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**Increase in vastus medialis cross-sectional area is associated with reduced pain,
cartilage loss and joint replacement risk in knee osteoarthritis**

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Running head: relationship of vastus medialis size with knee pain and structure

Abstract

Objective: Although there is evidence for a beneficial effect of increased quadriceps strength on knee symptoms, the effect on knee structure is unclear. This study examined the relationship between change in vastus medialis (VM) cross-sectional area (CSA) and knee pain, tibial cartilage volume and risk of knee replacement in subjects with symptomatic knee osteoarthritis (OA).

Methods: 117 subjects with symptomatic knee OA had a knee MRI at baseline, 2 years, and 4.5 years. VM CSA was measured at baseline and 2 years. Tibial cartilage volume was measured at baseline, 2 years, and 4.5 years. Knee pain was assessed by the Western Ontario and McMaster University Osteoarthritis Index at baseline and 2 years. Knee joint replacement over 4 years was determined.

Results: Baseline VM CSA was inversely associated with current knee pain ($r=-0.16$, $P=0.04$) and medial tibial cartilage volume loss from baseline to 2 years ($B=-10.9$, 95% CI -19.5 to -2.3), but not baseline tibial cartilage volume. In addition, an increase in VM CSA from baseline to 2 years was associated with reduced knee pain over the same time period ($r=0.25$, $P=0.01$), reduced medial tibial cartilage loss from 2 to 4.5 years ($B=-16.8$, 95%CI -28.9 to -4.6), and reduced risk of knee replacement over 4 years (OR=0.61, 95%CI 0.40-0.94).

Conclusion: In a symptomatic knee OA population, increased VM size was associated with reduced knee pain and beneficial structural changes at the knee, suggesting management of knee pain and optimizing VM size are important in reducing OA progression and subsequent knee replacement.

Knee osteoarthritis (OA), which commonly affects the medial knee compartment (1), is a chronic joint disorder imposing significant health care burden (2). Understanding the factors affecting disease progression may enable the development of disease modifying therapies. One such potential area is the role of quadriceps strength. The quadriceps muscle is a principal contributor to functional knee joint stability and provides shock absorption for the knee during ambulation (3, 4). The role of quadriceps muscle strength in mediating the development and progression of knee OA has been the focus of a number of investigations.

Cross-sectional studies have reported decreased quadriceps strength in individuals with knee OA compared with controls without knee OA (5-9), and that quadriceps weakness is associated with greater knee pain and impaired physical function (5, 6, 10-12). Nevertheless, evidence from longitudinal studies has been conflicting for the association between quadriceps strength and the development and progression of knee OA (13-18). While one study suggested an association between quadriceps weakness and incident radiographic knee OA in women (13), the Multicenter Osteoarthritis Study found that thigh muscle strength predicted incident symptomatic OA but not incident radiographic knee OA (14). Similarly, inconsistent findings exist for the association between quadriceps strength and radiographic progression of knee OA. While one study found no association (15), other studies reported greater quadriceps strength to be associated with increased tibiofemoral OA progression in malaligned knees and lax knees (16). In contrast, another study reported that quadriceps weakness was associated with the progression of joint space narrowing in women (18). The only magnetic resonance imaging (MRI) study found that increased quadriceps strength was associated with reduced cartilage loss in the lateral patellofemoral compartment with no association seen at the tibiofemoral compartment (17). In these studies, dynamometry has been used for assessing quadriceps strength (13-18). However, pain may mediate effort and

lead to inconsistent muscle strength results (19), and knee pain has been shown to predict decline in knee extension strength (20). Among the previous studies (13-18), only one study adjusted for baseline knee pain (14). Differences across study populations, particularly relating to the severity of knee OA and whether the participants had pain or were largely asymptomatic, may have contributed to the inconsistent findings of previous studies (13-18). Methods for assessing the progression of knee OA have varied in sensitivity to change, particularly where semi-quantitative radiological and MRI methods were used (21, 22). Given the inconclusive relationship between quadriceps strength and tibiofemoral OA progression and the methodological issues, further studies using novel methods to assess quadriceps strength and sensitive methods to assess OA progression will be needed.

Although dynamometry is widely used to assess muscle strength, the anatomical cross-sectional area (CSA) of a muscle has been validated as a measure of the force producing capability of that muscle (23, 24). For instance, the CSA of the quadriceps muscle group at the mid-thigh has been shown to be related to the maximal voluntary knee extensor force when measured by MRI (25) and computed tomography (26, 27). Importantly, differences between medial and lateral vastus muscles have been shown in people with knee OA. During walking, individuals with knee OA recorded greater ratio of lateral to medial vastus muscle activation compared with asymptomatic controls (9, 28, 29). The reduced activation of vastus medialis may lead to loss of the medial musculature and be implicated in the medial tibiofemoral OA disease process. In contrast, a recent study showed that higher vastus lateralis to vastus medialis CSA ratio was associated with better cartilage characteristics in preclinical knee OA (30). Thus the role of vastus medialis in the pathogenesis of knee OA is not well understood. Moreover, no study has examined the longitudinal change in vastus

medialis CSA in the context of knee OA and whether this change is associated with cartilage changes and patient-related outcomes.

Thus the aim of this study was to examine the change in vastus medialis CSA over 2 years in a population with symptomatic knee OA, and to investigate its relationship with pain, change in tibial cartilage volume assessed using MRI, and the risk of knee replacement over 4 years.

Patients and Methods

Study participants

Subjects with knee OA were recruited by using a combined strategy including advertising through local newspapers and the Victorian branch of the Arthritis Foundation of Australia, as well as in collaboration with general practitioners, rheumatologists, and orthopaedic surgeons (31). The study was approved by the ethics committee of the Alfred and Caulfield Hospitals in Melbourne, Australia. All subjects gave informed consent.

Inclusion criteria were age > 40 years and symptomatic knee OA (score of > 20% on at least one pain dimension of the Western Ontario and McMaster University Osteoarthritis Index (WOMAC) (32)) and presence of osteophytes (at least grade 1 osteophyte in either the tibiofemoral or patellofemoral compartment) according to the clinical and radiographic criteria of the American College of Rheumatology (33). Subjects were excluded if any other form of arthritis was present, if there were any contraindications to MRI (e.g. pacemaker, cerebral aneurysm clip, cochlear implant, presence of shrapnel in strategic locations, metal in the eye or claustrophobia), or if they were unable to walk 50 feet without the use of assistive devices, had hemiparesis of either lower limb or were planning to undergo total knee replacement.

Anthropometric and clinical data

Weight was measured to the nearest 0.1 kg (shoes and bulky clothing removed) using a single pair of electronic scales. Height was measured to the nearest 0.1 cm (shoes removed) using a stadiometer. Body mass index (BMI, kg/m^2) was calculated. Knee pain was assessed by WOMAC, analysed using 100 mm visual analogue scales (32). The pain subscale comprises 5 questions, each of which is assessed on a 100 mm visual analogue scale and summed to give a total pain score out of 500. Increase in the score corresponds with worsening of pain.

Physical activity

Current physical activity was assessed using a questionnaire in 3 categories: walking (1 = <0.5 miles/week; 2 = 0.5-5 miles/week; 3 = 5-10 miles/week; 4 = >10 miles/week), work (1 = sedentary; 2 = sedentary and occasional exercise; 3 = 50% sedentary and 50% active; or active housework; 4 = predominantly manual active all day), and sport (1 = none; 2 = 1 hour/week of golf, bowls, badminton, cycling, or swim; 3 = >2 hours/week of above activities; or >1 hour/week of fitness, aerobics, or squash; 4 = >2 hours/week of fitness, aerobics, or squash). A total physical activity score was created by adding up the above scores (34).

Knee angle

At baseline, each subject had a weight-bearing anteroposterior tibiofemoral radiograph taken of the symptomatic knee in full extension. Frontal plane knee angle was measured (35). Lines were drawn through the middle of the femoral shaft and through the middle of the tibial shaft: the angle subtended on the medial side was measured using Osiris software. The intra-observer reproducibility for agreement was 0.98 (35).

MRI examination

Each subject had an MRI performed on the symptomatic knee at baseline and approximately 2 and 4 years later. Knees were imaged in the sagittal plane on the same 1.5T whole-body MR unit (Signa Advantage HiSpeed; General Electric Medical Systems, Milwaukee, WI, USA) using a commercial receive-only extremity coil. The following sequence and parameters were used: a T₁-weighted, fat-suppressed, 3D gradient recall acquisition in the steady state; flip angle 55 degrees; repetition time 58 ms; echo time 12 ms; field of view 16 cm; 60 partitions; 512 x 192 matrix; and one acquisition, time 11 min 56 sec. Sagittal images were obtained at a partition thickness of 1.5 mm and an in-plane resolution of 0.31 x 0.83 mm. All the MRI assessments were performed blinded to subject identification, time sequences, and other knee structural measurements.

Vastus medialis cross-sectional area

Distal vastus medialis CSA was measured directly from axial MR images by one trained observer manually drawing disarticulation contours around the muscle boundaries using Osiris (Digital Imaging Unit, University Hospital of Geneva, Geneva, Switzerland) (36). The CSA was measured at the MR slice 37.5 mm superior to the quadriceps tendon insertion at the proximal pole of the patella, orthogonal to the long axis of the leg. This slice was chosen as it was the largest slice visible across all subjects. The intraobserver reliability for repeating vastus medialis CSA measurement on the same MR image, expressed as intraclass correlation coefficient (ICC), was 0.99, with the standard error of the mean (SEM) of 19.5 mm². The intraobserver reliability for repeating measurement of vastus medialis CSA change over 2 years, performed on 20 randomly selected subjects, expressed as ICC, was 0.99, with SEM of 21.9 mm². The reproducibility of vastus medialis CSA measurement for repeating MRI

examinations over a short time period (1-2 weeks), expressed as ICC, was 0.996, with SEM of 21.2 mm².

Cartilage volume

Medial and lateral tibial cartilage volumes were measured from the total volume, by manually drawing disarticulation contours around the cartilage boundaries on each section using Osiris (31). Two trained observers measured the cartilage volumes independently and the average of the results was used. The coefficients of variation for the medial and lateral tibial cartilage volume measures were 3.4% and 2.0%, respectively (31).

Bone area

Medial and lateral tibial plateau cross-sectional bone areas were directly measured from axial images using Osiris (37). The coefficients of variation for the medial and lateral tibial plateau bone area were 2.3% and 2.4%, respectively (37).

Identification of knee replacement

During the 4th year all subjects were contacted and asked whether they had undergone a knee replacement due to OA of the same knee in which they had the baseline MRI. This was confirmed by contacting the treating physician in all cases.

Statistical analyses

Annual change in tibial cartilage volume was calculated by cartilage volume change (follow up cartilage volume subtracted from initial cartilage volume) divided by time between MRI scans. Change in vastus medialis CSA was calculated by subtracting baseline CSA from follow-up CSA. Change in WOMAC pain was calculated by subtracting follow-up WOMAC

pain score from baseline score. Multiple linear regression was used to examine the relationship between vastus medialis CSA and continuous outcome variables (tibial cartilage volume, and annual change in tibial cartilage volume) adjusting for potential confounders including age, gender, BMI, tibial bone area and knee angle. Logistic regression was used to examine the relationship between vastus medialis CSA and the risk of knee replacement, adjusting for potential confounders. Multiple linear regression was also used to examine the associations of knee pain with vastus medialis CSA and its change over 2 years. A p-value of less than 0.05 (two-tailed) was regarded as statistically significant. All analyses were performed using the SPSS statistical package (standard version 19, SPSS, Chicago, IL, USA).

Results

One hundred and twenty-six eligible participants had baseline knee MRI for the assessment of knee structures. One hundred and seventeen (93%) participants completed the longitudinal MRI component of the study over 2.0 (SD 0.2, range 1.2-3.2) years (Table 1). Subjects lost to 2 year follow-up were more likely to be male, have more severe knee pain and higher lateral tibial cartilage volume compared with those who completed follow-up. Seventy-eight (62%) participants completed the 4.5 (SD 0.4, range 3.6-5.7) year follow-up. Subjects lost to 4.5 year follow-up had a greater BMI than those completing the study, but were not significantly different in terms of age, gender, knee cartilage and bone measures.

Relationship between vastus medialis CSA and knee pain

From baseline to 2 year follow-up, on average over the whole sample, vastus medialis CSA increased by 36.5 (SD 155.3) mm² (P=0.01), representing an increase of 9% (SD 28%) of the baseline CSA. Over 2 years, WOMAC pain score decreased by 17 (SD 49), with 84 (67%) participants showing an improvement in pain (WOMAC pain score decreased by ≥ 1). After

adjusting for age, gender, and BMI, there was a significant, inverse association between vastus medialis CSA and WOMAC knee pain score at baseline (Figure 1). The R^2 was 0.025 (i.e. correlation coefficient = 0.16), indicating a mild correlation. Over 2 years, a reduction in WOMAC knee pain score was associated with an increase in vastus medialis CSA, after adjusting for age, gender, BMI, and change in BMI (Figure 2). The R^2 was 0.059 (i.e. correlation coefficient = 0.24), representing a mild correlation. These results persisted after adjusting for physical activity.

Relationship between baseline vastus medialis CSA and baseline tibial cartilage volume and its change over 2 years

In univariate analysis, baseline vastus medialis CSA was positively associated with medial and lateral tibial cartilage volume at baseline (Table 2). After adjusting for age, gender, BMI, tibial plateau bone area, and knee angle, this association was no longer significant. In univariate analysis, there was no significant association between baseline vastus medialis CSA and annual change in tibial cartilage volume over 2 years in any tibiofemoral compartment (Table 2). However, after adjusting for age, gender, BMI, baseline tibial plateau bone area and cartilage volume, and knee angle, greater baseline vastus medialis CSA was associated with reduced medial tibial cartilage volume loss over 2 years (Table 2). Including baseline WOMAC pain score in the regression models did not alter the results (Table 2).

Relationship between increased vastus medialis CSA over 2 years and cartilage volume loss from 2 to 4.5 years and risk of knee replacement over 4 years

In both univariate analysis and after adjusting for age, gender, BMI, and initial cartilage volume, an increase in vastus medialis CSA from baseline to 2 year follow-up was associated with reduced medial tibial cartilage volume loss from 2 to 4.5 year follow-up (Table 3). No

significant association was observed in the lateral compartment. An increase in vastus medialis CSA from baseline to 2 year follow-up was also associated with a reduced risk of knee joint replacement over 4 years (Table 3). Including change in WOMAC pain score in the regression models did not alter the results significantly (Table 3). Neither change in physical activity nor change in BMI over 2 years significantly attenuated the above associations (data not shown). Including knee angle in the regression models did not alter the results (data not shown). There was no evidence for an effect modification of knee alignment on the association between increased vastus medialis CSA and cartilage volume loss or knee replacement risk.

Discussion

In this community-based population with symptomatic knee OA, we found that greater baseline vastus medialis CSA was associated with lower knee pain at baseline and reduced medial tibial cartilage loss over 2 years, and that an increase in vastus medialis CSA over 2 years was associated with reduced knee pain and subsequent medial tibial cartilage loss, and a reduced risk of knee replacement over 4 years. Taken together, these findings suggest that increased vastus medialis CSA in a population with symptomatic knee OA is associated with reduced knee pain and beneficial effects on knee structure which include reduced loss of tibial cartilage volume and delayed disease progression toward a knee replacement.

The inverse relationship between vastus medialis CSA and pain we observed is consistent with previous cross-sectional studies which reported associations between increased pain and reduced strength and impaired function of the quadriceps muscle (38, 39). In this symptomatic knee OA population we found an increase in vastus medialis CSA over 2 years was associated with a reduction in knee pain. A clinical trial showed that knee pain reduction

through either peripheral (local anaesthetic) or central mechanisms resulted in an increase in muscle strength and activation (40), while quadriceps strength training alone has been shown to reduce knee pain (41), highlighting the strong relationship between knee pain and quadriceps muscle function. In our study which is a natural history study of a population with knee pain, pain improvement could not be attributed to any particular treatment and is consistent with the fluctuating natural history of symptoms in OA and the tendency for symptoms to improve in subjects selected to have significant knee symptoms on recruitment.

No previous studies have reported an increase in quadriceps muscle size in a natural population with symptomatic knee OA. We would expect a decrease in muscle size over time due to ageing and reduced mobility resulted from knee pain. However, since OA is a continuous process with pain fluctuating over time, symptomatic improvement may result in improved mobility, and weight-bearing activities associated with daily living may have reversed some of the muscle effects related to the reduced knee loading due to knee pain. It is most likely that reduction in knee pain is associated with regain of muscle size back towards the person's own baseline rather than a true absolute increase in muscle size. A recent study examining the morphologic changes in vastus medialis muscle in patients with knee OA showed that all muscle specimens exhibited atrophy of type 2 fibers (42). In particular, selective atrophy of type 2 fibres in 68% of the specimens may result from pain-associated disuse as with pain-related immobilization of a limb (42). It may be that what we are seeing in our study is a reversal of some of these changes with improved ambulation associated with knee pain reduction.

We found that an increase in vastus medialis CSA was associated with beneficial knee structural changes at the tibiofemoral compartment and clinically significant patient-related

outcome: decreased rate of tibial cartilage volume loss and reduced risk of knee replacement. Whilst a recent MRI study found no significant relationship between quadriceps strength and tibiofemoral cartilage loss (17), this may reflect the less sensitive method used in the study for assessing structural change which is a semi-quantitative approach (43). Regarding the role of knee alignment in the relationship between quadriceps strength and OA progression, one study showed that increased quadriceps strength was associated with increased radiographic progression in malaligned or lax knees (16). However, another study that used MRI based cartilage assessments did not show a detrimental effect of muscle strength on tibial cartilage loss with increased varus alignment (17). In this current study we found that an increase in vastus medialis CSA over 2 years was associated with reduced cartilage volume loss over the next 2.5 years and also a reduction in the risk of knee replacement over 4 years, which was independent of knee angle. Our study examined a symptomatic knee OA population, used very sensitive methods for assessing knee structural change (i.e. quantitative assessment of cartilage volume) (43), and also investigated the clinically important outcome of reduced knee replacement risk. These findings provide strong evidence for the importance of maintaining knee muscle function in an effort to maintain knee joint health in OA.

A possible explanation for the beneficial effect of vastus medialis size on knee structure may be via muscles contributing to joint stability and load distribution of the knee in the medial-lateral plane (3, 4). Although yet to be investigated in an OA population, in the gait of normal healthy people the knee is well stabilised by the muscles, with the quadriceps contributing over 40%, and all knee muscles over 50%, of the peaking medial compartment loading (4). Therefore there is scope for the muscles to create an appropriate biomechanical environment to beneficially affect the articular cartilage. This is biologically plausible, since factors associated with large loading during walking have been implicated in cartilage loss and

disease progression (44, 45). Conversely, loading is important for cartilage integrity. At its extreme, it has been shown that young adults who become quadriplegic rapidly lose cartilage (46), and physical activity is important for cartilage gain in children (47). The strength and activation of the muscles may affect the balance that exists between an optimal and excess loading on the joint (3, 4, 6, 9, 28) in terms of optimizing cartilage health. This loading hypothesis is further supported by our findings of a beneficial effect of vastus medialis on the medial tibiofemoral compartment which is the compartment that is subjected to the greatest loading during weight-bearing activity (48).

While a strength of our study was that we obtained valid and reliable measurement of vastus medialis CSA on MRI, we did not examine the role of other components of the quadriceps muscles, such as vastus lateralis and intermedius. Due to the available MRI images and technical issues, the CSA of these quadriceps components could not be measured consistently in the converted axial MR images on all participants. The investigation of vastus medialis is similar to previous studies that have focussed specifically on the vastus medialis, reporting selective atrophy of type 2 fibres in end-stage knee OA (42) and changes in motor unit recruitment in OA patients compared to controls (49), as well as improved functional recovery with electrical stimulation of the vastus medialis muscle after total knee replacement (50). Moreover, there seems to be role imbalance between the vastus medialis versus vastus lateralis in the knee OA (9, 28, 29). This medial-lateral imbalance in activation may affect the atrophy of the vastus medialis and subsequent cartilage health. Furthermore, although we did not measure muscle strength directly, we measured the CSA of muscle as a surrogate for muscle strength, and we were able to measure the longitudinal change in muscle CSA from MRI with high reproducibility. We did not include joint laxity measures which may influence joint biomechanics. All our participants had knee pain and mild to moderate knee OA at

recruitment, so the findings may not be applicable to healthy population without knee OA or patients with severe disease.

In this population with symptomatic knee OA, an increase in vastus medialis CSA was associated with reduced knee pain, tibial cartilage volume loss, and knee replacement over 4 years. These findings suggest beneficial effects of increased vastus medialis size in subjects with knee OA. It may be that management of knee pain in order to optimize mobility and maintain vastus medialis size is important in reducing OA progression and subsequent knee replacement. These results have the potential to provide new insight into more effective therapeutic strategies for knee OA.

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Figure 1: Association between baseline vastus medialis cross-sectional area (cm²) and WOMAC pain score adjusted for age, gender and body mass index (P = 0.04)

Figure 2: Association between change in vastus medialis cross-sectional area (cm²) and reduction in WOMAC pain score over 2 years adjusted for age, gender, body mass index, and change in body mass index (P = 0.007)

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Table 1: Characteristics of the study participants

	n = 117
Age, years	63.7 (10.2)
Female, n (%)	68 (58)
Body mass index, kg/m ²	28.8 (5.1)
WOMAC pain score	81 (44)
Physical activity	6.3 (1.8)
Kellgren-Lawrence score ≥ 2 , n (%)	82 (73)
Knee angle, degrees	180.8 (5.8)
Vastus medialis cross-sectional area, mm ²	756 (247)
Medial tibial cartilage volume, mm ³	1738 (474)
Lateral tibial cartilage volume, mm ³	1923 (575)
Medial tibial plateau area, mm ²	2075 (393)
Lateral tibial plateau area, mm ²	1363 (257)
Values are reported as mean (SD) unless otherwise stated	

Table 2: Relationship between baseline vastus medialis cross-sectional area (cm²) and tibial cartilage volume at baseline and its change over 2 years

	Univariate	p-value	Multivariate	p-value	Multivariate	p-value
	Regression Coefficient		Regression Coefficient		Regression Coefficient	
	(95% CI)		(95% CI)		(95% CI)	
Baseline tibial cartilage						
volume (mm³)						
Medial	52.5 (21.1, 84.0)	0.001	3.2 (-29.7, 36.2) ¹	0.85	-5.0 (-37.4, 27.5) ²	0.76
Lateral	83.7 (43.1, 124.3)	< 0.001	29.4 (-12.2, 71.0) ¹	0.16	24.7 (-17.5, 66.9) ²	0.25
Annual change in tibial						
cartilage volume (mm³)						
Medial	-5.4 (-12.9, 2.2)	0.16	-10.9 (-19.5, -2.3) ³	0.01	-11.9 (-20.6, -3.2) ⁴	0.01
Lateral	8.9 (-0.7, 18.5)	0.07	5.1 (-5.2, 15.5) ³	0.33	4.5 (-6.0, 15.0) ⁴	0.40

¹adjusted for age, gender, body mass index, tibial plateau bone area, and knee angle in multivariate regression

²adjusted for age, gender, body mass index, tibial plateau bone area, knee angle, and WOMAC pain score in multivariate regression

³adjusted for age, gender, body mass index, baseline tibial plateau bone area and cartilage volume, and knee angle in multivariate regression

⁴adjusted for age, gender, body mass index, baseline tibial plateau bone area and cartilage volume, knee angle, and WOMAC pain score in multivariate regression

Table 3: Relationship between change in vastus medialis cross-sectional area from baseline to 2 years (cm²) and subsequent change in tibial cartilage volume and risk of knee replacement over 4 years

	Univariate	p-value	Multivariate	p-value	Multivariate	p-value
	Regression Coefficient/ Odds Ratio (95% CI)		Regression Coefficient/ Odds Ratio (95% CI)*		Regression Coefficient/ Odds Ratio (95% CI)**	
<i>Annual change in tibial cartilage volume from 2 to 4.5 years (mm³)¹</i>						
Medial	-14.5 (-26.6, -2.5)	0.02	-16.8 (-28.9, -4.6)	0.01	-14.6 (-26.9, -2.3)	0.02
Lateral	-8.3 (-20.9, 4.4)	0.20	-9.4 (-22.6, 3.8)	0.16	-9.3 (-22.9, 4.4)	0.18
<i>Knee replacement over 4 years (Yes/no)²</i>						
	0.62 (0.41, 0.96)	0.03	0.61 (0.40, 0.94)	0.03	0.65 (0.41, 1.02)	0.06

*adjusted for age, gender, body mass index, and initial tibial cartilage volume

**adjusted for age, gender, body mass index, initial tibial cartilage volume, and change in WOMAC pain score from baseline to 2 years

¹regression coefficient; ²odds ratio

Figure 1: Association between baseline vastus medialis cross-sectional area (cm²) and WOMAC pain score adjusted for age, gender and body mass index (P = 0.04)

Figure 2: Association between change in vastus medialis cross-sectional area (cm²) and reduction in WOMAC pain score over 2 years adjusted for age, gender, body mass index, and change in body mass index (P = 0.007)