classification.

Alignment Classification	N (%)	Alignment Angle		
		Mean (SD)	Minimum	Maximum
Varus	76 (48)	5.6 (3.4)	2.1	20.9
Neutral	42 (27)	1.2 (0.6)	0.0	2.0
Valgus	39 (25)	−2.7 (2.3)	−11.4	−0.1
BMI Classification	N (%)	Body Weight		
		Mean (SD)	Minimum	Maximum
Overweight	36 (23)	78.9 (8.7)	66.9	110.2
Class 1 Obese	67 (43)	82.2 (11.8)	69.9	113.5
Class 2+ Obese	54 (34)	102.3 (11.1)	84.0	145.6

Table 3

Mean (SD) bone-on-bone knee forces, and peak knee external moments during walking. Mean body weight = 912 N (93 kg). PF = patellofemoral.

Forces and Moments	**Mean (SD)**	**Minimum**	**Maximum**
Knee Compressive force (N)	2645 (873)	1241	6337
Knee Shear force (N)	408 (156)	88	894
PF Compressive Force (N)	430 (345)	1.3	2300
Knee Adduction Moment (Nm)	30 (13)	2.2	69
Knee Flexion Moment (Nm)	36 (22)	−12	122

Table 4

Least square means (Tukey-adjusted 95% CI) bone-on-bone forces and knee external moments during walking for BMI and alignment, controlling for gender and walking speed. The interaction between BMI and alignment was not statistically significant hence; the main effects of BMI and alignment are reported. Mean body weight = 912 N (93 kg).

Knee Joint Load	**BMI ($kg{\cdot}m^{-2}$)**				**Alignment**			
	27 – 29.9 Overweight	**30 – 34.9 Class 1 Obese**	**35 – 41.3 Class 2+ Obese**	**P-value BMI category**	**<0° Valgus**	**0°–2° Neutral**	**>2° Varus**	**P-value Alignment**
Compressive Force (N)	2411 (2182, 2639)	2772 (2602, 2943)	2993 (2796, 3190)	0.0006	2734 (2520, 2949)	2651 (2430, 2871)	2791 (2634, 2948)	0.58
Shear Force (N)	369 (322, 415)	418 (384, 453)	472 (432, 513)	0.004	394 (351, 438)	435 (390, 480)	429 (397, 461)	0.33
PF Force (N)	402 (292, 511)	459 (378, 540)	492 (398, 586)	0.45	452 (348, 555)	410 (305, 515)	491 (416, 565)	0.44
Knee Adduction Moment (Nm)	26.4 (22.6, 30.3)	30.4 (27.5, 33.3)	26.6 (23.3, 29.9)	0.12	18.7 (15.1, 22.4)	27.7 (24.0, 31.4)	37.0 (34.4, 39.7)	<0.0001
Knee Flexion Moment (Nm)	33.5 (26.6, 40.4)	36.7 (31.6, 41.9)	41.7 (35.8, 47.7)	0.17	35.6 (29.2, 42.1)	37.1 (30.4, 43.7)	39.2 (34.5, 43.9)	0.65

Pairwise significant differences:

Compressive force: Overweight vs Class 1, Overweight vs. Class 2+

Shear force: Overweight vs. Class 2+, Class 1 vs. Class 2+

Knee Adduction: All alignment categories were significantly different at a Tukey adjusted 0.05 level.