Title

508 Is Thigh Intramuscular Fat in Individuals without Radiographic Osteoarthritis or Frequent Pain associated with Knee Strength and Function? Data from the Osteoarthritis Initiative

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Publication Date

2024-04-01

DOI

10.1016/j.joca.2024.02.521

Table1: Performance of the models trained with MRI biomarkers against reference model

Groups	Group 1 (k=1113)			Group 2 (k=811)		Group 3 (k=810)		Group 4 (k=566)		
Metrics	M2	M2+ThC	M2+%dAB	M2	M2+BML	M2	M2+MT	M2	M2+ACL	All MRI
Accuracy	0.733	0.737	0.731	0.707	0.723	0.712	0.708	0.667	0.664	0.668
Sensitivity	0.352	0.377	0.322	0.406	0.426	0.412	0.411	0.478	0.459	0.503
Specificity	0.887	0.883	0.896	0.849	0.863	0.853	0.848	0.784	0.790	0.769
Precision	0.558	0.565	0.556	0.557	0.593	0.569	0.559	0.575	0.572	0.571
AUC	0.739	0.752	0.730	0.732	0.740	0.732	0.729	0.705	0.701	0.710
p-value	-	0.097	0.515	-	0.294	-	0.797	-	0.603	0.754

M2 refers to Model 2 based on TBT parameters adjusted for clinical (age, sex, BMI) covariates and radiological (Kellgren-Lawrence and medical joint space narrowing) scores.%dAB, ThC, BML, MT and ACL refer to Average cartilage thickness, percentage of cartilage area in the subchondral zone, bone marrow lesions, meniscus tears and damage in the anterior cruciate ligament, respectively

508

IS THIGH INTRAMUSCULAR FAT IN INDIVIDUALS WITHOUT RADIOGRAPHIC OSTEOARTHRITIS OR FREQUENT PAIN ASSOCIATED WITH KNEE STRENGTH AND FUNCTION? DATA FROM THE OSTEOARTHRITIS INITIATIVE

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Purpose (the aim of the study): While studies have shown that increased thigh *inter*muscular fat is associated with reduced muscle strength in knee osteoarthritis (OA), the impact of *intra*muscular on knee strength is not well understood. This study aims to assess thigh intramuscular fat based on MRI and its associations with knee strength (flexion and extension) and function, focusing specifically on individuals without radiographic OA or frequent pain in the knee and hip.

Methods: MR imaging (3 Tesla) was used to assess thigh intramuscular fat in 710 individuals (44.5%/55.5% males/females, mean age = 59.8 ± 9.0 years, mean BMI = 27.1 ± 4.3 kg/m^2), from the Osteoarthritis Initiative without knee or hip radiographic OA or total joint arthroplasty, and without frequent knee or hip pain. Axial T1-weighted spin echo images were assessed for intramuscular fat using the Goutallier Grading (GG) scale (0: normal muscle. 1: some fatty streaks. 2: less fat than muscle. 3: equal amounts of fat and muscle. 4: more fat than muscle). The following muscles were graded (right and left thighs): the knee extensors (quadriceps) included the vastus medialis (VM), vastus lateralis (VL), vastus intermedius (VI), rectus femoris (RF), and the knee flexors (hamstrings) included the semimembranosus (SM), semitendinosus (ST), and biceps femoris (BF). The maximum quadriceps grade was defined as the highest GG from VM, BL, VI, and RF, while the maximum hamstring grade was defined as the highest GG from SM, ST, and BF. Strength measurements (per thigh) included knee flexion force [N] and extension force [N]. Function measurements (per person) included the chair stand pace [stands/second].

Mixed effects models were used to separately assess the relationship between GG (predictor) and flexion/extension strength (outcomes). Models accounted for two thighs per person and were adjusted for BMI, age, and sex and Physical Activity Scale for the Elderly (PASE). Linear regression models were used to examine the association between GG (predictor) and chair stand pace (adjusting for age, sex, and BMI). Given that chair stand pace comprises a single measurement per person, accordingly, the average GG grades in the right and left thighs were computed for this analysis. To test if the associations between GG grade and outcomes of strength and function varied by sex, an interaction between GG grade and sex was added to each model described above.

Results: Greater intramuscular fat (GG grade) was significantly associated with lesser flexion and extension strength across various muscle types, as outlined in **Table 1** ($p < 0.05$ for a majority of the muscles) and illustrated in **Figure 1**. The coefficients, indicating the change in force per 1 unit increase in GG grade, ranged from -6.59 for the SM to -12.5 for the RF (flexion outcomes) and from -14.89 for the SM to -21.68 for the VM and VI (extension outcomes).

For the function outcome, greater intramuscular fat was significantly ($p < 0.05$) associated with a slower chair stand pace for all muscles except the RF (**Table 1**). Coefficients, representing the change in chair stand pace per 1 unit increase in GG grade, varied from -0.028 in the SM to -0.040 in the VI. There were no statistically significant interactions between GG and sex on strength or function outcomes ($p > 0.05$) suggesting that the associations between GG and strength and function did not vary by sex.

Conclusions: In individuals without radiographic hip or knee OA and without frequent pain, greater intramuscular fat was associated with lower flexion and extension strength and less function (based on chair stand pace). These results did not vary by sex. Overall, the associations between higher intramuscular fat and reduced muscle strength and function in a “normative” cohort may offer benchmarks and insights into potential mechanisms of obesity-related knee degeneration.

Goutallier Grade (predictor)	Flexion Force (N) Coefficient	95% CI		p-value	Extension Force (N) Coefficient	95% CI		p-value	Chair Stand Pace (stands/second) Coefficient	95% CI		p-value
Quadriceps	-7.329	-13.605	-1.053	**0.022**	-22.674	-33.193	-12.154	**<0.001**	-0.031	-0.049	-0.012	**0.001**
Vastus Medialis	-7.020	-14.113	0.073	0.052	-20.252	-32.327	-8.176	**0.001**	-0.037	-0.056	-0.018	**<0.001**
Vastus Lateralis	-7.694	-13.977	-1.411	**0.016**	-21.680	-32.172	-11.187	**<0.001**	-0.032	-0.051	-0.013	**0.001**
Vastus Intermedialis	-10.724	-17.803	-3.645	**0.003**	-21.684	-33.673	-9.695	**<0.001**	-0.040	-0.060	-0.020	**<0.001**
Rectus Femoris	-12.511	-19.360	-5.663	**<0.001**	-21.325	-32.927	-9.722	**<0.001**	-0.014	-0.035	0.006	0.169
Hamstrings	-5.967	-11.922	-0.012	0.050	-14.988	-24.871	-5.105	**0.003**	-0.028	-0.047	-0.009	**0.004**
Biceps Femoris	-9.262	-16.309	-2.216	**0.010**	-19.299	-31.137	-7.462	**0.001**	-0.031	-0.049	-0.012	**0.001**
Semimembranosus	-6.595	-12.413	-0.777	**0.026**	-14.896	-24.557	-5.236	**0.003**	-0.028	-0.049	-0.007	**0.008**
Semitendinosus	-6.957	-14.351	0.437	0.065	-12.114	-24.666	0.438	0.059	-0.029	-0.050	-0.008	**0.007**

Note: Force outcomes: mixed models adjusted for age, sex, BMI, PASE (accounting for two limbs per person)
Note: Chair stand outcome: regression models adjusted for age, sex, BMI (average Goutallier Grade over both limbs due to one chair stand outcome per person)

Table 1: Associations between Goutallier Grade (predictor) and strength and function (outcomes).

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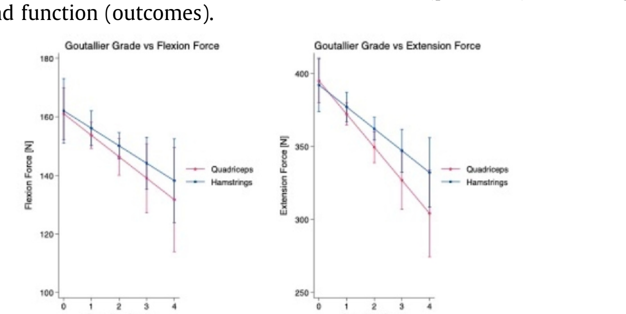

Figure 1: The graphs (based on mixed models) illustrate the associations between Goutallier Grade and Flexion and Extension Force.

Figure 1: The graphs (based on mixed models) illustrate the associations between Goutallier Grade and Flexion and Extension Force.

509

THE RELATIONSHIP BETWEEN ULTRA-PROCESSED FOOD INTAKE AND KNEE CARTILAGE THICKNESS IN MEN AND WOMEN:DATA FROM OSTEOARTHRITIS INITIATIVE

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Purpose (the aim of the study): Knee osteoarthritis (KOA) continues to be a burdensome disease on our globally aging population with increasing obesity. Compared to men, women with KOA appear to have higher rates of cartilage loss. Lifestyle is an important reason behind this sex discrepancy, for which diet is a modifiable factor. Earlier research has highlighted the importance of healthy diets for healthier joints. The prevalence of ultra-processed foods (UPF), defined as food items that are prepared using industrial-scale chemical processing methods is increasing in food markets. Their longer shelf life and increased palatability have increased their presence in our diets especially in the Western world. However, adverse health outcomes have been reported with increased UPF consumption. To date, the relationship between UPF and structural changes related to KOA has not been investigated. This study examined the relationship between UPF and cartilage thickness in men and women with or at risk for developing KOA.

Methods: Participants from the Osteoarthritis Initiative at enrollment (n= 4330, 1817 [42%] men; mean age= 61.3 ± 9.2; mean BMI = 28.6 ± 4.8 kg/m^2) without rheumatoid arthritis(n=66) or unplausible food frequency questionnaire (FFQ) data(n=400) were included.

Dietary information was assessed based on Block Brief 2000 FFQ. It consists of 102 questions on various foods and beverages and inquiries about the quantity (standard servings) and frequency (“everyday” to “never”) of their consumption during the past year. UPF intake was calculated as per NOVA Classification, which groups diet into four classes based on the degree of processing during preparation. NOVA-4 indicates UPF at the highest processing level. The predictor was the percentage of UPF proportion in the daily diet (servings) (NOVA-4/∑(NOVA1-4) x100/365) (**Fig. 1**), the outcome was cartilage thickness (both knees) at enrollment, quantified in 5 regions (medial and lateral tibia [MT-LT]/ femur [MF- LF] and patella) on 3T MRI.

Mixed effects models accounting for two knees/person and 5 regions/knee were used. To assess potential variations in the relationship between UPF and cartilage thickness based on sex and region, a triple interaction model between UPF-region-sex (along with corresponding two-way interactions) was employed. If the interaction was statistically significant ($p < 0.05$) sex- and region-stratified mixed models were employed. All models were adjusted for age, BMI, total daily caloric intake, sex, race, Physical Activity Score of Elderly (PASE), presence of medical insurance and depression. β coefficients represent the change in cartilage thickness (mm) for each 1% increase in UPF proportion (servings) in daily diet.

Results: There was a significant interaction between UPF-cartilage region and sex (p=0.037), suggesting that the association between UPF and cartilage thickness varies by both sex and region. In women, higher UPF was associated with thinner cartilage in MT (β=-0.50, $p < 0.001$), MF (β=-0.51, $p < 0.001$) and LF (β=-0.43, $p < 0.001$). In men, the association between UPF and thickness was not statistically significant in majority of the cartilage regions (β range: 0.10-0.23, $p > 0.05$); the association was significant in the MT (β= 0.40, p=0.016). **Fig. 2** illustrates the associations between UPF and cartilage thickness in men and women for each cartilage regions. **Table 1** outlines sex-stratified relationships between UPF and cartilage thickness in the five knee cartilage regions.

Conclusions: Higher UPF consumption may be associated with KOA in women that is evidenced by thinner cartilage, primary on the medial side of the joint, which may help explain the disproportionately higher disease burden in women. These findings suggest that the contents of our modern diet may be an independent factor affecting cartilage health.

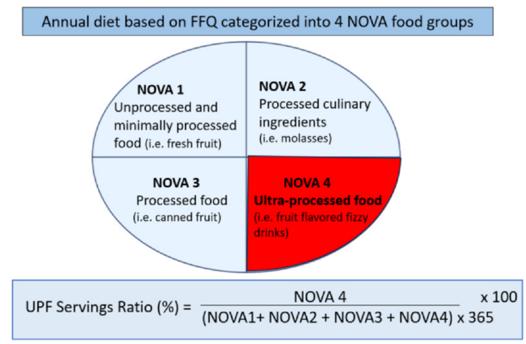

Figure 1. Assessment of the proportion of ultra-processed foods (the predictor) in the overall diet, based on Block Brief 2000 Food Frequency Questionnaire, according to the NOVA Classification of diet.

Figure 1

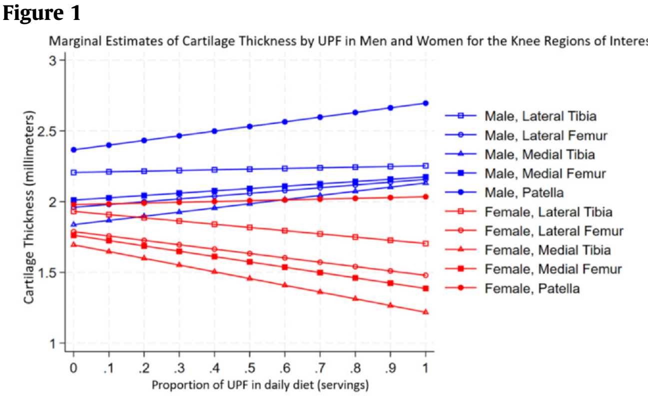

Figure 2: Marginal estimates of cartilage thickness by UPF in men and women for the five knee cartilage regions of interest derived from mixed effects models.

Figure 2

Table 1. Sex-stratified results from mixed effects models with annual UPF servings ratio in diet as predictor and individual cartilage thickness measurements for 5 regions in the knee as outcomes. Beta coefficients represent change in cartilage thickness (in millimeters) for each 1% increase in UPF proportion (servings) in daily diet.

		UPF Proportion (%) in Daily Diet (Predictor)			
Cartilage Thickness Outcomes (mm)		Women		Men	
		β (95%CI)	p-value	β (95%CI)	p-value
Cartilage Regions	Lateral Tibia	-0.22 (-0.51, 0.07)	0.130	0.11 (-0.28, 0.50)	0.528
	Lateral Femur	**-0.43 (-0.66, -0.19)**	**<0.001**	0.23 (-0.10, 0.56)	0.169
	Medial Tibia	**-0.50 (-0.74, -0.26)**	**<0.001**	**0.40 (0.08, 0.72)**	**0.016**
	Medial Femur	**-0.51 (-0.77 -0.25)**	**<0.001**	0.23 (-0.15 0.60)	0.232
	Patella	-0.003 (-0.35, 0.35)	0.988	0.10 (-0.02, 0.21)	0.090

Bold numbers indicate statistically significant results. All models are adjusted for age, race, BMI, PASE, total daily caloric intake, presence or absence of depression and medical insurance.

Table 1