

Knee Joint Loading in Knee Osteoarthritis: Influence of Abdominal and Thigh Fat

STEPHEN P. MESSIER^{1,3,8}, DANIEL P. BEAVERS², RICHARD F. LOESER^{1,7}, J. JEFFERY CARR⁵, SHUBHAM KHAJANCHI¹, CLAUDINE LEGAULT², BARBARA J. NICKLAS^{1,3}, DAVID J. HUNTER⁶, and PAUL DEVITA⁴

¹Department of Health and Exercise Science, Wake Forest University, Winston-Salem, NC; ²Department of Biostatistical Sciences, Wake Forest School of Medicine, Wake Forest University, Winston-Salem, NC; ³Section on Gerontology and Geriatric Medicine, Wake Forest School of Medicine, Wake Forest University, Winston-Salem, NC; ⁴Department of Exercise and Sport Science, East Carolina University, Greenville, NC; ⁵Department of Radiology, Wake Forest School of Medicine, Wake Forest University, Winston-Salem, NC; ⁶Department of Rheumatology, Royal North Shore Hospital and Kolling Institute, University of Sydney, Sydney, AUSTRALIA; ⁷Section on Molecular Medicine, Wake Forest School of Medicine, Wake Forest University, Winston-Salem, NC; and ⁸Department of Rheumatology and Immunology, Wake Forest School of Medicine, Wake Forest University, Winston-Salem, NC

ABSTRACT

MESSIER, S. P., D. P. BEAVERS, R. F. LOESER, J. J. CARR, S. KHAJANCHI, C. LEGAULT, B. J. NICKLAS, D. J. HUNTER, and P. DEVITA. Knee Joint Loading in Knee Osteoarthritis: Influence of Abdominal and Thigh Fat. *Med. Sci. Sports Exerc.*, Vol. 46, No. 9, pp. 1677–1683, 2014. **Purpose:** Using three separate models that included total body mass, total lean and total fat mass, and abdominal and thigh fat as independent measures, we determined their association with knee joint loads in older overweight and obese adults with knee osteoarthritis (OA). **Methods:** Fat depots were quantified using computed tomography, and total lean and fat mass were determined with dual energy x-ray absorptiometry in 176 adults (age, 66.3 yr; body mass index, 33.5 kg·m⁻²) with radiographic knee OA. Knee moments and joint bone-on-bone forces were calculated using gait analysis and musculoskeletal modeling. **Results:** Higher total body mass was significantly associated ($P \leq 0.0001$) with greater knee compressive and shear forces, compressive and shear impulses ($P < 0.0001$), patellofemoral forces ($P < 0.006$), and knee extensor moments ($P = 0.003$). Regression analysis with total lean and total fat mass as independent variables revealed significant positive associations of total fat mass with knee compressive ($P = 0.0001$), shear ($P < 0.001$), and patellofemoral forces ($P = 0.01$) and knee extension moment ($P = 0.008$). Gastrocnemius and quadriceps forces were positively associated with total fat mass. Total lean mass was associated with knee compressive force ($P = 0.002$). A regression model that included total thigh and total abdominal fat found that both were significantly associated with knee compressive and shear forces ($P \leq 0.04$). Thigh fat was associated with knee abduction ($P = 0.03$) and knee extension moment ($P = 0.02$). **Conclusions:** Thigh fat, consisting predominately of subcutaneous fat, had similar significant associations with knee joint forces as abdominal fat despite its much smaller volume and could be an important therapeutic target for people with knee OA. **Key Words:** OSTEOARTHRITIC GAIT, KNEE, FAT MASS, JOINT FORCES

The association between obesity and knee osteoarthritis (OA) was first documented in 1945 (20) and has been widely verified (10,45). Obesity is an important biomechanical risk factor for incident knee OA

primarily because of its tendency to increase knee joint loading (31). Sarcopenic obesity, a condition in which there is greater fat mass and decreased lean mass, is closely associated with knee OA (odds ratio (OR), 3.51) (19). The abdomen and hip–thigh regions store the most fat (41). Abdominal fat consists of subcutaneous, visceral, and intermuscular fat depots, and thigh fat consists primarily of subcutaneous fat. Although excessive abdominal visceral fat is a well-known risk factor for cardiovascular disease, little is known about the contributions that specific fat depots make to knee joint loading and how they affect the OA disease pathway (8).

Davids et al. (7) found that experimentally increasing thigh girth in an anthropometric model scaled to children increased knee joint compressive forces, independent of alignment.

Address for correspondence: Stephen P. Messier, Ph.D., J. B. Snow Biomechanics Laboratory, Department of Health and Exercise Science, Wake Forest University, Winston-Salem, NC 27109; E-mail: messier@wfu.edu.

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Thigh girth (a surrogate measure for thigh fat) was a significant predictor of the peak external adduction moment in middle-age adults without knee pain; however, this relation was not present when moments were normalized to body mass (34). The authors concluded that the presence of obesity, and not thigh or abdominal fat distribution, affected the adduction moment (34). The absence of a significant relation was possibly a consequence of concurrently normalizing the adduction moment to body mass ($\text{N}\cdot\text{m}\cdot\text{kg}^{-1}$) and statistically controlling for mass (kg), height (m), and body mass index (BMI) ($\text{kg}\cdot\text{m}^{-2}$).

We sought to investigate the relation between obesity and knee OA by partitioning obesity into discreet anatomical compartments. Three statistical models were used to determine the relations that total body mass, lean and fat mass, and regional fat mass depots have with knee joint loading in overweight and obese adults with knee OA. The importance of knowing the contribution that lean and fat mass and specific fat depots make to knee joint loading may help inform future knee OA rehabilitation techniques.

METHODS

Design

The Intensive Diet and Exercise for Arthritis trial was a single-blinded, 18-month, randomized controlled clinical trial conducted at Wake Forest University with the approval of the institutional review board and in accordance with the Helsinki declaration. An informed consent was obtained in writing from all participants.

Participants

Participants ($n = 454$) were randomized into one of three groups: exercise only, intensive dietary weight loss only, or intensive dietary weight loss plus exercise. The study described here used baseline data from a randomized subset of participants ($n = 176$); equal numbers from each group received computed tomography (CT) scans to measure fat depots in the thigh and abdomen.

Entry criteria included the following: (a) ambulatory persons age ≥ 55 yr, (b) Kellgren–Lawrence (K–L) grade 2 or 3 radiographic tibiofemoral OA of one or both knees, (c) $27 \text{ kg}\cdot\text{m}^{-2} \leq \text{BMI} \leq 41 \text{ kg}\cdot\text{m}^{-2}$, and (d) sedentary lifestyle. Study design and rationale are presented in detail elsewhere (25).

Measurements and Procedures

Gait analysis. Before 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 six times, and the freely chosen walking speed was calculated as

the mean of the six trials. This speed ($\pm 3.5\%$) was used in all subsequent gait evaluations.

Three-dimensional high-speed (60 Hz) motion analysis used a six-camera system (Motion Analysis Corp., Santa Rosa, CA) 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 joint moments 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 (9) and detailed elsewhere (23). To control for footwear effects, each participant wore the identical make and model of athletic shoes during testing.

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; and (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 (9,23). We have used our model extensively to estimate knee joint biomechanics (9,22–24). Our predictions for knee muscle and joint forces compare favorably with those of other predictive models (33,43) and are similar to measured forces from instrumented knee joint prostheses (12,26).

Fat depot measurements. Whole-body fat and lean mass were measured by dual energy x-ray absorptiometry using a fan-beam scanner (Delphi A; Hologic, Waltham, MA), following the manufacturer's recommendations for patient position and scan protocols and analysis. CT scans, using a GE 16-slice LightSpeed Pro, quantified thigh (intermuscular and subcutaneous) and abdominal (intramuscular, subcutaneous, and visceral) fat depots. All measures of depot volume were in cubic centimeters.

Participants were placed supine in the scanner with arms above the head and legs flat. Abdomen technique was 120 kVp, 320 mA, 2.5-mm thick slices, a helical pitch of 6.25 mm per rotation, and a gantry speed of 0.5 s. Scanning covered the lower abdomen, including the umbilicus and lower lumbar vertebra, using a 50-cm scan and display field that included the entire girth. To ensure consistent, standardized measurement of tissue volume, slices covering exactly 15 cm superior to inferior (head to foot) were analyzed. The first sacral segment was used as the inferior landmark to ensure comparable placement of the measurements between and within participants (30). Fat tissue was defined by CT numbers in the range of -190 to -30 . Fat depots were defined by technicians segmenting volumes on the basis of established anatomical boundaries. Subcutaneous fat was defined as outside the abdominal wall musculature; visceral fat, as within the inner aspect of the abdominal wall; and

TABLE 1. Total mass and abdominal and thigh fat measures for a 1-cm slice ($\text{cm}^3 \cdot \text{cm}^{-1}$).

	Mean	SD	95% CI
Total lean mass (kg)	55.9	11.6	54.1–57.7
Total fat mass (kg)	36.3	7.6	35.2–37.5
Total body mass (kg)	92.3	13.7	90.1–94.4
Abdominal fat mass ($\text{cm}^3 \cdot \text{cm}^{-1}$)	548.7	128.5	529.6–567.8
Abdominal subcutaneous fat ($\text{cm}^3 \cdot \text{cm}^{-1}$)	326.3	98.1	311.7–340.9
Abdominal visceral fat ($\text{cm}^3 \cdot \text{cm}^{-1}$)	205.5	87.8	192.4–218.5
Abdominal intermuscular fat ($\text{cm}^3 \cdot \text{cm}^{-1}$)	17.0	7.2	15.9–18.1
Thigh fat mass ($\text{cm}^3 \cdot \text{cm}^{-1}$)	188.1	59.7	179.3–197.0
Thigh subcutaneous fat ($\text{cm}^3 \cdot \text{cm}^{-1}$)	181.8	59.6	173.0–190.7
Thigh intermuscular fat ($\text{cm}^3 \cdot \text{cm}^{-1}$)	6.3	3.7	5.8–6.9
Thigh muscle mass ($\text{cm}^3 \cdot \text{cm}^{-1}$)	120.1	27.0	116.1–124.1

intermuscular fat, as within the abdominal and paraspinal musculature. The intraclass correlation coefficient of the measurement of visceral fat volume in our laboratory is 0.99 (30).

Bilateral thigh scans were conducted at 120 kVp, 350 mA, 10-mm helical with a pitch of 11.25 mm per rotation, and a gantry speed of 0.8 s. The femur, from head to medial condyle, was measured and divided into three equal lengths. Measurements were performed on 50-mm-long slices centered at the boundary of the proximal and middle third of the femur. In addition to total fat, analysts defined a boundary on each slice on the basis of the location of the musculature to define the subcutaneous and intermuscular depots. The side with the most affected knee was used in subsequent statistical analyses. To compare the relative contributions of abdominal and thigh fat to knee joint loads, CT images performed volumetrically (cm^3) were divided by the z dimension (15 cm for the abdomen and 5 cm for the thigh) to create the volume per 1 cm, or cubic centimeters per centimeter ($\text{cm}^3 \cdot \text{cm}^{-1}$) (an area measurement).

X-rays. Bilateral, semiflexed, posterior–anterior, weight-bearing knee x-rays were used to identify tibiofemoral arthritis. K–L grade (0–4) was used to quantify its severity (17). All participants had grades 2 or 3 in their most affected knee.

Statistical Analysis

All summaries of continuous data are presented using means, SD, and 95% confidence intervals (CI). Linear regression was used to model the relation between the outcome measures of force (knee compressive, shear, and patellofemoral forces) or moments (knee internal abduction and extension moments) and independent measures of body mass, lean and fat mass, and thigh and abdominal fat depots. A multivariable linear regression model (model 1) was first fit for each knee joint force and moment, with total body mass as the independent variable, controlling for Western Ontario and McMaster Universities Arthritis Index (WOMAC) pain, gender, and walking speed. Further regression models were then fit to determine the association between each force and moment outcome and total lean and fat mass simultaneously, controlling for WOMAC pain, gender, and walking speed (model 2). WOMAC pain was included as a covariate because it was previously shown to be related to knee joint loading (1,35).

In model 3, we compared the association between total abdominal and total thigh fat with each knee joint load and moment, adjusting for WOMAC pain, gender, walking speed, and thigh muscle volume. Significance was set at $P \leq 0.05$ for all analyses. All statistical analyses were conducted using the SAS 9.3 software (SAS Institute, Cary, NC).

RESULTS

BMI ($33.5 \pm 3.6 \text{ kg} \cdot \text{m}^{-2}$), gender (72% female), age (66.3 ± 6.3 yr), and walking speed ($1.21 \pm 0.19 \text{ m} \cdot \text{s}^{-1}$) did not differ significantly among the 176 study participants and the other 278 Intensive Diet and Exercise for Arthritis participants. Fat comprised 61% of the thigh fat plus thigh muscle volume, with 97% of the fat subcutaneous; subcutaneous fat accounted for 59% of the total abdominal fat. Table 1 shows mean (SD, 95% CI) values for all fat measures and thigh muscle mass. Total body fat was correlated with total thigh fat ($r = 0.65$, $P < 0.0001$) and total abdominal fat ($r = 0.67$, $P < 0.0001$). Total thigh fat was correlated with thigh subcutaneous fat ($r = 0.99$, $P < 0.0001$), and total abdominal fat was correlated with abdominal subcutaneous fat ($r = 0.71$, $P < 0.0001$). Thigh intermuscular fat was not significantly correlated with total thigh fat ($r = 0.06$, $P = 0.40$), but abdominal intermuscular fat was correlated with total abdominal fat ($r = 0.51$, $P < 0.0001$). Total abdominal fat was significantly correlated with abdominal visceral fat ($r = 0.63$, $P < 0.0001$).

Association of body mass with knee joint loads (model 1). Table 2 shows the mean peak knee joint forces and moments. Regression analyses adjusting for pain, gender, and walk speed revealed that total body mass was significantly associated ($P < 0.0001$) with peak knee compressive and shear forces and impulses, peak patellofemoral compressive force ($P = 0.006$), and peak knee extension moment ($P = 0.004$), with R^2 values ranging from 0.34 to 0.64. Body mass was also associated with quadriceps, hamstrings, and gastrocnemius muscle forces. In all cases, higher body mass was related to greater knee joint force, impulse, moment, or muscle force (Table 3). Total body mass was not significantly associated with peak abduction moment ($P = 0.22$) or impulse ($P = 0.81$).

Association of lean and fat mass with knee joint loads (model 2). When both lean and fat mass were included in a multiple regression model, fat mass was significantly

TABLE 2. Mean peak knee joint forces (in newtons (N) and multiples of body weight) and moments during walking (N·m).

Knee Joint Load	Mean (SD)	Body Weight Multiple
Compressive force (N)	2764 (890)	3.0
Shear force (N)	401 (150)	0.4
Patellofemoral force (N)	454 (344)	0.5
Internal abduction moment (N·m)	31 (14)	—
Internal extension moment (N·m)	35 (22)	—
Quadriceps force (N)	1284 (45)	
Hamstring force (N)	725 (27)	
Gastrocnemius force (N)	707 (12)	
Compression impulse (N·s)	1203 (24)	
Shear impulse (N·s)	160 (5)	
Knee abduction moment impulse (N·m·s)	10.4 (0.6)	
Knee extension moment impulse (N·m·s)	7.2 (5.6)	

Mean body weight was 908.5 N (men, 1027 N; women, 862 N), with 1 lb = 4.45 N.

TABLE 3. Associations of body mass, total lean and fat mass, and thigh and abdominal fat mass with knee joint loading.

		Model 1 ^a		Model 2 ^b		Model 3 ^c	
		Body Mass	Total Lean Mass	Total Fat Mass	Thigh Fat	Abdominal Fat	
Compressive force	<i>R</i> ²	0.62		0.62		0.58	
	<i>P</i>	<0.0001	0.002		0.0001	0.005	0.0008
Shear force	<i>R</i> ²	0.41		0.48		0.41	
	<i>P</i>	<0.0001	0.41	<0.001		0.0004	0.04
Patellofemoral compressive force	<i>R</i> ²	0.34		0.38		0.33	
	<i>P</i>	0.006	0.85	0.02		0.14	0.22
Abduction moment	<i>R</i> ²	0.11		0.12		0.13	
	<i>P</i>	0.22	0.06	0.62		0.03	0.12
Extension moment	<i>R</i> ²	0.34		0.38		0.35	
	<i>P</i>	0.004	0.93	0.01		0.02	0.41
Quadriceps force	<i>R</i> ²	0.47		0.52		0.47	
	<i>P</i>	<0.0001	0.46	<0.0001		0.01	0.05
Hamstring force	<i>R</i> ²	0.46		0.42		0.44	
	<i>P</i>	<0.0001	0.01	0.33		0.07	0.02
Gastrocnemius force	<i>R</i> ²	0.80		0.81		0.69	
	<i>P</i>	<0.0001	<0.0001	<0.0001		<0.0001	<0.0001
Compressive impulse	<i>R</i> ²	0.68		0.64		0.58	
	<i>P</i>	<0.0001	<0.0001	0.0002		<0.0001	0.0006
Shear impulse	<i>R</i> ²	0.38		0.36		0.35	
	<i>P</i>	<0.0001	0.01	0.01		<0.0001	0.25
Abduction moment impulse	<i>R</i> ²	0.14		0.16		0.15	
	<i>P</i>	0.81	0.35	0.57		0.23	0.21
Extension moment impulse	<i>R</i> ²	0.19		0.21		0.20	
	<i>P</i>	0.09	0.64	0.50		0.02	0.48

Regression equations control for WOMAC pain, gender, and gait speed. Model 3 also controls for thigh muscle volume.

^aModel for overall body mass associated with each joint load.

^bModel that includes both total lean and total fat mass.

^cModel that includes both thigh and abdominal fat and controls for thigh muscle volume.

associated with more knee loading variables than lean mass. Specifically, total lean and total fat mass were significantly associated with peak knee compressive force ($P_{lean} = 0.002$; $P_{fat} = 0.0001$), compressive impulse ($P_{lean} < 0.0001$; $P_{fat} = 0.0002$), and shear impulse ($P_{lean} = 0.01$; $P_{fat} = 0.01$); however, total fat mass was also related to peak knee shear force ($P < 0.001$), peak patellofemoral force ($P = 0.02$), and peak knee extension moment ($P = 0.01$), whereas total lean mass was not. Of the three muscle forces, the gastrocnemius had the strongest relation with lean and fat mass ($R^2 = 0.81$).

Association of thigh and abdominal fat with knee joint loads (model 3). Our third model included total thigh fat and total abdominal fat independent of total thigh muscle volume. The combination of thigh and abdominal fat in model 3 was significantly related to peak compressive force ($R^2 = 0.58$) and peak shear force ($R^2 = 0.41$), with both thigh ($P = 0.005$) and abdominal ($P = 0.0008$) fat significantly contributing to higher forces. Similar results were found for compressive and shear impulses; thigh fat made the larger contribution to shear force and shear impulse. Thigh fat was positively associated with peak knee extension moment ($P = 0.02$), knee extension moment impulse ($P = 0.02$), and peak abduction moment ($P = 0.03$). When total fat mass was entered into model 3, neither thigh nor abdominal fat was independently associated with any joint load measures (data not shown).

Abdominal fat was significantly associated with all muscle forces, with larger fat depots associated with higher forces. Thigh fat was similarly associated with quadriceps and gastrocnemius muscle forces but not with hamstring force. The strongest relation was between thigh and

abdominal fat and gastrocnemius muscle force, with an R^2 value of 0.69.

DISCUSSION

Several studies (6,24,34) confirm what seems intuitive—that higher body mass and greater lower extremity joint loading are positively associated. Consistent with our previous work (24), we found strong relations between bone-on-bone knee joint compressive and shear forces, compressive and shear impulses, patellofemoral forces, and peak knee extension moment and total body mass. Each muscle group in our musculoskeletal model, the quadriceps, hamstrings, and gastrocnemius had significant associations with total body mass, with the gastrocnemius having the highest R^2 value of 0.80.

Many knee OA studies have stressed the importance of the internal knee abduction moment as a surrogate measure of joint loading (4,16,37). In the presence of varus alignment, it has been associated with incidence and progression of knee OA (36,37). There is also support for the relation between the abduction moment and body mass in the case of massive weight loss after bariatric surgery (14). We found no significant relation between body mass and the internal abduction moment or the abduction moment impulse. Two factors may explain the lack of significance: (a) in previous studies, peak internal abduction moment was most strongly associated with varus-misaligned knees (2,3,15,28), and we included participants independent of knee alignment, thereby attenuating the strength of any relation with body mass, and (b) our participants had K–L scores of 2 or 3, and

Mündermann et al. (29) showed that internal abduction moment is significantly higher in patients with more severe knee OA ($K-L \geq 3$). Interestingly, in model 3 that included thigh and abdominal fat as independent measures adjusted for thigh muscle volume, thigh fat was associated with the internal abduction and extension moments, suggesting that excessive thigh fat is related to greater compressive knee loads, most likely acting as a wobbling or vibratory mass that increases knee joint moments. Taken together, these data suggest that total body mass and total fat mass have little influence on the internal abduction moment but thigh fat may play a significant role in increasing both joint forces and joint moments.

Body mass equals the sum of all lean and fat tissue. As independent measures in model 2, they were significantly related to bone-on-bone knee joint compressive force, with fat mass contributing more to the relation than lean mass. Only fat mass was related to peak shear and patellofemoral forces. Fat mass was also associated with the internal extension moment. Although weight loss in knee OA patients includes substantial loss of lean mass even in the presence of exercise (27), reducing fat mass likely plays a greater role in attenuating knee joint loads than reducing muscle mass.

Of the three muscle groups in our musculoskeletal model, total lean and total fat mass were most strongly associated with the gastrocnemius muscle force. The gastrocnemius plays a major role in generating knee joint forces and moments in an effort to control the forward motion of the leg throughout stance and to stabilize upper body mass (32). Hence, as obesity increases, the gastrocnemius muscle force must increase to stabilize the larger mass.

Normal muscle mass in older overweight and obese adults (i.e., nonsarcopenic obesity) is also related to a lower prevalence of knee OA (OR, 2.38) compared with that in adults of similar weight with low muscle mass (OR, 3.51) (19). Greater thigh muscle mass can effectively dissipate energy associated with total body mass and position through eccentric contractions and improve gait mechanics, helping to attenuate joint loads. However, Sharma et al. (36) suggested that strong quadriceps may exacerbate OA disease progression in the presence of varus misalignment. Our results indicate that lean mass is associated with increases in compressive knee joint forces and hamstring and gastrocnemius muscle forces. Recent work also found a positive association between skeletal muscle mass and the prevalence of knee OA, although the percentage of total muscle mass was negatively associated (42). We have argued that increased lower extremity muscle forces have beneficial effects on gait; however, our results do not eliminate the possibility, as Sharma suggested, that increased thigh muscle mass may also have a negative effect on the knee under certain conditions. Until more definitive evidence exists, preserving lean mass in older adults and reducing the ratio of fat mass to lean mass, as recommended by the American College of Sports Medicine, should remain a priority in the nonpharmacological treatment of knee OA (18).

A previous work, using the internal abduction moment as a measure of joint loading, concluded that excessive body mass and not the location of fat deposition increased the risk of knee OA (34). Indeed, when total fat mass was entered into model 3 with thigh and abdominal fat, only total fat mass was associated with knee joint load measures. However, the correlations between total fat and thigh fat ($r = 0.65$) and abdominal fat ($r = 0.67$) are moderate, suggesting that individual fat depots (i.e., abdominal and thigh) are, in some way, different than total fat mass. Using a more diverse set of joint loading and fat depot measures, our data suggest that despite the threefold larger volume of abdominal fat compared with that of thigh fat (549 cm^3 per 1-cm abdominal thickness vs 188 cm^3 per 1-cm thigh thickness) (Table 1), they were both significantly associated with peak knee compressive and shear forces. Moreover, it was thigh fat, not total fat or abdominal fat, that was significantly related to the knee abduction moment.

Thigh fat has little positive influence on gait mechanics. It is a noncontractile tissue that increases joint loading while providing minimal joint protection via shock absorption or joint stability (34). Thigh fat may also have a detrimental inflammatory effect on the pathophysiology of knee OA (13,19). This is not to underestimate the influence of abdominal fat depots on joint loading, which is substantial. Rather, the influence of thigh fat on joint loading combined with its location just proximal to the knee joint makes it a possible therapeutic target.

Although providing useful insights, all musculoskeletal models used to predict knee joint loads have limitations (21). Specifically, the absence of several knee ligaments, the assumption of no cocontraction by the hip flexors, and the use of a lumped muscle model are limitations of our model. However, our predicted joint force and muscle force curves are similar to those of other biomechanical models (21,38,43) and are highly similar to measured values using an instrumented knee prosthesis (26).

Our results confirm that reduced total body mass and total fat mass are associated with lower knee joint loading in older, overweight, and obese adults with knee OA. Partitioning of general body obesity into abdominal and thigh compartments revealed that thigh fat had similar significant associations with knee joint forces as abdominal fat despite its much smaller volume. Targeting reductions in thigh fat, however, has met with mixed results (11,39,40,44). Lean muscle mass was positively related to knee joint compressive loads, although the possibility that increased thigh muscle mass will have a negative effect on the knee by increasing joint stress (36) seems in contradiction to the harmful effects of sarcopenia in older adults (5,19). Future work should determine whether lower extremity strength training, with and without weight loss, can reduce thigh fat depots and increase thigh muscle mass and whether these changes result in either long-term protective or harmful effects on clinical (pain, function, and mobility) and structural (disease progression) outcomes in people with knee OA.

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S. P. M. conceived the study, participated in its design and coordination, carried out the biomechanical gait and strength analysis, and drafted the manuscript. D. P. B., C. L., and C. D. participated in its design and coordinated statistical analyses and data management. R. F. L. participated in its design and coordinated x-ray readings. P. D. participated in its design and helped coordinate the biome-

chanical gait analysis and musculoskeletal modeling. D. J. H. and B. J. N. participated in its design and coordination. J. J. C. coordinated and interpreted the computed tomography data. S. K. participated in data collection and interpretation of the results. All authors read and made comments on previous drafts of the manuscript and approved the final manuscript.

The trial registration number for this study is NCT00381290.

The authors have no conflicts of interest.

The results of this study do not constitute endorsement by American College of Sports Medicine.

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