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KNEE-JOINT LOADING IN KNEE OSTEOARTHRITIS: INFLUENCE OF ABDOMINAL AND THIGH FAT

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Abstract

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 determined with dual energy x-ray absorptiometry in 176 adults (age = 66.3 yr., BMI = 33.5

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There are no conflicts of interest for any of the authors

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CONFLICTS OF INTEREST

The authors have no conflicts of interest.

AUTHOR CONTRIBUTIONS

SPM conceived the study, participated in its design and coordination, carried out the biomechanical gait and strength analysis, and drafted the manuscript. DPB, CL, CD participated in its design, coordinated statistical analyses and data management. RFL participated in its design, and coordinated x-ray readings, PD participated in its design, helped coordinate the biomechanical gait analysis, and musculoskeletal modeling. DJH participated in its design and coordination. BJN participated in its design and coordination. JJC coordinated and interpreted the CT data. SK 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.

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 ($p = 0.0001$) 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 both were significantly associated with knee compressive and shear forces ($p = 0.04$). Thigh fat was associated with the 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.

Keywords

Osteoarthritic gait; knee; fat mass; joint forces

INTRODUCTION

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 due to 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 [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. While excessive abdominal visceral fat is a well-known risk factor for cardiovascular disease, little is known about the contributions specific fat depots make to knee joint loading and how they impact the OA disease pathway (8).

Dauids et al. (7) found that experimentally increasing thigh girth in an anthropometric model scaled to children increased knee joint compressive forces, independent of alignment. Thigh girth (a surrogate measure for thigh fat) was a significant predictor of the peak external adduction moment in middle aged adults without knee pain; however, this relationship 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 relationship was possibly a consequence of concurrently normalizing the adduction moment to body mass (Nm·kg⁻¹) and statistically controlling for mass (kg), height (m), and BMI (kg·m⁻²).

We sought to investigate the relationship between obesity and knee OA by partitioning obesity into discreet anatomical compartments. Three statistical models were used to

determine the relationships 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 lean and fat mass and specific fat depots make to knee-joint loading may help inform future knee OA rehabilitation techniques.

METHODS

The Intensive Diet and Exercise for Arthritis (IDEA) 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. Informed consent was obtained in writing from all participants.

Participants (N = 454) were randomized into one of 3 groups: exercise-only (E), intensive dietary weight loss-only (D), or intensive dietary weight loss-plus-exercise (D+E). 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: (a) ambulatory persons age ≥ 55 years; (b) Kellgren-Lawrence (K-L) grade 2 or 3 radiographic tibiofemoral OA of one or both knees; (c) $27 \text{ kg}\cdot\text{m}^{-2} \leq \text{BMI} < 41 \text{ kg}\cdot\text{m}^{-2}$; and (d) sedentary lifestyle. Study design and rationale are presented in detail elsewhere (25).

Measurements and Procedures

Gait Analysis—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 ($\pm 3.5\%$) was used in all subsequent gait evaluations.

Three-dimensional high-speed (60 Hz) motion analysis used a 6-camera system (Motion Analysis Corporation, 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; (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 to 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 (DXA) using a fan-beam scanner (Delphi A, Hologic, Waltham, MA) following the manufacturer's recommendations for patient position and scan protocols and analysis. Computed tomography (CT) scans, using a GE 16-slice Light Speed Pro, quantified thigh (intermuscular, subcutaneous) and abdominal (intramuscular, subcutaneous, visceral) fat depots. All measures of depot volume were in cm³.

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/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-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 based on established anatomical boundaries. Subcutaneous fat was defined as outside the abdominal wall musculature; visceral fat as within the inner aspect of the abdominal wall; 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/rotation and a gantry speed of 0.8 s. The femur, from head to medial condyle, was measured and divided into 3 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 based on 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 (cm³) were divided by the z dimension (15 cm for the abdomen, 5 cm for the thigh) to create the volume per 1 cm, or cm³·cm^{–1} (an area measurement).

X-rays—Bilateral, semi-flexed, 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, standard deviations, and 95% confidence intervals. Linear regression was used to model the relationship between the outcome measures of force (knee compressive, shear, and patellofemoral) or moments (knee

internal abduction and extension) 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 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 $p = 0.05$ for all analyses. All statistical analyses were conducted using SAS 9.3 software (Cary, NC).

RESULTS

BMI ($33.5 \pm 3.6 \text{ kg} \cdot \text{m}^{-2}$), gender (72% female), age (66.3 ± 6.3 yrs), 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 IDEA participants. Fat comprised 61% of the thigh fat + thigh muscle volume, with 97% of the fat subcutaneous; subcutaneous fat accounted for 59% of total abdominal fat. Table 1 shows mean (SD, %CI) values for all fat measures and thigh muscle mass. Total body fat was correlated with total thigh ($r=0.65$, $p<0.0001$) 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 0.34–0.64. 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 associated with more knee loading variables than lean mass. Specifically, total lean and total fat mass were significantly associated with peak knee compressive force ($p_{\text{lean}} = 0.002$; $p_{\text{fat}} = 0.0001$) compressive impulse ($p_{\text{lean}} < 0.0001$; $p_{\text{fat}} = 0.0002$), and shear impulse ($p_{\text{lean}} = 0.01$; $p_{\text{fat}} = 0.01$); 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 relationship with lean and fat mass ($R^2 = 0.81$).

Association of thigh and abdominal fat with knee-joint loads (Model 3)

Our 3rd 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 the 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 were 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 hamstring force. The strongest relationship 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 appears intuitive, that higher body mass and greater lower extremity joint loading are positively associated. Consistent with our previous work (24), we found strong relationships between bone-on-bone knee joint compressive and shear forces, compressive and shear impulses, patellofemoral forces, and peak knee extension moment with 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 relationship between the abduction moment and body mass in the case of massive weight loss subsequent to bariatric surgery (14). We found no significant relationship 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 malaligned knees (2;3;15;28); we included participants independent of knee alignment thereby attenuating the strength of any relationship with body mass; and (b) our participants had K–L scores of 2 or 3, and Mündermann et al. (29) showed that the internal abduction moment is significantly higher in patients with more severe knee OA (K–L = 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 relationship 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 the 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., non-sarcopenic obesity) is also related to a lower prevalence of knee OA (OR = 2.38) compared to similar weight adults 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 malalignment. 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 impact 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 non-pharmacologic treatment of knee OA (18).

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 ($r = 0.65$) and abdominal ($r = 0.67$) fat 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 3-fold larger volume of abdominal fat compared to thigh fat (549 cm³ per 1-cm abdominal thickness vs. 188 cm³ per 1-cm thigh thickness, see Table 1) they both were 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 non-contractile 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 make it a possible therapeutic target.

While 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 co-contraction 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 impact on the knee by increasing joint stress (36) appears 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, mobility) and structural (disease progression) outcomes in people with knee OA.

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Table 1

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

	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 ($\text{cm}^3\text{cm}^{-1}$)	548.7	128.5	(529.6, 567.8)
Abdominal subcutaneous fat ($\text{cm}^3\text{cm}^{-1}$)	326.3	98.1	(311.7, 340.9)
Abdominal visceral fat ($\text{cm}^3\text{cm}^{-1}$)	205.5	87.8	(192.4, 218.5)
Abdominal intermuscular fat ($\text{cm}^3\text{cm}^{-1}$)	17.0	7.2	(15.9, 18.1)
Thigh Fat Mass ($\text{cm}^3\text{cm}^{-1}$)	188.1	59.7	(179.3, 197.0)
Thigh subcutaneous fat ($\text{cm}^3\text{cm}^{-1}$)	181.8	59.6	(173.0, 190.7)
Thigh intermuscular fat ($\text{cm}^3\text{cm}^{-1}$)	6.3	3.7	(5.8, 6.9)
Thigh Muscle Mass ($\text{cm}^3\text{cm}^{-1}$)	120.1	27.0	(116.1, 124.1)

Table 2

Mean peak knee-joint forces (in Newtons [N] and multiples of body weight [BW]) and moments during walking (Nm).

Knee Joint Load	Mean (SD)	BW 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 (Nm)	31 (14)	--
Internal extension moment (Nm)	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 (Nm's)	10.4 (0.6)	
Knee extension moment impulse (Nm's)	7.2 (5.6)	

N = Newtons

Nm = Newton meters

s = seconds

Mean body weight was 908.5 N (men = 1027 N, women = 862 N). Note: 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. Regression equations control for WOMAC pain, gender, and gait speed. Model 3 also controls for thigh muscle volume.

	Model 1		Model 2		Model 3	
	R ²	P	R ²	P	R ²	P
Compressive Force						
	0.62	<0.0001	0.62	0.0001	0.58	0.0008
Shear Force						
	0.41	<0.0001	0.48	<0.001	0.41	0.04
Patellofemoral Comp Force						
	0.34	0.006	0.38	0.02	0.33	0.22
Abduction Moment						
	0.11	0.22	0.12	0.62	0.13	0.12
Extension Moment						
	0.34	0.004	0.38	0.01	0.35	0.41
Quadriceps Force						
	0.47	<0.0001	0.52	<0.0001	0.47	0.05
Hamstring Force						
	0.46	<0.0001	0.42	0.33	0.44	0.02
Gastrocnemius Force						
	0.80	<0.0001	0.81	<0.0001	0.69	<0.0001
Compressive Impulse						
	0.68	<0.0001	0.64	0.0002	0.58	0.0006
Shear Impulse						
	0.38	<0.0001	0.36	0.01	0.35	0.25

		Model 1		Model 2		Model 3	
		Body + mass		Total lean mass [‡]		Thigh Fat [*]	
				Total fat mass [‡]		Abdominal Fat [*]	
Abduction moment Impulse	R ²	0.14		0.16		0.15	
	P	0.81		0.35		0.23	
Extension moment Impulse	R ²	0.19		0.21		0.20	
	P	0.09		0.64		0.02	
				0.50		0.48	

⁺ Model for overall body mass associated with each joint load

[‡] Model that includes both total lean and total fat mass

^{*} Model that includes both thigh and abdominal fat and controls for thigh muscle volume