

Osteoarthritis and Cartilage



Longitudinal (4 year) change of thigh muscle and adipose tissue distribution in chronically painful vs painless knees – data from the Osteoarthritis Initiative

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SUMMARY

Objective: To evaluate 4-year longitudinal change in thigh muscle and adipose tissue content in chronically painful vs painless knees.

Methods: Knees from Osteoarthritis Initiative (OAI) participants with non-acceptable symptom status (numerical rating scale (NRS) ≥ 4) and frequent pain (≥ 6 months at baseline, year 2 and year 4 follow-up) were studied. These were matched with painless controls (bilateral NRS pain intensity ≤ 1 and \leq infrequent pain at all 3 timepoints). 4-year longitudinal changes in thigh muscle anatomical cross-sectional areas (CSAs), isometric muscle strength, and in subcutaneous (SCF) and intermuscular fat (IMF) CSAs were obtained from magnetic resonance images (MRI) and were compared between groups (paired *t*-tests).

Results: 43 participants fulfilled the inclusion criteria of chronic pain, had complete thigh muscle MRI acquisitions and strength measurements, and a matched control. Quadriceps CSAs, but not extensor strength, showed a significant longitudinal decrease in chronically painful knees (-3.9% ; 95% confidence interval [95 CI] -6.3% , -1.5%) and in painless controls (-2.4% ; 95% CI -4.1% , -0.7%); the difference in change was not statistically significant ($P = 0.33$). There was a significant 4-year gain in SCF in painful knees (8.1% ; 95% CI 3.1% , 13%) but not in controls (0.0% ; 95% CI -4.4% , $+4.4\%$) with the difference in change being significant ($P = 0.03$). The gain in IMF (-5.2%) was similar between painful and painless knees.

Conclusion: This is the first paper to show a significant impact of (chronic) knee pain on longitudinal change in local subcutaneous adipose tissue. The effect of pain on subcutaneous fat appeared stronger than that on intermuscular adipose tissue and on muscle status.

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Introduction

Knee osteoarthritis (KOA) is one of the most common causes of knee pain in the elderly¹ – particularly in obese patients^{2,3}. In patients with KOA, low thigh, and particularly quadriceps, muscle strength is commonly observed; this has been associated with limited knee function^{4,5} and a further increase in the body mass index (BMI)⁶. Thigh muscle strength, a potentially modifiable risk factor of KOA, has shown to exert beneficial effects on knee pain⁷,

but thigh muscle strength was apparently not protective of structural (radiographic) progression of KOA⁸.

Cross-sectional between-knee, within-person studies suggested that there is no significant relation between radiographic status and thigh muscle strength and did not find smaller quadriceps anatomical cross-sectional areas (CSAs) and extensor strength in limbs with advanced⁹ or with early¹⁰ radiographic alterations. In contrast, a strong association was found between knee pain and thigh muscle strength^{11,12} with smaller quadriceps CSAs and lower extensor strength found in limbs with frequently painful knees than in contralateral painless limbs¹². Further, cross-sectional cohort studies in >3000 participants suggested that knee pain, but not radiographic status, was significantly associated with extensor and flexor muscle strength¹¹, and that extensor and flexor strength both were significantly associated with limb function, as

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assessed by the Western Ontario McMaster Universities (WOMAC) function score⁴. In a first longitudinal study, Beattie *et al.* reported a significant decrease in quadriceps volume and a significant increase in thigh intermuscular fat (IMF) tissue content over 2 years in women with symptomatic KOA; however, the observed change did not exceed that in women without symptoms and radiographic change who had risk factors for KOA¹³.

Recent findings suggest that factors other than biomechanics may be involved in the etiology of KOA¹⁴ and these reported associations of pro-inflammatory adipokines (such as leptin) with cartilage degradation^{15,16} and with knee pain¹⁷. However, no study to date has examined the specific impact of (chronic) knee pain on longitudinal change in thigh subcutaneous fat (SCF) tissue content, IMF, muscle CSAs and muscle strength. Given the important relationship between obesity and KOA^{2,3} and the potential impact of local (thigh) adipose tissue content on knee pain¹⁸ and function¹⁹, the current study was designed to address the following specific questions:

1) Does 4-year change in thigh muscle CSAs and strength differ between limbs with high intensity chronic knee pain vs those with painless knees?

- 2) Does 4-year change in thigh SCF and IMF content differ between limbs with high intensity chronic knee pain vs those with painless knees?
- 3) To what extent are longitudinal changes in SCF and IMF associated with change in muscle CSA and strength, and/or with change in body mass?
- 4) Do the above longitudinal relationships differ between men and women?
- 5) Are there cross-sectional differences in thigh muscle, SCF, and IMF CSAs between limbs with high intensity chronic knee pain vs those with painless knees?

Methods

Participants

Participants for this study were drawn from the entire Osteoarthritis Initiative cohort ($n = 4796$; Fig. 1; <http://www.oai-ucsf.edu/datarelease/>; clinical data sets 0.2.2, 3.2.1, 6.2.2)²⁰. Healthy reference cohort participants ($n = 122$) and participants lacking axial thigh muscle MRIs at baseline or year 2 or year 4 follow-up ($n = 2536$) were excluded.

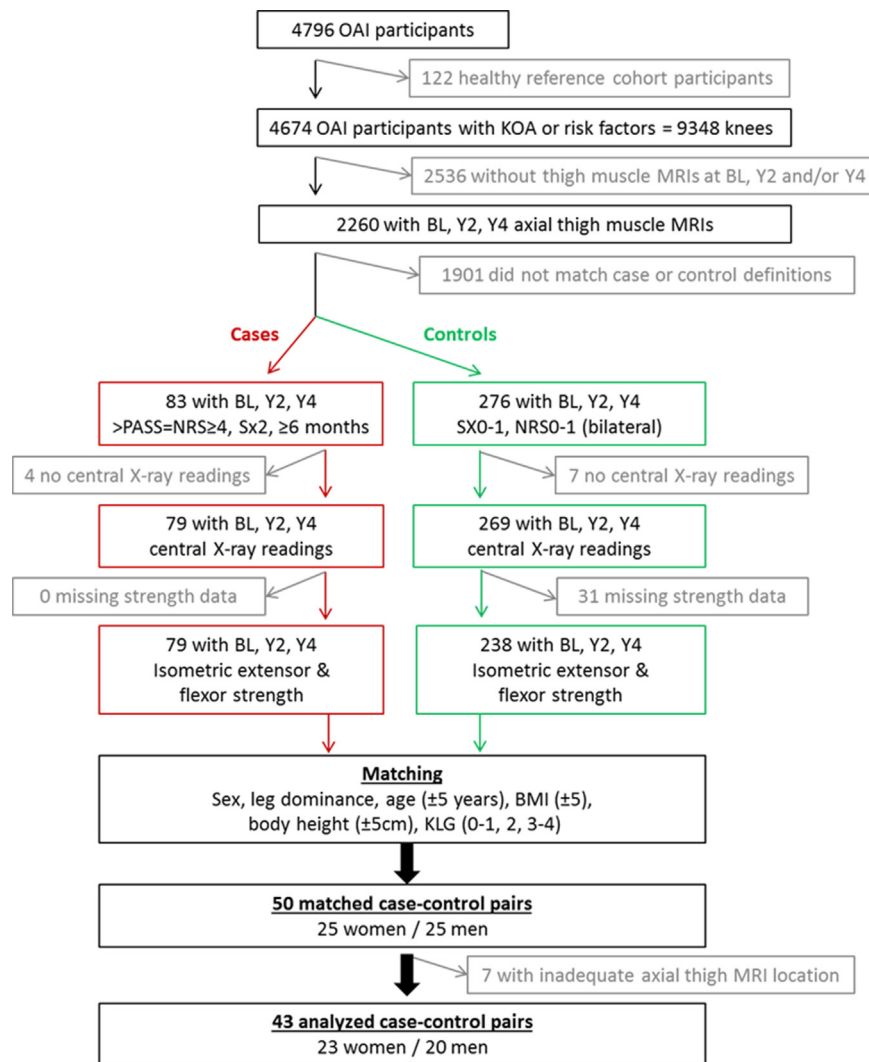


Fig. 1. Process used for selection of participants from the OAI data base. BL = baseline; Y2 = 2-year follow-up; Y4 = 4-year follow-up; PASS = Patient acceptable symptom status; KXSX = pain frequency (0 = no pain; 1 = pain, aching stiffness < half days of a month; 2 = pain aching, stiffness > half days of a month in the last 12 months); NRS = Numerical Rating Scale; BMI = body mass index; KLG = Kellgren–Lawrence grade.

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