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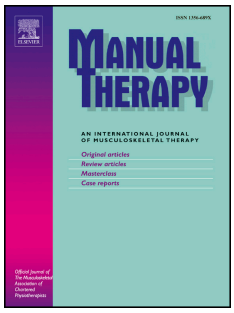

Increased Duration of Co-Contraction of Medial Knee Muscles is Associated with Greater Progression of Knee Osteoarthritis

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INCREASED DURATION OF CO-CONTRACTION OF MEDIAL KNEE MUSCLES IS ASSOCIATED WITH GREATER PROGRESSION OF KNEE OSTEOARTHRITIS

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INCREASED DURATION OF CO-CONTRACTION OF MEDIAL KNEE MUSCLES IS ASSOCIATED WITH GREATER PROGRESSION OF KNEE OSTEOARTHRITIS

ABSTRACT

Background: As knee osteoarthritis (OA) cannot be cured, treatments that slow structural disease progression are a priority. Knee muscle activation has a potential role in OA pathogenesis. Although enhanced knee muscle co-contraction augments joint stability; this may speed structural disease progression by increased joint load. **Objective:** This study investigated the relationship between cartilage loss and duration of co-contraction of medial/lateral knee muscles in medial knee OA. **Design:** Prospective cohort study. **Methods:** Medial (vastus medialis; semimembranosus) and lateral (vastus lateralis; biceps femoris) knee muscle myoelectric activity was recorded in 50 people with medial knee OA during natural speed walking at baseline. Medial tibial cartilage volume was measured from MRI at baseline and 12 months. Relationships between percent volume loss and duration of co-contraction of medial/lateral muscles around stance phase and ratio of duration of medial to lateral muscle co-contraction were evaluated with multiple linear regression. **Results:** Greater duration of medial muscle co-contraction and greater duration of medial relative to lateral co-contraction correlated positively with annual percent loss of medial tibial cartilage volume(P=0.003). Estimated cartilage loss was 0.14(95% confidence interval 0.23-0.05) greater for each increase in medial muscle co-contraction duration of 1% of the gait cycle. Lateral muscle co-contraction inversely correlated with cartilage loss. **Conclusion:** Data support the hypothesis that augmented medial knee muscle co-contraction underpins faster progression of medial knee OA. Increased duration of lateral muscle co-contraction protected against medial cartilage loss. Exercise and biomechanical interventions to change knee muscle activation patterns provide possible candidates to slow progression of knee OA.

Keywords: Disease progression; Knee osteoarthritis; Electromyography; Co-contraction.

INTRODUCTION

Knee osteoarthritis (OA) commonly affects the medial tibiofemoral compartment[1] and has significant morbidity and health care burden[2]. As it cannot be cured, treatments that slow disease progression are a priority. Understanding factors associated with structural deterioration in knee OA should assist development of novel disease-modifying interventions.

Increased medial knee joint load during walking (typically inferred from inverse dynamics), contributes to structural progression of knee OA[3,4]. As muscle forces contribute to joint loading[5,6], muscle activation in knee OA is likely to influence disease course. Knee muscle strength has been implicated in progression. Muscle weakness, particularly quadriceps, is common in knee OA[7]. Although longitudinal studies provide conflicting evidence for a relationship between strength and structural changes[8], recent studies using magnetic resonance imaging (MRI) cartilage measures suggest higher muscle strength may be protective of structural deterioration in early knee OA[9,10].

Coordination of muscle activity is a determinant of knee loading. From one perspective, increased co-contraction of knee muscles has been identified in individuals with subjective report of knee instability[11], and could compensate for joint laxity that has been identified in association with approximation of eroded joint surfaces[12]. Although beneficial in the short term to enhance joint protection[13], increased muscle co-contraction also elevates joint load[14,15], and this could underpin faster cartilage loss. Muscle activation patterns have been investigated in medial knee OA, but findings are inconsistent due to variation in study samples (e.g. disease severity, associated deformities) and methodological approaches to quantify muscle activity[13,16-19]. In knee OA, co-contraction of knee muscles is increased during walking[16,19,20] as quantified by greater amplitude[19,20], longer duration[19] and greater

co-contraction indices[21] than disease-free individuals. The relationship between knee muscle activation and prospectively measured changes in knee joint cartilage has not been studied.

Distribution of muscle activity could be relevant; bias of co-contraction to medial muscles might be more problematic than bias to lateral muscles in medial knee OA. During gait, ground reaction forces pass medially to the knee joint centre, creating an external knee adduction moment throughout stance that causes medial tibial plateau compression. This is magnified in varus knee deformity (bow legs) [22-24]. Bias of muscle activation to lateral muscles[25,26] could generate an internal abduction moment and reduce medial joint load (Fig. 1A). Conversely, bias towards medial muscles could increase medial joint load with detrimental effects. Cross-sectional data imply greater medial co-contraction in medial knee OA[13]. Longitudinal studies are necessary to investigate whether bias towards medial muscle co-contraction is related to greater cartilage loss and study the potential for causality.

We hypothesized that bias of knee muscle co-contraction to medial muscles would be associated with greater loss of medial cartilage volume over 12 months, and bias towards lateral muscle co-contraction would be protective. We tested this hypothesis in a prospective cohort study of individuals with symptomatic medial knee OA.

MATERIALS AND METHODS

Study design

This was a secondary analysis of structural measures of disease progression data from a subset of participants (n=50) enrolled in a randomized controlled trial that compared the effects of lateral wedge and control insoles[27]. Additional EMG measures were made at baseline in this subset and these data have not been reported previously. Only the group who received

control insoles were studied. Structural MRI outcomes were assessed at baseline and repeated 12 months later. EMG measures were made at baseline only and the investigator was blinded to structural measures.

Ethical Approval Statement

The Institutional Medical Research Ethics Committee approved the study. Procedures were in accordance with the Helsinki Declaration. Participants gave written informed consent.

Participants

Participants were recruited from the community via advertisements in local clubs, and print/radio media. Volunteers underwent telephone screening, a standardised semiflexed standing posteroanterior knee x-ray and clinical examination to determine eligibility. The most symptomatic (based on pain measures) knee was studied in those with bilateral disease.

Inclusion criteria were: age ≥50 years, average knee pain on walking of >3 on an 11-point numerical rating scale (0=no pain; 10=maximal pain) at screening, pain located over the medial knee compartment, medial compartment osteophytes or medial joint space narrowing on x-ray[28], and x-ray anatomical knee alignment ≤185° (mechanical axis hip-knee-ankle angle of ≤182° on a full leg x-ray, indicating neutral to varus knee joint alignment). Pain and physical function were measured using the Western Ontario and McMaster Universities (WOMAC) osteoarthritis index (higher scores - greater pain and physical dysfunction) [29].

Exclusion criteria were: Kellgren and Lawrence grades 1 and 4[30], predominant patellofemoral joint symptoms on clinical examination (indicated by pain location, pain provoking activities, tenderness on palpation, and pain during patella mobilisation[31]), knee surgery or intra-articular corticosteroid injection within 6 months, current or past (within 4 weeks) oral corticosteroids, systemic arthritic conditions, history of knee arthroplasty or osteotomy, other musculoskeletal or neurological condition affecting lower limb,

contraindications to MRI, planning to commence other treatment for knee OA, and regular use of a gait aid.

Measures of muscle activation

Recordings of myoelectric activity from lateral (biceps femoris [BF] and vastus lateralis [VL]) and medial (semimembranosus [SM], vastus medialis [VM]) muscles were made with surface electromyography (EMG) electrodes. Pairs of Ag/AgCl disc electrodes (Kendall Meditrace 100, Covidien, USA) were attached to the skin (2cm inter-electrode distance) longitudinally with respect to muscle fibres (Fig. 1B). Skin was shaved and cleaned with alcohol. EMG was amplified 2000x, band-pass filtered (20-500Hz) using a telemetered Noraxon Telemyo 900 system (Noraxon, USA) and digitized at 1080 samples/s using the 16-bit analog inputs of a Vicon M2/MX motion analysis system (Vicon, Oxford UK).

Gait measurement

At baseline, participants walked for five trials at self-selected speed in their normal footwear along a 10-m level walkway with speed monitored by two photoelectric beams. Adhesive reflective markers were attached according to the standard Vicon Plug-in-Gait model. Movement data were sampled at 120 samples/s by the 8-camera Vicon system. All data were imported into Matlab (Mathworks, USA).

Structural measures of disease progression

The knee was imaged in the sagittal plane using a 1.5-T whole body unit. The imaging sequence was a T1-weighted fat suppressed 3D gradient recall acquisition in the steady state (procedure detailed elsewhere[27]). Volume of the medial tibial cartilage plate was defined by manually drawing disarticulation contours around the cartilage boundary on each section (Orisis, HUG, Switzerland). Two trained blinded observers made measurements independently (cartilage volume coefficient of variation - 3.4%[32]). Annual change in medial tibial cartilage

volume was calculated by subtraction of the volume at 12 months from that at baseline, and division by time between scans. Annual change was divided by the baseline value to derive the percent annual change. To adjust for cartilage at baseline, baseline medial cartilage volume was normalized to medial tibial bone area to the power of 1.5[33]; cross-sectional bone area of the medial tibial plateau was measured on the input image reformatted in the axial plane[34].

Two machines were used; Philips (Eindhoven, The Netherlands) and GE (Signa Advantage HiSpeed GE Medical Systems, Milwaukee, Wisconsin, USA), due to decommissioning of the Philips machine. The same machine was used at baseline and follow-up for 35 (70%) participants. Machine change did not affect results[27].

Data analysis

Spatiotemporal gait parameters

Gait parameters were determined for the (most) symptomatic knee. Heel strikes (local minima of heel marker vertical position) and toe offs (local maxima of heel marker vertical velocity) were determined[35]. *Stride length* (difference in antero-posterior position of heel marker at consecutive heel strikes), *Stride width* (difference in medio-lateral position of heel markers between left and right heel strikes), *Stride time* (time between heel strikes), and *Stance time* (time between heel strike and following toe off on the same side) and *Walking speed* (average forward speed of the pelvis) were calculated and averaged across trials.

Temporal parameters of EMG

In view of problems with expression of co-contraction using EMG *amplitude* relative to maximal voluntary knee muscle activation (e.g. possible inability to maximally contract knee muscles for amplitude normalization during pain/fear of pain), temporal measures of duration of co-contraction of muscle pairs were used. There is some evidence of longer duration muscle activation in knee OA[19], but not with respect to specific muscle pairs or disease progression.

EMG was band pass filtered (20-500 Hz, 4th order Butterworth filter, bi-directional) and times of EMG onset and offset were detected using the approximated generalized likelihood ratio method[36]. This statistical method detects changes in EMG amplitude using a predefined threshold. Muscle activation occurred around stance and onsets and offsets were expressed relative to heel strike as a percentage of stride cycle.Events were visually inspected and any unrelated to the stance phase EMG burst were discarded.

The duration of co-contraction was calculated for predefined muscle pairs as the period of time both muscles were active (from EMG onset of last muscle of pair to activate and EMG offset of first muscle of pair to deactivate) and expressed as a percentage of stride cycle duration. Three co-contraction measures were calculated and averaged across strides: 1) medial knee muscle co-contraction (VM and SM co-contraction); 2) lateral knee muscle co-contraction (VL and BF co-contraction); and 3) relative co-contraction – ratio of medial co-contraction to lateral co-contraction.

Statistical analysis

Statistical analysis was undertaken with Stata (StatCorp LP, Texas, USA). Significance was set at $P<0.05$. To investigate the association between disease progression (percent annual change in medial tibial cartilage volume; dependent variable) and co-contraction measures (independent variable), a model was built using multiple regression analysis including confounders (sex, age, BMI and baseline medial cartilage volume). Other potential confounders (knee alignment, Kellgren and Lawrence grade, and MRI machine) were excluded from the final analysis after confirming they contributed little to variance, and to limit the number of variables. After regression estimation, model assumptions were tested: multicollinearity (high correlation between two or more predictor variables in a multiple

regression model), homoscedasticity (constant variance), normality of the model residuals (Shapiro-Wilk test) and outliers (>2×SD of model residuals).

RESULTS

Participant characteristics

Table 1 shows cohort characteristics at baseline. Spatiotemporal gait parameters are also presented.

Medial and lateral muscle co-contraction and cartilage volume loss

For illustration, data are shown in Fig. 2 for participants divided into tertiles based on the percent annual change in tibial cartilage volume (slow: -1.2 to 3.7%; medium: -4.0 to -1.5%; fast: -11.4 to -4.6%). When potential confounders were accounted for in the regression model, the duration of medial muscle co-contraction during stance was positively correlated with annual loss of medial tibial cartilage volume *(P*=0.003) (Fig. 3A). The estimated loss of cartilage volume increased 0.14% (95% confidence interval -0.23% -0.05%) for each increase in medial muscle co-contraction duration of 1% of the gait cycle duration when other independent variables in the model are fixed. Lateral muscle co-contraction tended to be inversely correlated with medial cartilage loss (estimated 0.08% (95% CI -0.01% 0.16%) less cartilage volume loss for each 1% increased in lateral co-contraction duration; *P*=0.065). The model explained 24.8% (*P*=0.046) of the variation of the annual change in medial tibial cartilage volume (Table 2). Values for annual loss of medial cartilage volume were >2×SD outside the regression model residuals for five participants. After revision of the model excluding these outliers, the model explained 43.3% (*P*=0.001) (Table 2) of the variance, and the cartilage volume loss remained positively correlated with the medial co-contraction duration (*P*<0.001) and inversely correlated with the lateral co-contraction duration (*P*=0.018).

The confounding variable "sex" became significant; females lost 1.86% (95% CI -3.24 -0.49) more cartilage than males (*P*=0.009).

Ratio of medial-to-lateral muscle co-contraction and cartilage volume loss

When potential confounders were accounted for in the regression model, the duration of medial relative to lateral co-contraction was positively correlated with annual medial cartilage volume loss (*P*=0.014) (Fig. 3B). Although the model explained 19.3% of the variation of the annual change in tibial cartilage volume, it was not significant (*P*=0.084) (Table 3). After revision of the model without participants with data >2×SD outside the regression model residuals (n=3), the ratio remained positively correlated with disease progression (3.60% (95% CI -6.24 -0.96) greater annual cartilage volume loss for a one unit increase in the ratio (i.e. bias to greater medial co-contraction); *P*=0.009). The model explained 28.4% of the variance in annual medial cartilage volume loss (*P*=0.015) (Table 3). "Sex" was a significant confounder; females lost 1.61% (95% CI -3.11 -0.11) more cartilage than males (*P*=0.036).

DISCUSSION

These data provide the first evidence that temporal features of muscle activation are prospectively related to disease progression of medial knee OA. These longitudinal data show not only that a longer period of co-contraction of medial knee muscles during stance phase is associated with greater loss of medial tibial cartilage volume over 12-months, but that greater duration of lateral knee muscle co-contraction is protective against this loss. Although temporal measures don't enable direct estimation of knee joint load, increased load would be the plausible consequence of increased duration of co-activity. The congruence of observed greater medial cartilage loss and greater medial muscle co-contraction strengthens the argument that

distribution of knee joint load, secondary to the pattern of knee muscle activation, is relevant for joint cartilage health.

Distribution of knee muscle activation in gait is related to progression of knee OA

Although knee joint load cannot be determined from temporal measures of muscle activation, it is reasonable to speculate that joint load is at least partly related to when a muscle is active. The relationship between muscle activation and joint load in knee OA is debated. Compressive knee load likely plays a major role in knee OA development and progression, as supported by *in vivo* animal experiments[37] and the positive relationship of knee OA to obesity[38,39] and occupations involving repetitive knee bending[40]. Increased muscle activation could also contribute, as muscle forces, reflected indirectly by activation, are a determinant of knee joint load[5,6]. However, even using state-of-the-art EMG-driven modeling methods the relationship between muscle activation is not straightforward as a consequence of complexities such as muscle geometry, strength, and the length and velocity relationships[41].

Additional activation of knee muscles, including increased co-contraction[12], is likely in knee OA to control the knee joint in the presence of functional knee instability[11,42-44]. If this strategy increases knee joint load, such muscle activation could have negative long-term consequences for disease progression. Greater medial knee joint load, estimated from the external knee adduction moment[3,4], is associated with more rapid disease progression. Internal moments cannot be inferred from external moments, and internal adduction and abduction moments from different combinations of muscle activation could compound or counteract, respectively, the effect of external moments on knee joint load.

As highlighted earlier, a limitation of the present data is the inability to directly relate temporal measures of muscle activation to knee joint load. For instance, peak knee joint load

could be greater for individuals with short periods of medial muscle activation, if activation magnitude is high. This cannot be excluded using the present analysis. Despite the inability to directly infer joint loading, our data provide evidence that temporal features of co-activation of knee muscles may be important in structural disease progression; bias towards longer periods of medial muscle co-contraction contributes to more rapid progression, whereas greater periods of lateral co-contraction appears to spare cartilage.

Cross-sectional data have provided conflicting results regarding activation patterns in knee OA. Although some show greater medial muscle co-contraction (ratio of activity) in medial joint disease[13], greater lateral muscle activation (co-contraction ratio) during gait has been reported in knee OA than controls[45]. Others have reported generalised co-activation of quadriceps and hamstrings muscles with severe OA, but greater lateral muscle co-activity in moderate OA[46]. These data could imply worse outcome with bias to lateral muscles, but are difficult to interpret as the OA groups were not restricted to those with medial compartment OA, and measures were made at a single time point, without considering disease progression. Results from a recent modelling study indicate that although selective activation of lateral muscles did not reduce medial knee load, the authors speculated that greater lateral muscle activation could enhanced knee joint control without further increase to the peak medial joint load, and thus provide benefit[47]. Taken together these and other contrasting observations suggest heterogeneity in muscle activation in knee OA[17], with potential definable subgroups. We argue that a subgroup with medial knee OA and a bias towards medial muscle co-contraction could benefit from neuromuscular or biomechanical interventions that challenge this bias, but this intervention would not be appropriate for all subgroups.

Our data have implications for interpretation of neuromuscular adaptation in knee OA. Despite the potential short-term benefit of increased muscle co-contraction to enhance knee

joint stability, the data imply this might underpin long-term consequences. A novel aspect is the confirmation that whether these consequences are positive or negative relates to subtle features of the pattern of inter-muscle coordination. It is unclear why some individuals use greater duration of lateral co-contraction whereas others use greater duration of medial co-contraction. Further, it remains to be tested whether these adaptations cause the difference in progression or are a response to differences in progression, and the mechanism is unclear (see[48]).

Methodological considerations

Several methodological issues require consideration. First, this is a secondary analysis from a RCT and although the group size was relatively small, significant relationships were found. Second, participants had predominantly medial joint changes with a Kellgren and Lawrence grade of 2 or 3 and the results cannot be generalized to other groups. Third, knee muscle co-contraction was evaluated as temporal characteristics. Although knee joint loading or muscle force cannot be directly inferred from these parameters, timing of activation will influence muscle-induced joint load. Previous work has reported relevance of even small changes in timing of muscle activation on estimated load for other joints[49]. Temporal measures of muscle activation were chosen over measures of activation amplitude, as the latter may be problematic in this population for several reasons (e.g. normalization of EMG measures to maximum might be compromised by muscle inhibition or avoidance of maximal efforts because of pain/fear of pain[7,50]). The present work provides a foundation for future studies that could consider more direct estimation of knee joint load from biomechanical modelling.

Clinical implications

These observations provide initial evidence of a potentially modifiable risk factor for progression of medial tibial OA in people with neutral to varus alignment. Several authors have argued that, in view of the potential negative impact of increased co-contraction on knee load and disease progression, exercise interventions should aim to reduce co-contraction to minimise joint load[13,18]. However, this is based on an over-simplified model of knee control, which considers co-contraction as an "all-or-none" phenomenon. This fails to consider the variety of muscle activation strategies available to control the knee joint, and that temporal features of muscle activation may be relevant. As co-contraction and timing of muscle activation is changed by specific types of exercise (e.g. exercise that draws on motor learning/skill learning principles[51]), and biomechanical interventions (e.g. bracing[52]), it is plausible to consider that the duration of medial co-contraction or the relative duration of co-contraction of medial to lateral muscles might be trainable. Whether such interventions slow progression of cartilage volume loss should form the basis of future work for this specific subgroup with knee OA at risk of more rapid progression.

Conclusion

An interpretation of the present results is that adaptations to enhance control of a diseased knee joint, may have negative long term consequences for joint structure. Some modifications of muscle coordination were associated with more rapid joint disease progression whereas others were associated with protection. There is a need to determine whether interventions to bias co-contraction to lateral muscles reduce disease progression in medial knee OA.

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FIGURE LEGENDS

Fig. 1 **A. Internal and external knee joint moments.** Direction of internal moments (solid line) generated by activation of medial (top panel: vastus medialis and semimembranosis) and lateral (bottom panel: vastus lateralis and biceps femoris) muscle activation. External knee adduction moment is shown as dashed line. **B. EMG electrode placement.** Semimembranosis - midway between ischial tuberosity (IT) and medial tibial condyle (MC); Biceps femoris - Midway between IT and lateral tibial condyle (LC); Vastus medialis - area of greatest muscle bulk, approx 8 cm from medial epicondyle (ME); Vastus lateralis - area of greatest muscle bulk, approx 15 cm from lateral epicondyle (LE).

Fig. 2 **Onset and offset of muscle activity.** For the purposes of illustration, data are shown for participants divded into tertiles based on the percent annual change in tibial cartilage volume (slow: -1.2 to 3.7%; medium: -4.0 to -1.5%; fast: -11.4 to -4.6%). Time of onset and offset of EMG are shown for individual participants (dots) and for each tertile group (mean and SD; veritcal line and box, respectively). The duration of co-contraction (from latest EMG onset of a muscle of the medial [upper panels] or lateral [lower panels] muscle pairs to the earliest EMG offset of a muscle in the pair) is indicated. Dashed lines indicate duration of co-contraction for the participants who progressed fastest and solid lines for the participants who progressed slowest. Note the shorter period of co-contraction for the slower progressing group.

Fig. 3 **Relationship between annual medial tibial cartilage volume loss and co-contraction measures. A.** Relationship between percentage annual medial tibial cartilage volume loss and duration of co-contraction of the medial muscles. **B.** Relationship between percentage annual medial tibial cartilage volume loss and ratio of

duration of co-contraction of the medial and lateral muscles. Regression lines and the 95% confidence intervals are shown.

TABLES

Table 1 Baseline characteristics of participants (mean (SD) or number (%))

Characteristics	**(n=50)**
Age (years)	66 (8)
Sex (females)	24 (49%)
Body mass index (kg/m^2)	29.1 (4.6)
Kellgren & Lawrence grade	
Grade 2	28 (56%)
Grade 3	22 (44%)
Anatomical alignment (deg)	180.7 (3.2)
Pain (WOMAC; 0-20)	7.0 (2.8)
Physical function (WOMAC; 0-68)	22.7 (10.5)
Walking speed ($ms^{-1)}$	1.02 (0.04)
Stride length (m)	1.26 (0.11)
Stride width (m)	0.11 (0.03)
Stride time (s)	1.23 (0.09)
Stance duration (s)	0.78 (0.05)
Stance duration (% stride cycle)	63.4 (1.9)

Table 2 Multiple regression analysis: Duration of medial and lateral knee co-contraction

Model: Annual medial tibial cartilage volume change = Intercept + β_1 × medial CC + β_2 × lateral CC + β_3 × Age + β_4 × Sex + β_5 × BMI

Overall model test		Test of model assumptions		
		Shapiro-Wilk test of		
F(6,43)	2.36	*residuals*	z = -1.586	*P* = 0.944
P > F	0.046	*Homoscedasticity*	chi2 = 2.2	*P* = 0.138
R-squared	0.248	*Variance inflation factors*	All < 1.91	

Predictor	β	Std. Err.	t	*P*>t	95% Conf.	Interval
Medial CC (VM-SM)	-0.14	0.04	-3.16	0.003	-0.23	-0.05
Lateral CC (VL-BF)	0.08	0.04	1.89	0.065	-0.01	0.16
Baseline cartilage volume	-80.73	125.67	-0.64	0.524	-334.18	172.72
Age	0.05	0.06	0.80	0.426	-0.07	0.17
Sex	-1.33	0.88	-1.52	0.137	-3.10	0.44
BMI	-0.08	0.10	-0.82	0.416	-0.28	0.12
Intercept	-0.58	5.47	-0.11	0.916	-11.61	10.44

Model: excluding outliers (n=5) Annual medial tibial cartilage volume change = Intercept + β_1 × medial CC + β_2 × lateral CC + β_3 × Age + β_4 × Sex + β_5 × BMI

Overall model test		Test of model assumptions		
		Shapiro-Wilk test of		
F(6,38)	4.84	*residuals*	z = -0.092	*P* = 0.537

P > F	0.001	*Homoscedasticity*	chi2 = 0.95 *P* = 0.329
R-squared	0.433	*Variance inflation factors*	All < 1.82

Predictor	β	Std. Err.	t	*P*>t	95% Conf. Interval	
Medial CC (VM-SM)	-0.15	0.04	-3.95	0.000	-0.22	-0.07
Lateral CC(VL-BF)	0.08	0.03	2.48	0.018	0.01	0.14
Baseline cartilage volume	-121.25	102.33	-1.18	0.243	-328.41	85.91
Age	0.03	0.05	0.55	0.585	-0.07	0.12
Sex	-1.86	0.68	-2.74	0.009	-3.24	-0.49
BMI	0.01	0.08	0.12	0.906	-0.16	0.18
Intercept	-0.60	4.44	-0.13	0.894	-9.58	8.39

VM – vastus medialis; VL – vastus lateralis; SM – semimembranosus; BF – biceps femoris; CC – co-contraction; BMI – body mass index; **β**– coefficient; Std. Err. – standard error; 95% Conf. Interval – 95% confidence interval.

Table 3 Multiple regression analysis: Ratio of medial to lateral knee co-contraction

Model: Annual medial tibial cartilage volume change = Intercept + β_1 × medial CC / lateral CC + β_2 × Age + β_3 × Sex + β_4 × BMI

Overall model test		Test of model assumptions		
		Shapiro-Wilk test of		
F(5,44)	2.1	*residuals*	z = -1.545	*P* = 0.939
P > F	0.084	*Homoscedasticity*	chi2 = 1.77	*P* = 0.184
R-squared	0.193	*Variance inflation factors*	All < 1.16	

Predictors	**β**	Std. Err.	t	*P*>t	95% Conf.	Interval
Medial CC / lateral CC	-4.07	1.59	-2.56	0.014	-7.28	-0.87
Baseline cartilage volume	-10.55	119.22	-0.09	0.930	-250.82	229.71
Age	0.03	0.06	0.54	0.593	-0.08	0.15
Sex	-1.48	0.89	-1.66	0.104	-3.28	0.32
BMI	-0.07	0.10	-0.68	0.500	-0.27	0.14
Intercept	1.49	5.88	0.25	0.802	-10.37	13.34

Model: excluding outliers (n=3) Annual medial tibial cartilage volume change = Intercept + β_1 × medial CC / lateral CC + β_2 × Age + β_3 × Sex + β_4 × BMI

Overall model test		Test of model assumptions		
		Shapiro-Wilk test of		
F(5,41)	3.25	*residuals*	z = -0.650	*P* = 0.742
P > F	0.015	*Homoscedasticity*	chi2 = 0.16	*P* = 0.687

R-squared 0.284 *Variance inflation factors* All < 1.15

Predictors	**β**	Std. Err.	t	*P*>t	95% Conf.	Interval
Medial CC / lateral CC	-3.60	1.31	-2.75	0.009	-6.24	-0.96
Baseline cartilage volume	24.80	97.78	0.25	0.801	-172.68	222.28
Age	0.02	0.05	0.34	0.739	-0.08	0.11
Sex	-1.61	0.74	-2.17	0.036	-3.11	-0.11
BMI	0.06	0.09	0.72	0.477	-0.11	0.24
Intercept	-1.99	4.84	-0.41	0.682	-11.77	7.78

VM – vastus medialis; VL – vastus lateralis; SM – semimembranosus; BF – biceps femoris; CC – co-contraction; BMI – body mass index; **β** – coefficient; Std. Err. – standard error; 95% Conf. Interval – 95% confidence interval.

Fig. 1

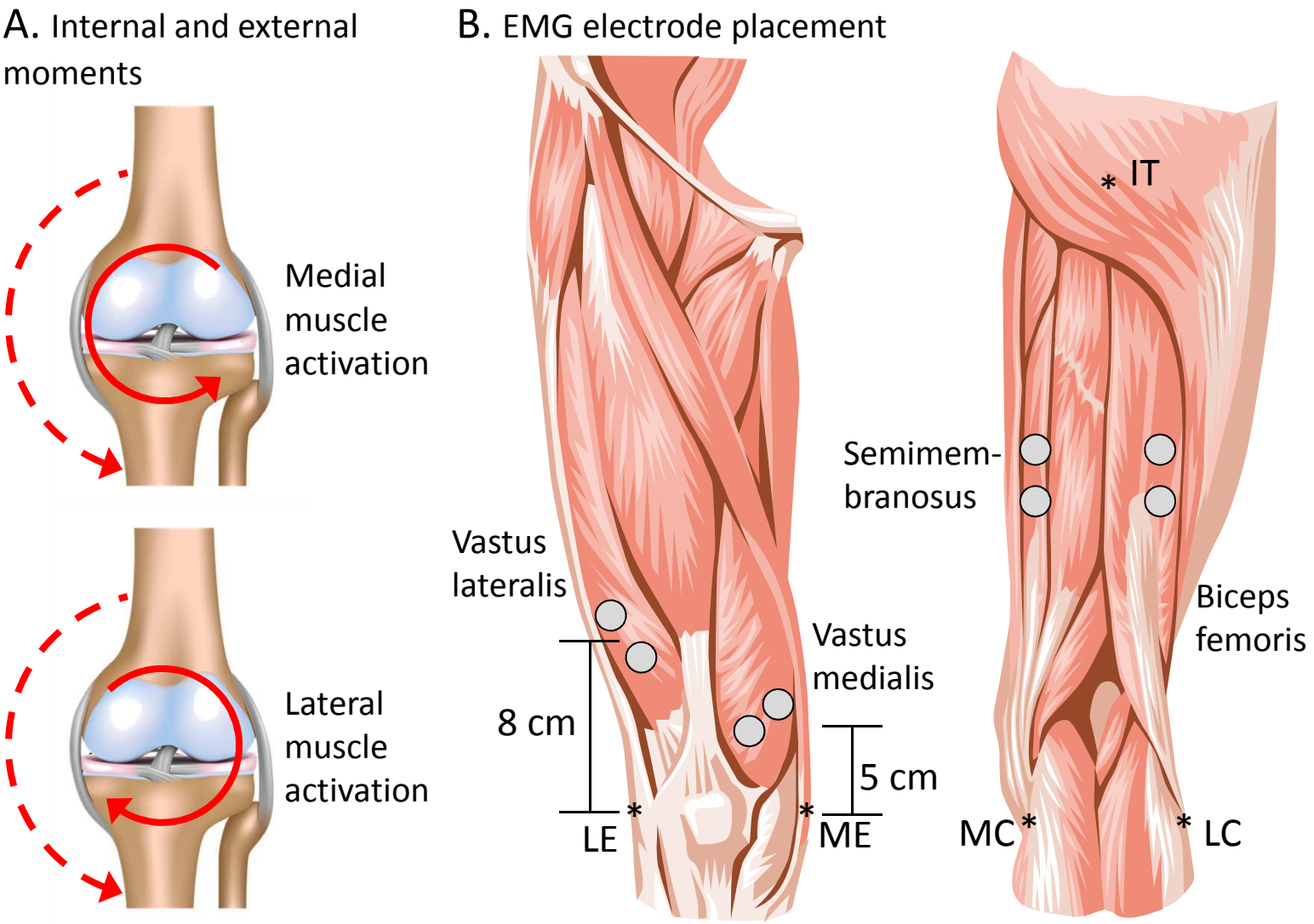


Fig. 2

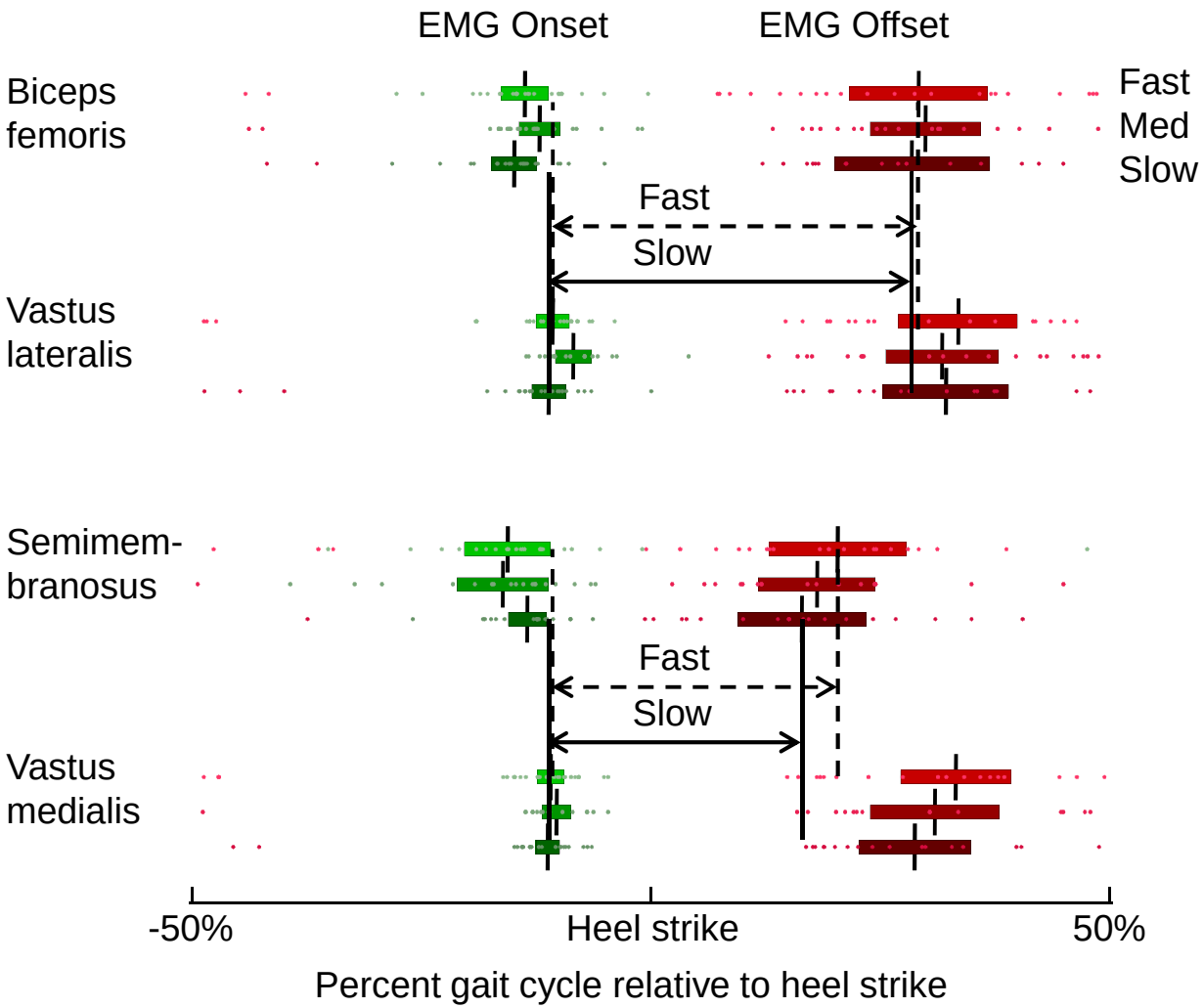
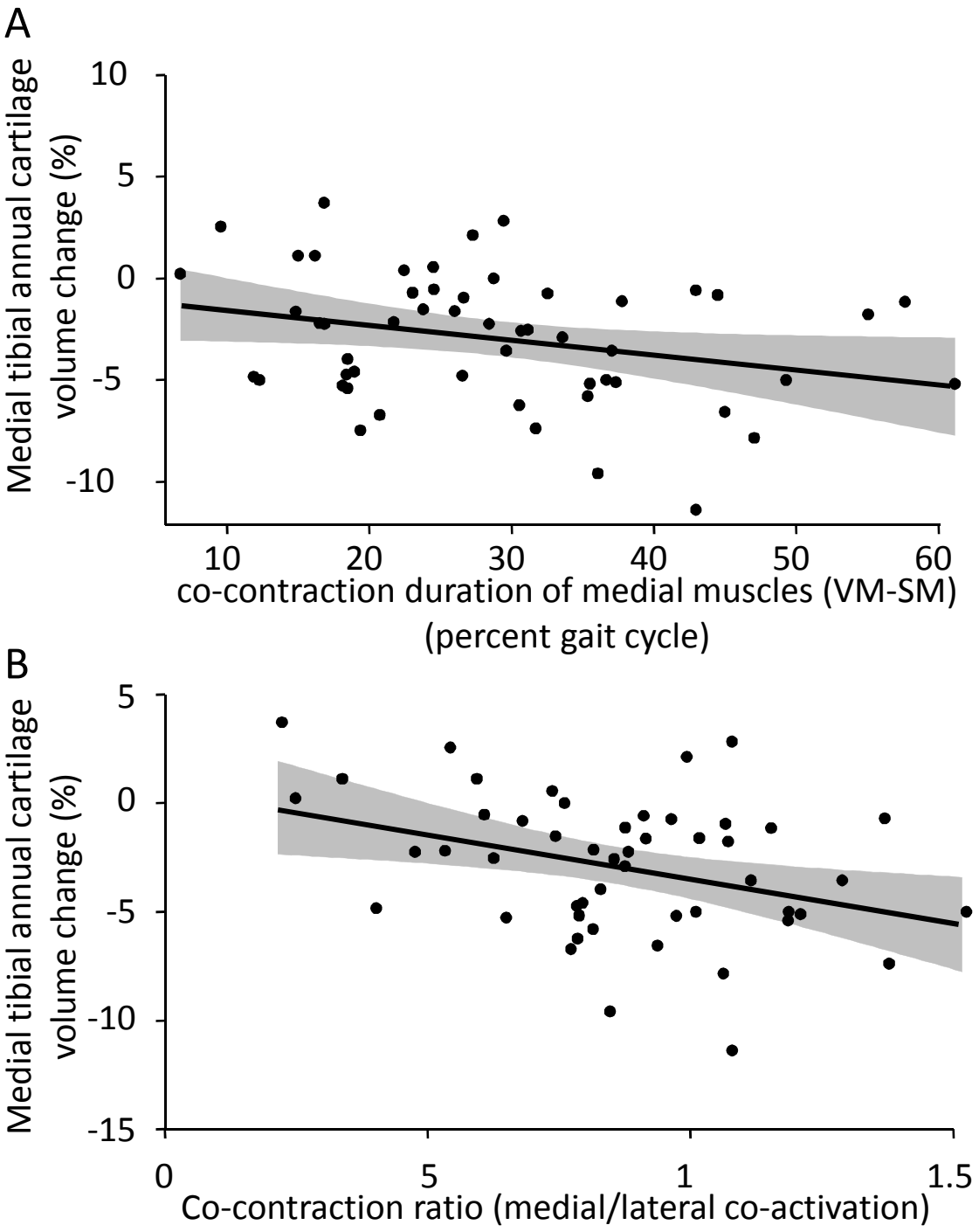


Fig. 3



Highlights

- *Prospective study of cartilage loss and co-contraction of knee muscles in knee OA*
- *Temporal parameters of knee muscle EMG during gait were measured at baseline*
- *Change in medial tibial cartilage volume measured over 12 months*
- *Longer medial knee muscle co-contraction duration relates to greater cartilage loss*
- *Longer duration of lateral muscle co-contraction relates to slower OA progression*

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