

ABSTRACT

Objectives

This study aimed to (i) compare the volumes of vastus medialis, vastus lateralis, vastus intermedius and rectus femoris and the ratio of vastus medialis and vastus lateralis (VM/VL) volumes between asymptomatic controls and patellofemoral joint osteoarthritis (PFJ OA) participants; and (ii) assess the relationships between cross-sectional area (CSA) and volumes of the vastus medialis and vastus lateralis in individuals with and without PFJ OA.

Methods

Twenty-two participants with PFJ OA and 11 controls aged ≥ 40 yrs were recruited from the community and practitioner referrals. Muscle volumes of individual quadriceps components were measured from thigh magnetic resonance (MR) images. The CSA of the vastus medialis and lateralis were measured at 10 equally distributed levels (femoral condyles to lesser femoral trochanter).

Results

PFJ OA individuals had smaller normalized vastus medialis (mean difference $0.90 \text{ cm}^3.\text{kg}^{-1}$, $\alpha=0.011$), vastus lateralis ($1.50 \text{ cm}^3.\text{kg}^{-1}$, $\alpha=0.012$) and rectus femoris ($0.71 \text{ cm}^3.\text{kg}^{-1}$, $\alpha=0.009$) volumes than controls. No differences in the VM/VL ratio were observed. The CSA at the 3rd level (controls) and 4th level (PFJ OA) above the femoral condyles best predicted vastus medialis volume, whereas the vastus lateralis volume was best predicted by the CSA at the 7th level (controls) and 6th level (PFJ OA) above the femoral condyles.

Conclusion

2 Reduced quadriceps muscle volume was a feature of PFJ OA. Muscle volume could be predicted from CSA measurements at specific levels in PFJ OA patients and controls.

4

Keywords

6 Vastus medialis, Vastus lateralis, Vasti, Knee, Patella, Arthritis, Muscle size

INTRODUCTION

The patellofemoral joint (PFJ) is the compartment most commonly affected in symptomatic knee osteoarthritis (OA)¹ and is the dominant source of symptoms associated with knee OA^{2,3}. Contemporary clinical guidelines recommend tailored OA management strategies to optimize clinical outcomes, yet there is little known about modifiable impairments that could guide effective management of PFJ OA. Quadriceps weakness plays an important role in the pathogenesis of knee OA⁴ and appears to be more important in the progression of PFJ disease than tibiofemoral joint (TFJ) disease⁵. Dynamometry provides an indication of the force produced by the entire quadriceps; however, the limitations of this technique include an inability to evaluate contributions of the individual quadriceps subregions. This may be important for PFJ OA, since imbalance of the medial (vastus medialis) and lateral (vastus lateralis) quadriceps force may affect PFJ alignment⁶ and hence PFJ contact pressure⁷. Considering that increased PFJ contact pressure is likely to be associated with the initiation and progression of PFJ OA, an imbalance in the force generating capacity of the medial and lateral vasti in people with PFJ OA may be a potentially modifiable factor associated with the development or progression of PFJ OA.

Magnetic resonance (MR) imaging is one technique that is capable of evaluating the force generating capacity of the individual vasti components. While measurement of muscle cross-sectional area (CSA) from MR imaging is gaining popularity as a surrogate measure of individual vasti muscle strength⁸⁻¹⁰, more meaningful information may be obtained from measures of muscle volume. A muscle's force generating capacity, sometimes also referred to as peak isometric muscle strength or peak isometric force¹¹, is related to its volume and its physiological cross sectional area (PCSA)¹². However, prior studies⁸⁻¹⁰ obtained anatomical CSAs of muscles at various levels that may not be representative of the muscles' PCSAs. In a

2 pennate muscle, the anatomical CSA does not account for angle of muscle pennation or
muscle fiber length and hence, may not be a true representative of muscle force. The CSA
4 level of a muscle that has a strong correlation with the muscle's volume should provide an
indication of the muscle's strength. The CSA at this level would provide a measurement that
6 could be used to estimate peak isometric muscle force, and would negate the necessity to
measure the entire muscle volume using MR, which can be expensive and time consuming.

8

The present study aimed to (i) compare the volumes of the individual quadriceps components
10 (vastus medialis, vastus lateralis, vastus intermedius and rectus femoris) and the ratio of
vastus medialis and vastus lateralis (VM/VL) volumes between controls and PFJ OA
12 participants; and (ii) assess the relationships between CSA and volumes of the vastus
medialis and vastus lateralis in individuals with and without PFJ OA.

14

MATERIALS AND METHODS

16 *Participants*

Twenty-two participants with PFJ OA (symptomatic and radiographic) and 11 controls
18 (asymptomatic and no radiographic OA) ≥ 40 years of age were recruited for the study. The
PFJ OA eligibility criteria were based on a previous study protocol¹³. Patients were included
20 if they exhibited clinical symptoms arising from the PFJ (anterior or retropatellar knee pain
severity ≥ 4 on an 11-point numerical pain scale during \geq two PFJ loading activities: stair
22 ambulation, squatting and rising from sitting; aggravating activities, symptoms present on
most days during the past month) and radiographic criteria (Kellgren and Lawrence (KL)
24 grading¹⁴ applied to the lateral PFJ ≥ 2 from skyline views³. While the PFJ OA patients may
have exhibited TFJ OA, PFJ OA patients were excluded if they exhibited a KL grading ≥ 2
26 from postero-anterior views in order to eliminate those with moderate-severe TFJ OA and

2 hence limit our cohort to those with predominant PFJ OA. The control participants had no
lower limb complaints, were physically active and had no radiographic OA (KL grade 0 in all
4 compartments). Exclusion criteria for all participants included major surgery (including
arthroplasty or osteotomy, but not arthroscopy); knee injections (within 3 months); current or
6 previous physiotherapy for knee pain (within 12 months); planned lower limb surgery
(following 6 months); history of hip or knee fractures; current conditions affecting the ability
8 to walk normally; concomitant pain from other knee structures, hips, ankles, feet or lumbar
spine; neurological or medical conditions; fibromyalgia; and contraindications for MR. Ethics
10 approval for the study was obtained from the University of Melbourne Human Research
Ethics Committee and the Department of Human Services Victoria Radiation Safety
12 committee. All participants provided written informed consent. Age, gender, height, body
weight and body mass index (BMI) were recorded for all subjects. The pain subscale of the
14 Knee Injury and Osteoarthritis Outcome Score (KOOS-pain) was used to score knee
osteoarthritis pain¹⁵.

16

Measurement of quadriceps volume

18 MR imaging was performed in the supine position on the most symptomatic leg in the PFJ
OA group and the dominant leg in the control group. Both knees were fully extended to
20 ensure uniformity of positioning between subjects. The MR images were recorded on a
Siemens (Erlangen Germany) 3T Trio MR scanner using a T2-weighted fat-suppressed
22 (water excitation) MEDIC (multi-echo data image combination) gradient echo sequence (TE
= 12 ms, TR = 23 ms, NEX = 1, Flip angle 12 degrees, 155Hz/Px, Parallel imaging GRAPPA
24 2) with a slice thickness of 1 mm isotropic voxels. This sequence was chosen because it was
fast and gave reasonable delineation of muscle, cartilage and bone. The in-plane image
26 resolution was 397 x 916 pixels. The number of coronal images ranged from 300 to 400 for

2 each participant depending on their height. Acquisition time was approximately 25 minutes
per subject.

4

The CSAs of the vastus medialis, vastus lateralis, vastus intermedius and rectus femoris
6 muscles were measured on axial MR images from the origin of the muscle to the insertion by
manually digitizing muscle boundaries using commercially available software (Amira 5.2,
8 Visage Imaging, Berlin). For each muscle, the CSAs of each axial slice were summed and the
total sum of the muscle CSAs was then multiplied by the slice thickness to obtain the muscle
10 volume (Fig 1A). For each participant, the CSAs of the vastus medialis and vastus lateralis
were recorded at ten evenly spaced levels from the femoral condyles through to the lesser
12 trochanter (Fig 1B).

14

16

The intra-rater reliability of the muscle volume measurement technique was quantified in
18 nine randomly selected subjects (5 PFJ OA; 4 controls). The reliability coefficients obtained
for vastus lateralis (ICC=0.998; 95% CI: 0.991 to 1.00), vastus medialis (ICC=0.998; 95%
20 CI: 0.991 to 1.00), vastus intermedius (ICC=0.997; 95% CI: 0.987 to 0.999) and rectus
femoris (ICC=0.994; 95% CI: 0.975 to 0.999) indicate excellent repeatability of the
22 measures. Accordingly, the standard error of measurement (SEM) was acceptably low (vastus
lateralis $0.10 \text{ cm}^3 \cdot \text{kg}^{-1}$; vastus medialis $0.06 \text{ cm}^3 \cdot \text{kg}^{-1}$; vastus intermedius $0.14 \text{ cm}^3 \cdot \text{kg}^{-1}$; rectus
24 femoris $0.05 \text{ cm}^3 \cdot \text{kg}^{-1}$).

26 *Statistical analysis*

2 All data were analyzed with the Statistical Package for the Social Sciences (PASW Statistics
18, SPSS Inc., Chicago, IL) and $\alpha < 0.05$. Between-group differences in participant
4 characteristics were assessed using independent t-tests or chi square tests as appropriate. The
ratio of vastus medialis to vastus lateralis (VM/VL) muscle volume was calculated for both
6 the control and PFJ OA groups. To control for the influence of body weight and gender,
muscle volumes ($\text{cm}^3 \cdot \text{kg}^{-1}$) were normalized to body weight and all between-group
8 comparisons of muscle volumes were performed using an Analysis of Covariance (with and
without gender as a covariate). Radiographic disease severity and knee pain are also potential
10 confounders, and the univariate association of radiographic disease severity of the PFJ
(measured with the KL grading system¹⁴) and the KOOS-pain subscale with the individual
12 muscle volumes was determined using the Spearman's rho correlation coefficient. Regression
analyses were performed on the ten equally-spaced CSAs (from the femoral condyles to
14 lesser trochanter of the femur) of vastus medialis and vastus lateralis to determine the CSA
that best predicted the muscle volume in the control and PFJ OA groups. To evaluate whether
16 dominance influenced vasti muscle size, the CSA that best represented the medial and lateral
vasti was also calculated for the non-dominant leg of the control group, and these were
18 compared to the dominant leg using a paired t-test.

20 **RESULTS**

Participant and disease characteristics

22 The control group (n = 11; age 53 ± 5 years, body weight 71 ± 14 kg, BMI 25 ± 3 $\text{kg} \cdot \text{m}^{-2}$) and
the PFJ OA group (n = 22; age 57 ± 11 years, weight 77 ± 13 kg, BMI 27 ± 4 $\text{kg} \cdot \text{m}^{-2}$) were
24 matched for all participant characteristics ($p > 0.05$). There were more females than males in
both groups (female: male ratios in the control and PFJ OA groups were 7:4 and 15:7,
26 respectively), with no difference in the frequencies ($\chi^2 = 0.546$; p-value = 0.07). No

2 association was observed between muscle volumes and PFJ radiographic disease severity
(vastus medialis: $r_s = -0.291$; $p = 0.189$; vastus lateralis: $r_s = -0.156$; $p = 0.487$; VM/VL ratio:
4 $r_s = -0.202$; $p = 0.367$), or KOOS-pain (vastus medialis: $r_s = -0.135$; $p = 0.550$; vastus
lateralis: $r_s = -0.119$; $p = 0.598$; VM/VL ratio: $r_s = 0.212$; $p = 0.344$).

6

Between-group comparison of quadriceps volume

8 Individuals with PFJ OA had smaller normalized muscle volumes of vastus medialis (mean
difference $0.90 \text{ cm}^3.\text{kg}^{-1}$, 95% confidence interval [0.22 to 1.57]; $\alpha = 0.011$), vastus lateralis
10 ($1.50 \text{ cm}^3.\text{kg}^{-1}$, [0.35 to 2.64]; $\alpha = 0.012$), and rectus femoris ($0.71 \text{ cm}^3.\text{kg}^{-1}$, [0.19 to 1.22; α
= 0.009) than controls (Table 1). No differences were observed in vastus intermedius (0.56
12 $\text{cm}^3.\text{kg}^{-1}$, [-0.59 to 1.71]; $\alpha = 0.331$). These results were reflected in peak isometric muscle
strength comparisons (see Supplementary Material). The ratio of VM/VL muscle volumes in
14 the PFJ OA group (0.66 ± 0.08) and the control group (0.64 ± 0.06) were not different (0.27,
[-0.50; 1.05]; $\alpha = 0.47$).

16

Relationship between vastus medialis and lateralis volumes and cross-sectional areas

18 For the vastus medialis, regression modeling revealed that the CSA at the 3rd level ($r^2 =$
 0.936 ; $B = 17$; $\alpha < 0.001$) and 4th level above the femoral condyles ($r^2 = 0.668$; $B = 18$; $\alpha <$
20 0.001) were the best predictors of muscle volume in the controls and PFJ OA participants,
respectively. For the vastus lateralis, muscle volume was predicted by the CSA at the 7th level
22 above the femoral condyles ($r^2 = 0.916$; $B = 26$; $\alpha < 0.001$) in the controls, and at the 6th level
above the femoral condyles ($r^2 = 0.705$; $B = 17$; $\alpha < 0.001$) in the PFJ OA participants. These
24 levels generally represented the largest CSA for each muscle.

26 *Comparison of muscle size between dominant and non-dominant limbs*

2 For the vastus medialis, the CSA at the 3rd level of the dominant leg ($20 \pm 6 \text{ cm}^2$) was not
significantly different from the non-dominant leg ($21 \pm 7 \text{ cm}^2$); $p = 0.161$. Similarly, for the
4 vastus lateralis there was no significant difference between the CSA at the 7th level for the
dominant leg ($28 \pm 5 \text{ cm}^2$) and the non-dominant leg ($27 \pm 6 \text{ cm}^2$); $p = 0.184$.

6

DISCUSSION

8 The volumes of the vastus medialis and vastus lateralis, normalized to body weight, were
significantly smaller in the PFJ OA group (approximately 20%) than the control group.
10 However, we found no difference in the ratio of VM/VL volumes between those with and
without PFJ OA. In both the PFJ OA and the control group, the ratio of VM/VL was
12 approximately 0.67, indicating that the vastus medialis volume was approximately 2/3 that of
the vastus lateralis in both groups. Based on the evidence from cadaveric and modeling
14 studies, indicating that imbalance of the medial and lateral vasti contributes to heightened
lateral PFJ stress^{16,17}, we considered that there may have been a lower ratio of VM/VL
16 volumes in those with PFJ OA. Our finding of no difference in the VM/VL ratio implies that
the force generating capacity of the vastus medialis is not affected to a greater extent than
18 that of the vastus lateralis in our population with PFJ OA.

20 While we did not observe between-group differences in the relative muscle volume between
the two heads of the vasti, it is possible that altered coordination and activation of the vastus
22 medialis and lateralis may exist in those with PFJ OA. Indeed, modeling studies have
identified that delayed activation of the medial quadriceps (relative to the lateral quadriceps)
24 increases lateral patellar malalignment^{18,19}, leading to areas of heightened contact pressure
across the lateral PFJ^{16,17}. However, it is also possible that our findings may be more aligned
26 with studies that did not observe differences in the onset timing of the medial and lateral vasti

2 between those with and without generalized knee OA²⁰⁻²². While the current study cannot be
compared to those studies that have investigated temporal aspects of the vasti activations in
4 people with generalized knee OA, further investigation is required to establish whether the
imbalances in activations of the vasti muscles, observed in younger people with
6 patellofemoral pain^{23,24}, are also a feature of PFJ OA.

8 The finding of lower size in three of the four quadriceps in the PFJ OA group reflects
previous reports of association between reduced quadriceps strength and PFJ OA^{5,25}. Muscle
10 weakness is influenced by muscle atrophy and the capacity to fully activate the muscle⁴.
Hence, our findings suggest that vastus medialis, vastus lateralis and rectus femoris atrophy
12 may be a feature of PFJ OA and likely contribute to torque deficits observed in these
individuals. Smaller quadriceps muscles may have reduced capacity to absorb shock²⁶ or
14 provide integrated sensorimotor function to the knee joint²⁷, thus rendering the joint more
susceptible to damage²⁸. Furthermore, results from a longitudinal cohort study⁵ and an animal
16 model²⁸ indicate that the PFJ is more susceptible to joint degeneration than the TFJ in the
presence of lower quadriceps strength. Due to the cross-sectional nature of our research
18 design it is not possible to determine whether the pain and structural changes associated with
PFJ OA leads to muscle disuse and atrophy, or whether reduced muscle activity contributes
20 to PFJ OA onset. However, our findings indicate that a program designed to improve strength
in the vastus medialis and vastus lateralis, in addition to the rectus femoris, may benefit those
22 with PFJ OA. However, such programs could also overload the PFJ²⁹, with potential to
increase pain; thus, progression of load should be carefully managed. Further studies are
24 required to confirm whether quadriceps strengthening could reduce symptoms or disease
progression in people with PFJ OA.

26

2 We used MR imaging to quantify muscle size, which expanded on previous studies that
evaluated the strength of the quadriceps when represented as one whole muscle-tendon unit.
4 Since our study did not detect any imbalance in the relative contributions of the medial and
lateral vasti, it is not clear whether measurement of the sizes of the individual quadriceps
6 subregions provides greater value than overall quadriceps strength measures obtained from
dynamometry. Furthermore, MR imaging of the entire thigh is expensive and the segmenting
8 of muscle volumes is time-consuming. However, dynamometry is not readily available in the
clinical setting, and this instrumentation is expensive to purchase. Our results indicate that
10 CSAs of the VM and VL (at specified levels) may provide a valid indication of muscle size
for those clinicians and researchers without access to dynamometry.

12

Our study highlights that the VM CSA at approximately 8 cm (control) and 12 cm (PFJ OA)
14 above the femoral condyles were the best predictors of VM volume, while VL CSA at
approximately 24 cm (control) and 20 cm (PFJ OA) best predicted VL volume. The gross
16 anatomies of the two muscles are quite distinct, which was reflected in the disparate levels
that best represent the corresponding muscle volume. Indeed, these levels generally represent
18 the largest CSA for each individual vastus. However, previous studies have described vasti
CSA at a single level, with distances ranging from 3.8 cm^{8,9} to 15 cm¹⁰ superior to the
20 proximal patella pole, which may not represent the muscle volumes and force capacities of
these muscles. These studies ought to consider the specific CSA of the muscle that is most
22 representative of the muscle's volume, in addition to controlling for the effects of gender and
body weight.

24

In the current study, we investigated muscle size for the individual quadriceps components in
26 people with and without symptomatic radiographic PFJ OA. The quantification of muscle

2 volume used in the current study provides a better estimate of the force generating capacity of
the muscles than measuring anatomical CSAs, which may not be representative of the
4 muscle's PCSA. Our calculations of muscle volume, PCSA and peak isometric force values
in the control group (Table 1 and Supplementary Table) were in reasonable agreement with
6 those in the literature³⁰⁻³². For example, our average muscle volume and PCSA of the controls
for vastus lateralis (505.1 cm³ and 80.7 cm², respectively) were of similar magnitudes to
8 those of Friedrich and Brand (1990) (514.0 cm³ and 64.4 cm², respectively)³¹, while our
average muscle volume and PCSA of rectus femoris (206.7 cm³ and 32.9 cm², respectively)
10 compare favorably to data reported by Klein Horsman et al. (2007) (226.3 cm³ and 28.9 cm²,
respectively)³⁰.

12

There are a number of limitations of our study that should be considered. The MR images
14 were performed under non-weight bearing conditions at full knee extension, which is
standard protocol for clinical imaging of the knee; however, it is not known whether the
16 results would have been the same if a weight-bearing activity (involving quadriceps
activation) was simulated. While these limitations may have influenced the calculations of
18 muscle volume, they are unlikely to have affected the between-group comparisons. The use
of the dominant leg to calculate muscle volume in the control group and the most
20 symptomatic leg in the PFJ OA may have resulted in bias. However, we performed some
preliminary analyses to confirm that the CSA for vastus medialis and vastus lateralis were not
22 different between legs in the control group. Therefore, it is unlikely that meaningful between-
leg differences in the control group would have affected our between-group comparisons. A
24 further limitation is the lack of detailed MR data, from which to score additional features of
osteoarthritis. For example, the radiographs cannot reveal features such as cartilage or bone
26 marrow lesions, synovitis or effusion. Therefore, we cannot rule out that some participants in

2 the control group may have had signs of OA that were not detectable on radiographs.
However, currently radiographic definitions of OA remain the gold standard, and we can be
4 confident that our control group was free of radiographically detected OA.

6 It is also acknowledged that neuromuscular factors contribute to a muscle's strength and that
the strength and size of other antagonistic or synergistic muscles also influence the load on
8 the PF joint, and therefore may be important for people with PFJ OA. Finally, the cross-
sectional nature of the study design precludes any conclusions regarding the temporal
10 relationship between muscle size and PFJ OA. Longitudinal studies are required to ascertain
the role of quadriceps muscle size in the etiology and progression of PFJ OA.

12

CONCLUSION

14 There was no difference in the ratio of VM/VL volumes between those with and without PFJ
OA. The volumes of the vastus medialis, vastus lateralis and rectus femoris, normalized to
16 body weight, were approximately 20% smaller in the PFJ OA than the control group. Further
studies are required to ascertain whether imbalance in the activations of the vastus medialis
18 and lateralis is a feature of PFJ OA, and whether quadriceps strengthening can reduce
symptoms or disease progression in people with PFJ OA.

Author Contributions

Harvi F Hart performed all analyses of quadriceps muscle volume and contributed to the writing of the paper

David C Ackland assisted with all data analyses, calculations of peak isometric force and contributed to the writing of the paper

Marcus G Pandy assisted with the calculations of peak isometric force and contributed to the writing of the paper

Kay M Crossley assisted with the data collection, statistical analyses and contributed to the writing of the paper

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Conflict of interest

HFH, DCA, MGP and KMC do not have any conflicts of interest to declare

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FIGURE CAPTIONS

Fig 1: **(A)** Delineation of the vastus medialis (yellow), vastus lateralis (green), vastus intermedius (orange) and rectus femoris (purple) on axial MR images, where i) represents segmented and unsegmented proximal axial MR image, ii) represents segmented and unsegmented mid thigh axial MR image and iii) represents segmented and unsegmented distal axial MR image. **(B)** Cross-sectional areas of the vastus medialis and vastus lateralis were obtained at ten evenly spaced levels from the femoral condyles to the lesser trochanter of the femur (dashed lines). The solid black lines identify the levels that were the strongest predictors of muscle volume for the controls, whereas the solid gray lines identify the levels that were the strongest predictors of muscle volume for the PFJ OA participants.

FIGURES

Figure 1

(Separate file attachment)

TABLES

Table 1: Averaged muscle volumes of the quadriceps for the PFJ OA and control groups. Muscle volume and muscle volume normalized to subject mass are given, along with standard deviations (SD). Significant differences ($p < 0.05$) in normalized muscle volume between the PFJOA subjects and control subjects are indicated.

Muscle		Muscle volume (SD) (cm ³)	Normalized muscle volume (SD) (cm ³ /kg)
Vastus lateralis	PFJOA	453.1 (173.2)	$p = 0.012$ $\left\{ \begin{array}{l} 5.8 (1.6) \\ 7.3 (1.4) \end{array} \right.$
	Control	505.1 (202.7)	
Vastus medialis	PFJOA	292.9 (100.9)	$p = 0.011$ $\left\{ \begin{array}{l} 3.7 (0.9) \\ 4.6 (0.9) \end{array} \right.$
	Control	325.2 (129.3)	
Vastus intermedius	PFJOA	397.4 (173.7)	5.0 (1.6)
	Control	418.3 (191.4)	5.6 (1.3)
Rectus femoris	PFJOA	177.9 (71.3)	$p = 0.009$ $\left\{ \begin{array}{l} 2.3 (0.7) \\ 3.0 (0.7) \end{array} \right.$
	Control	206.7 (81.1)	