Title

Association between hamstring coactivation during isokinetic quadriceps strength testing and knee cartilage worsening over 24 months

Journal

Osteoarthritis and Cartilage, 30(6)

ISSN

1063-4584

Authors

Murphy, MT
Wang, N
Felson, DT
et al.

Publication Date

2022-06-01

DOI

10.1016/j.joca.2022.03.002

Peer reviewed

HHS Public Access

Author manuscript

Osteoarthritis Cartilage. Author manuscript; available in PMC 2022 September 07.

Published in final edited form as:

Osteoarthritis Cartilage. 2022 June ; 30(6): 823–831. doi:10.1016/j.joca.2022.03.002.

Association between Hamstring Coactivation during Isokinetic Quadriceps Strength Testing and Knee Cartilage Worsening over 24 Months

Michael T. Murphy, MD,
Department of Rehabilitation Medicine, University of Kansas Medical Center, 3901 Rainbow Boulevard, Mailstop 1046, Kansas City, KS, 66160

Na Wang, MA,
Department of Biostatistics and Epidemiology, Boston University, Boston, MA, USA

David T. Felson, MD, MPH,
Department of Epidemiology, Boston University, Boston, MA, USA

Michael C. Nevitt, PhD, MPH,
Department of Epidemiology and Biostatistics, University of California-San Francisco, San Francisco, CA, USA

Cora E. Lewis, MD, MSPH, FACP, FAHA,
Department of Epidemiology, University of Alabama at Birmingham, Birmingham, AL, USA

Laura Frey-Law, PhD,
Department of Physical Therapy and Rehabilitation Science, University of Iowa, Iowa City, IA, USA

Ali Guermazi, MD, PhD,
Department of Radiology, Boston University, Boston, MA, USA

Neil A. Segal, MD, MS
Department of Rehabilitation Medicine, University of Kansas Medical Center, Kansas City, KS, USA

Abstract

P: (913) 485-7838, mmurphy11@kumc.edu.

Author contributions:
Micheal T. Murphy: drafting of the article, critical revision of the article for important intellectual content, final approval of the article
Na Wang: statistical expertise, analysis and interpretation of data
David T. Felson: statistical expertise conception of design; analysis and interpretation of data, final approval of the article
Michael C. Nevitt: conception of design
Cora E. Lewis: conception of design
Laura Frey-Law: conception of design, critical revision of the article for important intellectual content, final approval of the article
Neil A. Segal: conception of design, analysis and interpretation of data, drafting of the article, critical revision of the article for important intellectual content, final approval of the article

Competing Interests:
The authors declare no competing interests.

Objective: This study aimed to determine longitudinal associations, including sex-specific differences, between greater knee flexor antagonist coactivation and worsening cartilage morphology in knees with or at risk for OA.

Design: Baseline measurements were collected at the 60-month visit of a longitudinal osteoarthritis study following community-dwelling participants (MOST). Knee flexor and extensor muscle activity were measured with surface electromyography during a maximal isokinetic knee extension task. MRI analyzed knee cartilage morphology at baseline and 24-month follow-up. Multivariable adjusted logistic regression models were used to assess associations between coactivation level and cartilage morphology worsening .

Results: Analysis of 373 women (mean±SD age 67.4±7.3 years and BMI 29.7±5.0 kg/m^2) and 240 men (66.5±7.8 years and 29.9±4.5 kg/m^2) revealed that women had greater medial ($p<0.001$), lateral $p<0.001$), and combined ($p<0.001$) hamstring coactivation than men. In both sexes, combined hamstring coactivation was associated with patellofemoral cartilage morphology worsening [1.23 (1.02, 1.49)] and to a less significant degree with whole knee cartilage morphology worsening [1.21 (0.98, 1.49)]. In men, greater combined hamstring coactivation was associated with increased risk for whole knee [1.59 (1.06, 2.39)] and patellofemoral [1.38 (1.01, 1.88)] cartilage morphology worsening and point estimates suggested association between medial hamstring coactivation and medial tibiofemoral cartilage morphology worsening. No significant associations were detected between greater hamstring coactivation and cartilage morphology worsening in women.

Conclusions: These findings suggest a longitudinal relationship between antagonist hamstring coactivation during isokinetic knee extensor testing and worsening of cartilage morphology over 24 months in men with or at risk for knee OA.

Keywords

Muscle Activation; Knee; Osteoarthritis; Epidemiology

Introduction:

Knee osteoarthritis (OA) is a painful chronic disease affecting the entire knee joint, and its severity impacts patients' physical function, mental health, and quality of life. The term, muscle coactivation, describes the simultaneous activation of an antagonist muscle group during activation of an agonist muscle supporting a given joint[1]. In young healthy individuals coactivation of the quadriceps and hamstring muscles occurs predominately in early stance and terminal swing phase and to a lesser extent at push-off[2]. Physiologic levels of coactivation are important for knee joint stability. Hamstring muscles play a key role in knee flexion control by protecting against hyperextension in terminal swing and early stance[3]. However, previous work has revealed that greater hamstring coactivation is associated with lower knee extensor strength[4] and evidence suggests that higher levels of coactivation during walking lead to increased joint loading[5], which may be due to joint laxity[6], pain[7], or instability [8].

Knee OA leads to structural joint degeneration which is associated with altered biomechanical features of gait and clinical symptoms. One such biomechanical feature

is increased muscle coactivation which occurs in moderate[9, 10] and severe knee OA[11] and is associated with greater progression of knee osteoarthritis[1213–15]. It has been posited that coactivation of knee antagonist muscles during walking serves as a stability strategy[16]. In OA patient populations, this is evidenced by a stereotypical knee-stiffening gait pattern to reduce knee joint motion variability[17, 18]. However, excessive coactivation may be an inefficient and even a counterproductive strategy for joint stabilization and may actually lead to a sense of joint instability[19] and even disease worsening. Assessment of muscle coactivation during strength testing provides a reproducible means of assessing neuromuscular control, defined as the efferent motor response to sensory input from the somatosensory system, visual system, and vestibular system, and has been shown to occur in a generalized manner across joints and test paradigms[1]. Thus, as a potential risk factor for knee joint worsening, coactivation during a controlled strength assessment may provide a reproducible and standardized means of assessing neuromuscular control both within and between individuals.

Historically, in people with knee OA, gait biomechanics have been used to model joint loading and assess joint function. However, these studies are often confounded by variables such as walking speed[20], obesity[21], and pain[7] which have the potential to mask relationships with structural changes. Additionally, women have a higher incidence of knee OA and demonstrate greater pain sensitivity than males [22]. Thus, this study investigated one of the hypotheses of the Multicenter Osteoarthritis Study (MOST), that greater coactivation of the knee flexor muscles during a knee maximal extension task is associated with worsening of ipsicompartmental cartilage morphology . To inform therapies, targeted at modifiable risk factors for worsening of knee OA, this study characterized the extent to which sex-specific muscle coactivation was associated with knee cartilage damage.

Methods:

Participants and Characteristics

MOST is a longitudinal cohort study of community-dwelling adults with or at elevated risk for knee OA, who were between the ages of 55 and 84 years at the baseline visit for this study (60-month visit for MOST). Enrollment in MOST was described previously[23]. In brief, participants volunteered for the study through responding to mass mailings or advertisements. After volunteering, participants were screened via telephone for risk factors including age, sex, previous knee injury or surgery or overweight/obese status. Framingham Heart Study cohort percentiles were used for determining overweight/obese status[23]. Participants in this cohort were eligible for the current study if they had usable sEMG measurements, coactivation data and a readable MRI for the corresponding knee with sEMG. If they did not meet these requirements, they were excluded from analysis.

Assessments

Body mass index (BMI) was calculated from body mass and body height as previously described[23]. Varus alignment was measured using hip-knee-ankle axis on full-limb coronal radiographs. Coronal malalignment was defined as a ≥2° difference from neutral[19]. Radiographic Kellgren-Lawrence (KL) grades were used for assessing OA severity[24].

The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain sub-score[25, 26] , which uses a 0-20 scale with 0 representing no pain and 20 representing the worst self-reported knee-related pain, was used to measure pain.

Strength

As previously described,[4] we measured strength in the right lower limb except in participants who had total knee replacement on the right, in which case the left side was measured. Participants completed four repetitions of alternating maximal knee flexion and extension at 60°/second on an isokinetic dynamometer (Cybex 350, CSMi, Stoughton, MA). Strength measurements were excluded if the maximal extensor strength was measured to be less than 20Nm, as all participants were independently ambulatory, indicating greater strength than this nominal value. Therefore, a measurement this low indicated that the participant did not give adequate effort for strength and co-activation testing. Further details of the testing protocol and strength testing exclusion criteria have been described previously[27, 28].

Muscle Activation

Quadriceps and hamstring muscle activation levels were measured using a 4-channel surface electromyography (sEMG) system (Delsys, Boston, MA). Measurements were made during the isokinetic knee extensor strength test and normalized to the maximal extensor or flexor activation level, for quadriceps and hamstring muscles, respectively.

The protocol for sEMG followed internationally developed standards[29]. First, the skin over the mid-bellies of the medial and lateral quadriceps muscles: vastus medialis and vastus lateralis; and the medial and lateral hamstrings muscles: biceps femoris and semitendinosus muscles, were cleaned with isopropol alcohol. The small surface electrodes (41×20×5mm) were applied to the skin over each muscle using medical-grade double-sided adhesive strips provided by the sEMG manufacturer. The electrodes were positioned in line with the muscle fibers, so that the 1 cm Ag-AgCl recording bars were perpendicular to the muscle fibers. The lateral hamstring sEMG electrode (biceps femoris) was placed along the lateral posterior thigh, halfway between the ischial tuberosity and the lateral femoral condyle. The medial hamstring (semimembranosis) electrode was applied mid-way down the posterior thigh, between the ischial tuberosity and the medial femoral condyle, consistent with prior methods[30]. For more details and a photo, see Segal et al (2015)[19]. A reference electrode was placed over the bony prominence of the opposite ankle.

The differential bar electrodes had a fixed inter-electrode spacing of 1 cm and were pre-amplified by a gain of 10. Variable post-amplification gains ranged from 100 to 10,000 and the signal was bandpass filtered between 20-450 Hz. The signals were collected at a sampling frequency of 1000Hz, sufficiently high to detect mean activation amplitude over time while minimizing data storage requirements, using a 12-bit data acquisition card (National Instruments, Austin, TX). The rectified sEMG signals were averaged across 200ms moving windows, acting as a low-pass filter. The mean activation of each muscle was assessed over a 1400ms period centered on the 1500 ms contractions (90 degrees at 60 degrees/sec) performed during the maximal knee extension and flexion efforts.

Medial and lateral hamstring sEMG during extension efforts were standardized to the peak sEMG value obtained during flexion efforts (i.e., % of voluntary maximum activation). The mean activation of the hamstring muscles across the 4 contractions was used as the measure of muscle coactivation[19]. Specifically, the sEMG signals were standardized to their maximal activation when acting as an agonist, which allowed control for between-subject differences in impedance, allowing each muscle's activation to be assessed as a percent of its maximum activation[1, 31]. While there are multiple indices of coactivation in the literature, this approach was chosen as it is not confounded by choice of agonist muscle (e.g. medial vs lateral quadriceps muscles) which is necessary when assessing coactivation during submaximal tasks to account for reduced overall muscle activation. The square root of the difference between the squares was used to adjust for baseline noise, as outlined in Equation (1)[19].

$$\text{Hamstring Antagonist Coactivation} = \sqrt{\left\{(\text{Antagonist Amplitude})^2 - (\text{Mean Baseline Amplitude})^2\right\}} \quad \text{Equation 1}$$

Antagonist amplitude is the mean activation of the medial or lateral hamstrings during repetition of maximal quadriceps torque, as a percent of the maximal medial or lateral hamstring activation during agonistic (flexion) contraction. Baseline amplitude is the mean baseline amplitude as a percent of the maximal activation of the medial or lateral hamstring during rest. If recorded baseline amplitude was greater than recorded antagonist amplitude, hamstring coactivation was considered to be zero. Combined hamstring coactivation was calculated as the root mean square of the medial and lateral hamstring coactivation levels (see Equation (2))[19].

$$\text{Combined Hamstring Coactivation} = \sqrt{\frac{\left\{(\text{Medial Hamstring Coactivation})^2 + (\text{Lateral Hamstring Coactivation})^2\right\}}{2}} \quad \text{Equation 2}$$

MRI

The magnetic resonance imaging (MRI) protocol, including pulse sequences, has been previously described[32]. The MRIs were read by radiologists for cartilage morphology using Whole-Organ Magnetic Resonance Imaging Score (WORMS)[33]. There were five medial and five lateral tibiofemoral joint regions: central and posterior femoral subregions, and anterior, central, and posterior tibial subregions. These subregions were grouped into medial tibiofemoral cartilage morphology (MTF) and lateral tibiofemoral cartilage morphology (LTF) by combining femoral and tibial subregions in the medial and lateral compartments.[34] There were four patellofemoral joint subregions: medial and lateral anterior femoral and medial and lateral patellar subregions. These regions were grouped as patellofemoral cartilage morphology (PF). Cartilage morphology was graded from grade 0-6, with increasing grades indicating greater damage. Knees with a readable pair of 60- and 84-month MRIs were selected for reading based on the quality and suitability of the paired images for assessing change in cartilage, menisci, bone marrow lesions and other OA features. In cases in which a participant had a readable MRI for both knees, one knee

was randomly selected for reading. Only participants with MRI available for the knee with sEMG were included.

Definition of Knee Worsening

Whole knee cartilage morphology (WK) worsening was defined as worsening in any subregion: LTF, MTF, or PF between the 60- and 84-month visits, other than development of non-specific signal (change from grade 0 to grade 1).

Statistical Analyses

Sex-specific univariate distributions were calculated for age, BMI and hamstring coactivation and frequencies were calculated for sex and KL grade. To determine if greater coactivation of knee flexor muscles during a maximal knee extension task increases the risk of cartilage morphology worsening in the ipsilateral knee, we constructed crude and sex-specific logistic regression models with the dichotomous dependent variable being worsening over the 24-month period and the continuous independent variable being coactivation, adjusted for age, study site, BMI, history of knee injury or surgery, side assessed and KL grade to reduce the chances of bias in interpretation of the study findings. Specifically, to pair cartilage regions with the muscle groups thought to have the greatest impact on them, models tested relationships between medial hamstring coactivation and MTF cartilage morphology, lateral hamstring coactivation and LTF cartilage morphology, combined hamstring coactivation and WK cartilage morphology, and combined hamstring coactivation and PF cartilage morphology. Odds ratio estimates per one standard deviation unit and 95% confidence limits were calculated and tests for linearity between coactivation and risk for cartilage worsening were completed. Confirmatory analyses employed generalised estimating equations to assess worsening of cartilage in each individual WORMS subregion to expand the number of worsening outcomes. All analyses were completed using SAS Version 9.4 (SAS Inc, Cary, NC).

Results:

From the MOST 60-month follow-up visit, 613 participants were included in analyses. The mean±SD age and BMI of the 373 women and 240 men included in addition to other participant characteristics are presented in Table 1.

Of those excluded from analyses, as depicted in Figure 1, 27% of participants were ineligible due to not completing sEMG assessment or having unusable coactivation data while 55.3% of participants did not have cartilage morphology readings. Of those without cartilage morphology data, the majority were due to sEMG having been collected on the side contralateral to that of the cartilage morphology readings for MOST and 573 or 20.5%, had undergone total knee replacement by the 84-month visit.

In the full sample of participants, multivariable adjusted logistic regression results [odds ratio estimate per one standard deviation (95% confidence limits)] did not reveal relationships between medial hamstring coactivation and MTF cartilage morphology worsening [1.06 (0.87-1.29), p = 0.558] or lateral hamstring coactivation and LTF cartilage morphology worsening [0.93 (0.75, 1.17), p = 0.539]. However, a relationship was evident

between combined hamstring coactivation and PF cartilage morphology worsening with an effect size of [1.23 (1.02, 1.49), p = 0.035]. A smaller magnitude of association was found between combined hamstring coactivation and WK cartilage morphology worsening [1.21 (0.98, 1.49), p = 0.076].

Results for sex-specific multivariable adjusted logistic regression, presented in Table 2, demonstrated a significant relationship in men between combined hamstring coactivation and WK cartilage morphology worsening with an effect size indicated by odds ratios of 1.59 (95%CI 1.06, 2.39) and for combined hamstring coactivation and PF cartilage morphology worsening, OR of 1.38 (1.01, 1.88). Additionally, point estimates suggested an association between medial hamstring coactivation and MTF cartilage morphology worsening in men. A histogram of coactivation levels for the full study sample and by sex is presented in Supplementary Figures 1–6. Sex-specific unadjusted logistic regression results are available in Supplementary Table 1. Unadjusted and adjusted sex-specific multivariable generalized estimating equation (GEE) analyses were performed and closely mirrored logistic regression results (Supplementary Tables 2 and 3).

Discussion:

This study characterized the extent to which greater knee flexor muscle coactivation during a maximal knee extension task was longitudinally associated with worsening compartment-specific cartilage morphology over a 24-month period in community-dwelling adults with or at risk for knee OA. By controlling for age, study site, BMI, history of knee injury or surgery, side assessed and KL grade, this study also allowed investigation of additional risk factors potentially associated with antagonist coactivation and knee cartilage worsening.

Muscle co-activation is associated with knee OA severity[35, 36]. Quadriceps muscle weakness is a known risk factor for the development of symptomatic knee OA as well as worsening of joint space narrowing[23, 28], and increased hamstring loading has been shown to contribute to patellar malalignment by increasing lateral shift and tilt of the patella, thus contributing to overloading of the lateral cartilage[37]. Furthermore, a prior MOST analysis demonstrated that net quadriceps strength was attenuated by hamstring coactivation in women but not men[4]. Thus, we hypothesized that greater hamstring coactivation would be associated with knee OA worsening, likely with a female predominance.

Our results demonstrated no significant relationships between medial hamstring and lateral hamstring coactivation and MTF and LTF cartilage worsening, respectively, but did show associations between combined hamstring coactivation and PF cartilage worsening and WK cartilage worsening, respectively. Based on the effect sizes reflected by the point estimates and confidence intervals for the odds ratios, sex-specific analyses revealed significant associations between hamstring coactivation and worsening cartilage morphology in men despite women having greater medial, lateral, and combined hamstring coactivation. Specifically, men with greater antagonist knee flexor coactivation demonstrated a higher magnitude of association with WK and PF cartilage worsening.

Previous studies have found that women not only have greater hamstring coactivation [1, 38] but also are at elevated risk for cartilage loss[39]. Our findings partially diverge from these studies suggesting that muscle strength differences between men and women may play a role in OA progression. Sistante *et al.* reported that in addition to greater quadriceps strength, men had significantly greater prevalence of knee injury and knee surgery[4]. Even after controlling for knee injury and knee surgery in the present study, men with greater coactivation exhibited a significant association with worsening knee cartilage morphology. Increased joint loading is a known risk factor for knee OA progression[1, 8–11] and men have been shown to have greater baseline quadriceps strength[4]. Importantly, although beyond the scope of the current study, additional analyses stratifying by strength suggest that while there is some collinearity between co-activation and strength, the effect of coactivation was largely independent of quadriceps strength (Appendix 1). Thus, it is plausible that greater quadriceps strength combined with greater hamstring coactivation could increase joint loading, facilitating disease progression. However, muscle strength differences alone likely do not fully explain the findings in the present study.

Women have been found to have less prominent anterior medial and lateral femoral condyles, greater Q-angles, and reduced medial-lateral:anterior-posterior aspect ratios[39–41]. Despite the presence of these anatomical differences, no casual link between them and knee OA has been established. Nevertheless, the possibility that sex-specific anatomical differences play an adaptive or maladaptive role in knee OA persists. Future studies need to examine these differences in relation to the development of knee OA.

In addition to anatomical variations, gender differences may be influenced by other factors such as knee pain and knee instability[22]. Knee pain is commonly associated with knee OA[1, 42, 43], and women have been found to have significantly greater WOMAC knee pain scores and knee OA severity based on KL grade in comparison to men[44]. Additionally, greater pain sensitization has been associated with greater overall and medial hamstring co-contraction during knee extension[45]. While we did not investigate associations between knee pain and coactivation, by controlling for KL grade, our findings do provide additional support to Fitzgerald *et al.* who suggest that knee OA (KL>2) and knee pain contitrubute to both coactivation as well as knee instability[46]. It appears likely that a complex interplay between peripheral and central nervous system processes and alterations in pain sensitization, motor pathways (i.e. hamstring coactivation)[1], and knee OA severity exists. Additional research is needed to better understand the reasons for these differences between men and women.

To our knowledge, the current study is the first to examine associations between antagonist hamstring coactivation and worsening of knee cartilage morphology. It has previously been posited that elevated levels or greater duration of coactivation serve as protective mechanisms in response to pain (or anticipated pain) or to stabilize a potentially unstable joint in those with knee OA[47]. It also has been suggested that elevated levels of coactivation may concurrently contribute to disease progression through increased joint loading[6, 9–11, 13]. Alternatively, having excessive or insufficient hamstring coactivation could confer elevated risk. Our findings in conjunction with the aforementioned studies provide evidence that certain risk factors for knee OA worsening, namely strength differences, anatomical

variations, and pain perception, may be sex-specific. Given that these associations were detected in an observational study, further assessment should be considered in interventional studies to better determine the effect of modifying antagonist hamstring coactivation on risk for cartilage worsening as well as potentially the mechanism for the effects detected.

Study Strengths

This study had several strengths, including clinical relevance and generalizability. MOST is the largest and most comprehensive epidemiological study of knee OA completed to date that included measures of muscle coactivation. The focus on symptomatic disease in MOST in addition to radiographic evidence of disease contrasted with prior epidemiologic studies and enhanced the relevance to adults who present for clinical care. Additionally, recruitment in MOST maintained a distribution of age and sex in proportion to the U.S. population by selecting a community-acquired sample of men and women aged 55-89 at the baseline visit for the current study, rather than a clinic-based sample, who had or were at elevated risk for knee OA[23]. This, coupled with the fact that MOST was conducted in two different regions of the United States, enhances the relevance and generalizability of the study findings.

Study Limitations

Limitations of this study included potential technical complications with sEMG, muscle activation data collection during a seated isokinetic task, rather than a more functional strength test, and incomplete data collection. Knee extensor and flexor muscle activation during attempted maximal concentric isokinetic contractions while seated may not represent how these muscle groups are used during functional activities, such as ambulation. However, coactivation measurements during both seated and dynamic activities have been reported previously in several populations with associated merits and drawbacks[6, 31, 48, 49]. While a more functional test would be of interest, the use of a very standardized test in this cohort of thousands of individuals allowed reproducible measurements on a large scale. Additionally, due to an inability to time lock the EMG with the isokinetic testing equipment, the center of each contraction was chosen. If able, future studies should investigate hamstring co-activation during the initial acceleration and final deceleration phases. Conversely, in some participants, the EMG sensors may have caused discomfort during testing, potentially impacting coactivation responses; however pain at the electrode sites was not reported by participants, who were queried about pain during the strength test immediately after completing it. Future studies comparing co-activation assessed during standardized testing and functional tasks may better delineate this relationship.

Although the protocol for sEMG followed internationally developed standards, extraneous electrical noise is an inherent problem for accurate assessment of sEMG. Challenges such as electrode-skin contact, extraneous electrical signals, and cross-talk due to volume conduction can reduce signal-to-noise characteristics. For example, greater thigh subcutaneous adipose tissue, which is more characteristic in women,[50] could contribute to poorer quality sEMG signals and thus prevented detection of significance in women. However, sEMG signal quality was manually evaluated on a 3-point scale as good, moderate or poor. Only those with moderate or good quality signals were considered. While most point estimates for effect sizes are relatively small (close to 1.0), confidence intervals

include what could be clinically important effects, particularly in men. Statistical power for the study was limited, due to 27% of MOST participants could not be included due to failure to complete sEMG assessment or having unusable coactivation data and approximately half of participants had MRI measurements on the side contralateral to sEMG measurements, resulting in inability to include those participants. Since the side of MRI reading was randomly selected for most of these participants, the data were missing at random.

Implications

This study provided evidence for associations between antagonist hamstring coactivation and cartilage worsening in men, but not in women. While it remains unclear whether hamstring coactivation serves an adaptive or maladaptive role in knee OA, the associations observed in this study suggest a sex-specific relationship.

Conclusion

This study demonstrated longitudinal associations between greater levels of antagonist hamstring coactivation and worsening of cartilage morphology over 24 months in men. This supports the premise that sex-specific differences, possibly attributable to neuromuscular activation, anatomical factors and peripheral and central pain mechanisms, exist and confer variable protective and/or deleterious effects on individuals in the development or worsening of knee OA. Future investigations should explore these differences and their influence on hamstring coactivation in individuals at risk for worsening knee CM.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments:

The authors acknowledge the contributions of the participants and staff of the Multicenter Osteoarthritis Study (MOST).

Role of funding source:

This study was supported by NIH grants to: Boston University (David Felson - AG18820); the University of Iowa (James Torner and Neil Segal - AG18832); University of Alabama at Birmingham (Cora E. Lewis - AG18947); University of California San Francisco (Michael Nevitt - AG19069). The authors have no professional relationships with companies or manufacturers who will benefit from the results of the present study.

Appendix 1:

Given that 1) muscle co-activation was found to be associated with worsening cartilage morphology, 2) quadriceps muscle weakness is a known risk factor for worsening of tibiofemoral joint space narrowing, 3) net quadriceps strength is attenuated by hamstring coactivation in women but not men, and 4) in men, greater hamstring coactivation is associated with elevated risk of cartilage loss, a set of follow-up analyses were completed to assess the extent to which the findings of the current study (i.e. that greater coactivation is associated with cartilage loss in men but not in women) relates to the presence of both higher strength and coactivation. To evaluate the extent to which the effect of hamstring muscle co-activation on cartilage loss is independent of quadriceps muscle strength, sex-

stratified and strength-stratified (upper and lower halves) logistic regression models (GEE) were constructed. Longitudinal associations between baseline hamstring coactivation level (per 1SD) and the presence of cartilage worsening in the whole knee over 24-month follow-up was modeled while adjusting for maximal quadriceps strength, age, BMI, clinic site and history of knee injury or surgery and odds ratios (OR) and 95% confidence intervals (CI) were calculated per 1 standard deviation of the predictor variables.

In men, both greater coactivation and lower strength were associated with whole knee cartilage worsening after adjustment for each other and there was no significant interaction. In both men and women, lower strength was associated with elevated risk for worsening cartilage damage. In fully adjusted models, subgroup analyses revealed that, in men in the higher half of the distribution of strength, antagonistic hamstring coactivation was associated with whole knee cartilage worsening as detailed in the table below. This provided confirmatory evidence that greater hamstring coactivation is associated with cartilage worsening in men, while clarifying that this effect persists even after adjusting for the significant association between lower quadriceps strength and cartilage worsening.

	Outcome N/Total N	OR (95% CI)	p-value
Stronger Men	217/436	1.55 (1.11, 2.16)	0.0109
Weaker Men	94/168	1.14 (0.83, 1.57)	0.4057
Stronger Women	189/392	1.04 (0.81, 1.34)	0.7500
Weaker Women	148/254	0.99 (0.76, 1.28)	0.9112

Abbreviations:

BMI	body mass index
CM	cartilage morphology
GLM	general linear model
KL grade	Kellgren-Lawrence grade
LTF	lateral tibiofemoral
MOST	Multicenter Osteoarthritis Study
MRI	magnetic resonance imaging
MTF	medial tibiofemoral
OA	osteoarthritis
PF	patellofemoral
sEMG	surface electromyography
WK	whole knee

WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index
WORMS	Whole-Organ Magnetic Resonance Imaging Score

References

1. Frey-Law LA, Avin KG. Muscle coactivation: a generalized or localized motor control strategy? Muscle Nerve 2013; 48: 578–585. [PubMed: 24037745]
2. Strazza A, Mengarelli A, Fioretti S, Burattini L, Agostini V, Knaflitz M, et al. Surface-EMG analysis for the quantification of thigh muscle dynamic co-contractions during normal gait. Gait Posture 2017; 51: 228–233. [PubMed: 27825072]
3. Perry J, Burnfield JM. Gait Analysis: Normal and Pathological Function. J Sports Sci Med 2010; 9: 353.
4. Sisante JF, Wang N, Felson DT, Nevitt MC, Lewis CE, Frey-Law L, et al. Influence of Antagonistic Hamstring Coactivation on Measurement of Quadriceps Strength in Older Adults. PM R 2020; 12: 470–478. [PubMed: 31585496]
5. Trepczynski A, Kutzner I, Schwachmeyer V, Heller MO, Pfitzner T, Duda GN. Impact of antagonistic muscle co-contraction on in vivo knee contact forces. J Neuroeng Rehabil 2018; 15: 101. [PubMed: 30409163]
6. Lewek MD, Rudolph KS, Snyder-Mackler L. Quadriceps femoris muscle weakness and activation failure in patients with symptomatic knee osteoarthritis. J Orthop Res 2004; 22: 110–115. [PubMed: 14656668]
7. Henriksen M, Alkjaer T, Lund H, Simonsen EB, Graven-Nielsen T, Danneskiold-Samsoe B, et al. Experimental quadriceps muscle pain impairs knee joint control during walking. J Appl Physiol 2007; 103: 132–139. [PubMed: 17412791]
8. Dixon PC, Gomes S, Preuss RA, Robbins SM. Muscular co-contraction is related to varus thrust in patients with knee osteoarthritis. Clin Biomech (Bristol, Avon) 2018; 60: 164–169.
9. Childs JD, Sparto PJ, Fitzgerald GK, Bizzini M, Irrgang JJ. Alterations in lower extremity movement and muscle activation patterns in individuals with knee osteoarthritis. Clinical Biomechanics 2004; 19: 44–49. [PubMed: 14659929]
10. Hubley-Kozey CL, Deluzio KJ, Landry SC, McNutt JS, Stanish WD. Neuromuscular alterations during walking in persons with moderate knee osteoarthritis. J Electromyogr Kinesiol 2006; 16: 365–378. [PubMed: 16213159]
11. Hubley-Kozey C, Deluzio K, Dunbar M. Muscle co-activation patterns during walking in those with severe knee osteoarthritis. Clinical biomechanics (Bristol, Avon) 2008; 23: 71–80.
12. Lewek MD, Ramsey DK, Snyder-Mackler L, Rudolph KS. Knee stabilization in patients with medial compartment knee osteoarthritis. Arthritis Rheum 2005; 52: 2845–2853. [PubMed: 16142714]
13. Hodges PW, van den Hoorn W, Wrigley TV, Hinman RS, Bowles KA, Cicuttini F, et al. Increased duration of co-contraction of medial knee muscles is associated with greater progression of knee osteoarthritis. Man Ther 2016; 21: 151–158. [PubMed: 26254263]
14. Davis EM, Hubley-Kozey CL, Landry SC, Ikeda DM, Stanish WD, Astephen Wilson JL. Longitudinal evidence links joint level mechanics and muscle activation patterns to 3-year medial joint space narrowing. Clin Biomech (Bristol, Avon) 2019; 61: 233–239.
15. Costello KE, Astephen Wilson JL, Stanish WD, Urquhart N, Hubley-Kozey CL. Differences in Baseline Joint Moments and Muscle Activation Patterns Associated With Knee Osteoarthritis Progression When Defined Using a Clinical Versus a Structural Outcome. J Appl Biomech 2020: 1–13.
16. Davidson BS, Judd DL, Thomas AC, Mizner RL, Eckhoff DG, Stevens-Lapsley JE. Muscle activation and coactivation during five-time-sit-to-stand movement in patients undergoing total knee arthroplasty. J Electromyogr Kinesiol 2013; 23: 1485–1493. [PubMed: 23953763]
17. Gustafson JA, Robinson ME, Fitzgerald GK, Tashman S, Farrokhi S. Knee motion variability in patients with knee osteoarthritis: The effect of self-reported instability. Clin Biomech (Bristol, Avon) 2015; 30: 475–480.

18. Astephen Wilson JL, Stanish WD, Hubley-Kozey CL. Asymptomatic and symptomatic individuals with the same radiographic evidence of knee osteoarthritis walk with different knee moments and muscle activity. J Orthop Res 2017; 35: 1661–1670. [PubMed: 27775183]
19. Segal NA, Nevitt MC, Welborn RD, Nguyen US, Niu J, Lewis CE, et al. The association between antagonist hamstring coactivation and episodes of knee joint shifting and buckling. Osteoarthritis Cartilage 2015; 23: 1112–1121. [PubMed: 25765501]
20. Landry SC, McKean KA, Hubley-Kozey CL, Stanish WD, Deluzio KJ. Knee biomechanics of moderate OA patients measured during gait at a self-selected and fast walking speed. Journal of biomechanics 2007; 40: 1754–1761. [PubMed: 17084845]
21. Runhaar J, Koes BW, Clockaerts S, Bierma-Zeinstra SMA. A systematic review on changed biomechanics of lower extremities in obese individuals: a possible role in development of osteoarthritis. Obesity Reviews 2011; 12: 1071–1082. [PubMed: 21812903]
22. Henriksen M, Christensen R, Alkjaer T, Lund H, Simonsen EB, Bliddal H. Influence of pain and gender on impact loading during walking: a randomised trial. Clin Biomech (Bristol, Avon) 2008; 23: 221–230.
23. Segal NA, Nevitt MC, Gross KD, Hietpas J, Glass NA, Lewis CE, et al. The Multicenter Osteoarthritis Study: opportunities for rehabilitation research. PM R 2013; 5: 647–654. [PubMed: 23953013]
24. Felson DT, Niu J, Guermazi A, Sack B, Aliabadi P. Defining radiographic incidence and progression of knee osteoarthritis: suggested modifications of the Kellgren and Lawrence scale. Ann Rheum Dis 2011; 70: 1884–1886. [PubMed: 21908453]
25. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. J Rheumatol 1988; 15: 1833–1840. [PubMed: 3068365]
26. Marsh JD, Bryant DM, Macdonald SJ, Naudie DD. Patients respond similarly to paper and electronic versions of the WOMAC and SF-12 following total joint arthroplasty. J Arthroplasty 2014; 29: 670–673. [PubMed: 23953392]
27. Segal NA, Glass NA, Torner J, Yang M, Felson DT, Sharma L, et al. Quadriceps weakness predicts risk for knee joint space narrowing in women in the MOST cohort. Osteoarthritis Cartilage 2010; 18: 769–775. [PubMed: 20188686]
28. Segal NA, Torner JC, Felson D, Niu J, Sharma L, Lewis CE, et al. Effect of thigh strength on incident radiographic and symptomatic knee osteoarthritis in a longitudinal cohort. Arthritis and Rheumatism 2009; 61: 1210–1217. [PubMed: 19714608]
29. Hermens HJ, Freriks B, Disselhorst-Klug C, Rau G. Development of recommendations for SEMG sensors and sensor placement procedures. Journal of Electromyography & Kinesiology 2000; 10: 361–374. [PubMed: 11018445]
30. Rainoldi A, Melchiorri G, Caruso I. A method for positioning electrodes during surface EMG recordings in lower limb muscles. J Neurosci Methods 2004; 134: 37–43. [PubMed: 15102501]
31. Biscarini A, Benvenuti P, Botti FM, Brunetti A, Brunetti O, Pettorossi VE. Voluntary enhanced cocontraction of hamstring muscles during open kinetic chain leg extension exercise: its potential unloading effect on the anterior cruciate ligament. Am J Sports Med 2014; 42: 2103–2112. [PubMed: 24918112]
32. Felson DT, Niu J, Gross KD, Englund M, Sharma L, Cooke TD, et al. Valgus malalignment is a risk factor for lateral knee osteoarthritis incidence and progression: findings from the Multicenter Osteoarthritis Study and the Osteoarthritis Initiative. Arthritis Rheum 2013; 65: 355–362. [PubMed: 23203672]
33. Peterfy CG, Guermazi A, Zaim S, Tirman PF, Miaux Y, White D, et al. Whole-Organ Magnetic Resonance Imaging Score (WORMS) of the knee in osteoarthritis. Osteoarthritis Cartilage 2004; 12: 177–190. [PubMed: 14972335]
34. Neogi T, Felson D, Niu J, Lynch J, Nevitt M, Guermazi A, et al. Cartilage loss occurs in the same subregions as subchondral bone attrition: a within-knee subregion-matched approach from the Multicenter Osteoarthritis Study. Arthritis and rheumatism 2009; 61: 1539–1544. [PubMed: 19877101]

35. Hubley-Kozey CL, Hill NA, Rutherford DJ, Dunbar MJ, Stanish WD. Co-activation differences in lower limb muscles between asymptomatic controls and those with varying degrees of knee osteoarthritis during walking. Clin Biomech (Bristol, Avon) 2009; 24: 407–414.
36. Rutherford DJ, Hubley-Kozey CL, Stanish WD. Changes in knee joint muscle activation patterns during walking associated with increased structural severity in knee osteoarthritis. J Electromyogr Kinesiol 2013; 23: 704–711. [PubMed: 23357547]
37. Elias JJ, Kirkpatrick MS, Saranathan A, Mani S, Smith LG, Tanaka MJ. Hamstrings loading contributes to lateral patellofemoral malalignment and elevated cartilage pressures: an in vitro study. Clin Biomech (Bristol, Avon) 2011; 26: 841–846.
38. Sharma L, Felson D, Dunlop D, Nevitt M, Buckwalter J, Hietpas J, et al. Knee buckling and its relationship with physical function in knee osteoarthritis (OA). Arthritis and Rheumatism 2005; 52: S396–S396.
39. Hame SL, Alexander RA. Knee osteoarthritis in women. Curr Rev Musculoskelet Med 2013; 6: 182–187. [PubMed: 23471773]
40. Conley S, Rosenberg A, Crowninshield R. The Female Knee: Anatomic Variations. JAAOS - Journal of the American Academy of Orthopaedic Surgeons 2007; 15.
41. Merchant AC, Arendt EA, Dye SF, Fredericson M, Grelsamer RP, Leadbetter WB, et al. The female knee: anatomic variations and the female-specific total knee design. Clinical orthopaedics and related research 2008; 466: 3059–3065. [PubMed: 18820981]
42. Maly MR, Costigan PA, Olney SJ. Determinants of self-report outcome measures in people with knee osteoarthritis. Arch Phys Med Rehabil 2006; 87: 96–104. [PubMed: 16401446]
43. Sharma L, Felson D, Dunlop D, Nevitt M, Buckwalter J, Hietpas J, et al. Knee buckling and its relationship with physical function in knee osteoarthritis (OA). Arthritis and Rheumatism 2005; 52: S396–S396.
44. Glass N, Segal NA, Sluka KA, Torner JC, Nevitt MC, Felson DT, et al. Examining sex differences in knee pain: the multicenter osteoarthritis study. Osteoarthritis Cartilage 2014; 22: 1100–1106. [PubMed: 24999111]
45. Stefanik JJ, Frey-Law L, Segal NA, Niu J, Lewis CE, Nevitt MC, et al. The relation of peripheral and central sensitization to muscle co-contraction: the MOST study. Osteoarthritis Cartilage 2020; 28: 1214–1219. [PubMed: 32585174]
46. Fitzgerald GK, Piva SR, Irrgang JJ. Reports of joint instability in knee osteoarthritis: its prevalence and relationship to physical function. Arthritis Rheum 2004; 51: 941–946. [PubMed: 15593258]
47. Lewek MD, Rudolph KS, Snyder-Mackler L. Control of frontal plane knee laxity during gait in patients with medial compartment knee osteoarthritis. Osteoarthritis Cartilage 2004; 12: 745–751. [PubMed: 15325641]
48. Krishnan C, Allen EJ, Williams GN. Effect of knee position on quadriceps muscle force steadiness and activation strategies. Muscle Nerve 2011; 43: 563–573. [PubMed: 21404288]
49. LaBella C Patellofemoral pain syndrome: evaluation and treatment. Prim Care 2004; 31: 977–1003. [PubMed: 15544830]
50. Bredella MA. Sex Differences in Body Composition. Adv Exp Med Biol 2017; 1043: 9–27. [PubMed: 29224088]

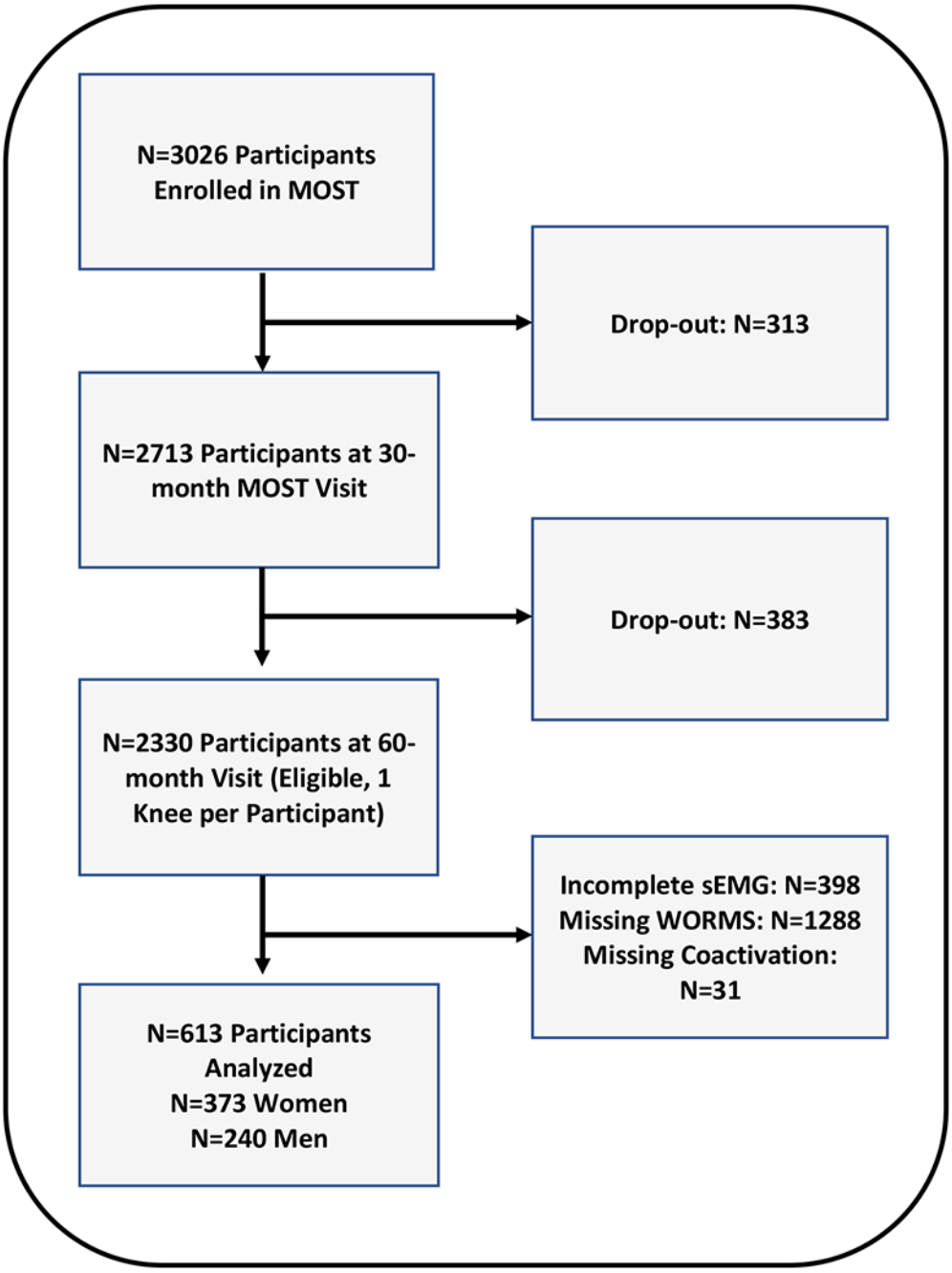

Figure 1.
Sample Available for Analysis

Table 1.

Participant Characteristics

	Women (n=373)	Men (n=240)
Age, years	67.4 ± 7.3	66.5 ± 7.8
BMI, kg/m^2	29.7 ± 5.0	29.9 ± 4.5
WOMAC Pain Sub-Score (median, IQR)	1 (0, 4)	1 (0, 2.5)
History of Surgery, %	7%	13%
History of Injury, %	24%	33%
KL grade, %		
0	35%	46%
1	17%	20%
2	25%	13%
3	21%	16%
4	2%	5%
Medial Hamstring Coactivation, %max	10.0 ± 10.2‡	6.2 ± 7.7
Lateral Hamstring Coactivation, %max	18.8 ± 13.3‡	10.9 ± 10.5
Combined Hamstring Coactivation, %max	16.0 ± 10.6‡	9.7 ± 8.3
MTF Worsening (n=593)	84 (23%)	58 (25%)
LTF Worsening (n=608)	67 (18%)	38 (16%)
PF Worsening (n=529)	87 (27%)	53 (23%)
WK Worsening (n=546)	171 (51%)	177 (55%)

Values presented as mean ± standard deviation, median (IQR), or percent (%);

‡= p <0.001;

BMI = body mass index; WOMAC Pain Sub-score: where 0 represents no pain and 20 represents the worst self-reported knee-related pain; KL = Kellgren Lawrence grade; Medial hamstring coactivation = root mean square of sEMG signal of medial hamstring coactivation during maximal isokinetic knee extension task; Lateral hamstring coactivation = root mean square of sEMG signal of lateral hamstring coactivation during maximal isokinetic knee extension task; Combined hamstring coactivation = root mean square of sEMG signal of medial and lateral hamstring coactivation during maximal isokinetic knee extension task; MTF worsening = distribution of medial tibiofemoral cartilage morphology worsening; LTF worsening = distribution of lateral tibiofemoral cartilage morphology worsening; PF worsening = distribution of patellofemoral cartilage morphology worsening; WK worsening = distribution of whole knee cartilage morphology worsening

Table 2.

Overall and Sex-specific Associations between Hamstring Coactivation and Cartilage Morphology

	Women (n=373)	Men (n=240)	Overall
Medial Hamstring vs. Medial Cartilage Morphology Worsening	0.96 (0.74, 1.24)	1.20 (0.88, 1.65)	1.06 (0.87, 1.29)
Lateral Hamstring vs. Lateral Cartilage Morphology Worsening	0.91 (0.68, 1.21)	0.97 (0.66, 1.41)	0.93 (0.75, 1.17)
Combined Hamstring vs. Whole Knee Cartilage Morphology Worsening	1.06 (0.82, 1.37)	**1.59 (1.06, 2.39)** †	1.21 (0.98, 1.49)
Combined Hamstring vs Patellofemoral Cartilage Morphology Worsening	1.15 (0.89, 1.49)	**1.38 (1.01, 1.88)** †	**1.23 (1.02, 1.49)** †

Sex-specific, multivariable adjusted associations (logistic regression model adjusted for age, study site, BMI, history of knee injury or surgery, side assessed and KL grade); odds ratio estimates per one standard deviation (95% confidence limits);

† $p < 0.05$