



## Research article

# Relative distribution of quadriceps head anatomical cross-sectional areas and volumes—Sensitivity to pain and to training intervention



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## ABSTRACT

**Introduction:** Quadriceps heads are important in biomechanical stabilization and in the pathogenesis of osteoarthritis of the knee. This is the first study to explore the relative distribution of quadriceps head anatomical cross-sectional areas (ACSA) and volumes, and their response to pain and to training intervention.

**Methods:** The relative proportions of quadriceps heads were determined in 48 Osteoarthritis Initiative participants with unilateral pain (65% women; age 45–78 years). Quadriceps head volumes were also measured in 35 untrained women (45–55 years) before and after 12-week training intervention. Cross-sectional areas of the vastus medialis (VM), inter-medius (VIM), and lateralis (VL), and of the rectus femoris (RF) were determined from axial T1-weighted MR images.

**Results:** The proportion of the VM on the total quadriceps ACSA increased from proximal to distal. The difference in quadriceps ACSA of painful (vs. pain-free) limbs was –5.4% for the VM ( $p < 0.001$ ), –6.8% for the VL ( $p < 0.01$ ), –2.8% for the VIM ( $p = 0.06$ ), and +3.4% for the RF ( $p = 0.67$ ) but the VM/VL ratio was not significantly altered. The muscle volume increase during training intervention was +4.2% ( $p < 0.05$ ) for VM, +1.3% for VL, +2.0% for VIM ( $p < 0.05$ ) and +1.6% for RF.

**Conclusion:** The proportion of quadriceps head relative to total muscle ACSA and volume depends on the anatomical level studied. The results suggest that there may be a differential response of the quadriceps heads to pain-induced atrophy and to training-related hypertrophy. Studies in larger samples are needed to ascertain whether the observed differences in response to pain and training are statistically and clinically significant.

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## 1. Introduction

Loss of quadriceps muscle strength is known to have adverse effects on knee joint biomechanics, and to increase joint loading (Andriacchi et al., 2009; Hortobágyi et al., 2004; Jefferson et al., 1990; Lattanzio et al., 1997; Radin et al., 1991; Segal and Glass, 2011; Skinner et al., 1986; Winby et al., 2009). Further,

reduction in quadriceps strength was found to contribute to functional disability and knee pain (McAlindon et al., 1993; O'Reilly et al., 1998; Sattler et al., 2012). Although it is still controversial whether muscle strengthening exercise can effectively reduce the incidence and progression of knee symptoms (Segal and Glass, 2011; Segal et al., 2012, 2009a, 2009b) and structural (particularly radiographic) incidence and progression of knee osteoarthritis (Amin et al., 2009; Brandt et al., 1999; Ding et al., 2008; Eckstein et al., 2013; Mikesky et al., 2006; Roos et al., 2011; Ruhdorfer et al., 2013; Segal and Glass, 2011; Segal et al., 2010b, 2009a, 2012, 2010a; Sharma et al., 2003; Thorstensson et al., 2004), muscle strengthening exercise is currently recommended by the Osteoarthritis Research Society International (OARSI) therapeutic guidelines for knee osteoarthritis (Bennell et al., 2009; Roos et al., 2011; Zhang et al., 2008).

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Anatomically, the quadriceps consists of three heads (vastus medialis [VM], intermedius [VIM], and lateralis [VL]) originating from the femur and inserting via the quadriceps tendon, patellar bone, and patellar tendon at the tibial tuberosity. The fourth head, the rectus femoris (RF), in contrast, originates from the inferior anterior iliac spine and, therefore, not only extends the knee, but also flexes the hip. The VM is known to play an important role in biomechanical stabilization of the femoropatellar joint by pulling the patella medially, keeping contact pressure in the lateral patella facet within limits, and preventing the patella from lateral (sub)luxation relative to the trochlear groove (Elias et al., 2009). Yet, several studies reported that VM strength variation had only a limited effect on patello-femoral biomechanics (Lee et al., 2002; Lorenz et al., 2012). However, the VM and VL have also been proposed to have antagonistic functions with regard to rotating the femur relative to the tibia; and have been suggested to maintain rotational stability of the knee and to be important in prevention of knee injuries (Schmitt and Mittelmeier, 1978). The quadriceps heads (specifically the VM) hence are suspected to play a role in pain and degenerative changes in the femoropatellar (Berry et al., 2008a, 2008b) and femorotibial joints (Fink et al., 2007; Hinman et al., 2002; Pan et al., 2011).

Recent cross sectional studies in participants with “pre-clinical” osteoarthritis suggested that larger VM (versus VL) ACSAs were associated with more cartilage defects in the patella (Berry et al., 2008a; Pan et al., 2011) and with inferior compositional cartilage properties (i.e. magnetic resonance imaging [MRI] transverse relaxation times; T2) in the femorotibial joint (Pan et al., 2011); these studies therefore indicated that a high VL/VM ratio was beneficial to cartilage health. A recent longitudinal study (Wang et al., 2012), in contrast, reported that the baseline VM ACSA was inversely associated (and hence protective) of current knee pain and of longitudinal medial tibial cartilage volume loss. Further, the longitudinal increase in VM ACSA from baseline to year 2 follow-up was found to be associated with a concurrent reduction in knee pain, with reduced medial tibial cartilage loss from 2 to 4.5 years follow-up, and with reduced risk of knee replacement over 4 years (Wang et al., 2012). The authors suggested that optimizing VM ACSA was important in reducing progression of knee osteoarthritis and knee replacement (Wang et al., 2012).

We previously reported that, in patients with the same grade of bilateral radiographic knee osteoarthritis, quadriceps ACSAs and isometric strength were significantly smaller in limbs with frequent knee pain, relative to a contralateral reference knee without pain (Sattler et al., 2012). We further reported that a supervised 12-week training intervention in untrained perimenopausal women (Ring-Dimitriou et al., 2009) involved a statistically significant increase in quadriceps ACSAs and volume (Hudelmaier et al., 2010). However, it is currently unknown whether, and if yes to what extent, there is a differential response of the quadriceps heads. In the current study, we therefore aimed to explore the relative distribution of the heads (i.e. the VL, VIM, VM, RF) to total quadriceps anatomical cross-sectional area (ACSA) and volume, and their individual response to pain and to training intervention.

## 2. Materials and methods

### 2.1. Subjects

We examined data from two cohorts that were previously described in detail, one from the US-based Osteoarthritis Initiative (Eckstein et al., 2014, 2012) that suffered from unilateral frequent knee pain (Sattler et al., 2012), and the other from a 12-week training intervention study performed in Salzburg, Austria (Hudelmaier et al., 2010; Ring-Dimitriou et al., 2009).

The unilateral knee pain sample comprised 48 participants who fulfilled the following criteria: frequent pain (i.e. pain, aching or stiffness in or around the knee for at least 1 month during the past 12 months) in one knee, no pain at all during the past 12 months in the contralateral knee, the same grade of radiographic knee osteoarthritis on fixed flexion radiographs (i.e. Kellgren Lawrence grade [KLG] 2 or 3 in both knees), and availability of thigh muscle MRIs and muscle strength measurements from the OAI data base (Sattler et al., 2012). This sample comprised 17 men and 31 women, aged 45–78 years (mean  $\pm$  standard deviation [SD]  $63 \pm 9.3$  years), and a body mass index (BMI) ranging from 21 to 44 ( $29.9 \pm 4.8$ ). Twenty-one participants displayed bilateral KLG2, and 27 bilateral cKLG3 (Sattler et al., 2012). This intra-individual, between-knee comparison revealed that frequent knee pain was associated with an approximately 5% reduction in quadriceps ACSA relative to the painless limb; this “response” was similar between men and women, and similar between bilateral KLG2 or KLG3 cases (Sattler et al., 2012). The side differences in quadriceps ACSAs were also associated with side differences in extensor strength, but no reduction in hamstring ACSAs or flexor muscle strength were observed in painful limbs (Sattler et al., 2012).

The training intervention study was performed in Salzburg, Austria (Ring-Dimitriou et al., 2009) and recruited 41 untrained women with a physical activity level of less than 1 h a week, no history of organized sports participation, and at the end of their menopause. The participants were assigned to three different training intervention groups: Strength training (ST;  $n = 16$ ), endurance training (ET;  $n = 19$ ) and autogenic training (controls;  $n = 6$ ). The women selected were 45–55 years old ( $50.8 \pm 3.2$  years) with a BMI of  $26.5 \pm 5.2$  kg/m<sup>2</sup> (Ring-Dimitriou et al., 2009). The participants had supervised training sessions 3 times per week for 60 min over 12 weeks (Ring-Dimitriou et al., 2009). The ST intervention significantly improved muscle quality, and both the ST and ET intervention improved cardiorespiratory fitness (i.e. VO(2)peak) (Ring-Dimitriou et al., 2009). Acquiring thigh MRIs before and after the training intervention, a 3.1% increase in total quadriceps volume was recorded after 12 weeks of ST, and a 3.7% increase after ET. There was no relevant or statistically significant change observed with AT (Hudelmaier et al., 2010).

### 2.2. Magnetic resonance imaging (MRI) and muscle segmentation

The analysis of the unilateral knee pain sample relied on the public-use baseline MRI data (O.E.1) from the Osteoarthritis Initiative (Eckstein et al., 2014, 2012). Fifteen axial contiguous 0.5 cm slices ( $0.98 \text{ mm} \times 0.98 \text{ mm}$  in-plane resolution) of both thighs were acquired using a T1-weighted spin echo sequence (TR 500 ms, TE 10 ms; Fig. 1) and a 3 Tesla Magnetom Trio scanner (Siemens Healthcare Erlangen, Germany). The image acquisition started 10 cm proximal to the distal femoral epiphysis and extended 7.5 cm proximally (Fig. 1). Details regarding the MRI techniques and protocols are available online ([www.oai.ucsf.edu/datarelease/operationsmanuals.asp](http://www.oai.ucsf.edu/datarelease/operationsmanuals.asp)) and have been described previously (Eckstein et al., 2014, 2012; Sattler et al., 2012). It is important to note that, due to the fixed (10 cm) distance between the distal femoral epiphysis and the most distal MRI slice acquired, the position of the images relative to the femur and thigh muscles was variable, depending on individual femur length and body height. This variability prevented us from performing a volumetric assessment of the quadriceps (heads) in this part of the study, given lack of comparability between participants. Because the quadriceps heads can be better distinguished distally than proximally (see below), we selected the most distal slice that could be identified to be in an anatomically consistent location across all study participants (given their variability in body height – Fig. 1); this was based on a previously established relationship between femoral length,

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