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Knee adduction moment relates to medial femoral and tibial cartilage morphology in clinical knee osteoarthritis

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ABSTRACT

The objective was to determine the extent to which the external peak knee adduction moment (KAM) and cumulative knee adductor load explained variation in medial cartilage morphology of the tibia and femur in knee osteoarthritis (OA). Sixty-two adults with clinical knee OA participated (61.5 ± 6.2 years). To determine KAM, inverse dynamics was applied to motion and force data of walking. Cumulative knee adductor load reflected KAM impulse and loading frequency. Loading frequency was captured from an accelerometer. Magnetic resonance imaging scans were acquired with a coronal fat-saturated sequence using a 1.0 T peripheral scanner. Scans were segmented for medial cartilage volume, surface area of the bone–cartilage interface, and thickness. Forward linear regressions assessed the relationship of loading variables with cartilage morphology unadjusted, then adjusted for covariates. In the medial tibia, age and peak KAM explained 20.5% of variance in mean cartilage thickness ($p < 0.001$). Peak KAM alone explained 12.3% of the 5th percentile of medial tibial cartilage thickness (i.e., thinnest cartilage region) ($p = 0.003$). In the medial femur, sex, BMI, age, and peak KAM explained 44% of variance in mean cartilage thickness, with peak KAM contributing 7.9% ($p < 0.001$). 20.7% of variance in the 5th percentile of medial femoral cartilage thickness was explained by BMI and peak KAM ($p = 0.001$). In these models, older age, female sex, greater BMI, and greater peak KAM related with thinner cartilage. Models of KAM impulse produced similar results. In knee OA, KAM peak and impulse, but not loading frequency, were associated with cartilage thickness of the medial tibia and femur.

1. Introduction

Joint loading is implicated in knee osteoarthritis (OA) progression (Andriacchi et al., 2009). Over six years, an increase by 25% of the peak knee adduction moment (KAM) corresponded with a 6.46 times greater risk for progressive joint space narrowing in knee OA (Miyazaki et al., 2002). Similar findings have been produced with magnetic resonance imaging (MRI). In 180 people with medial knee OA, more severe cartilage defects were associated with higher peak KAM (Creaby et al., 2010). Five-year changes in medial tibial cartilage thickness were predicted by baseline peak KAM and peak knee flexion moment in 16 people with knee OA (Chehab et al., 2014). However, the peak KAM does not always relate with cartilage damage. Peak KAM was unrelated to progression of cartilage defects over 12 months in medial knee OA (Bennell et al., 2011). It may be unreasonable to expect that a laboratory measure captured during a single instant would share a relationship with cartilage features that reflect long-term loading.

The magnitude, duration and repetition of weight-bearing activities dictate the responses of cartilage to mechanical loads (Pearle et al., 2005; Maly et al., 2012). Compared to peak KAM, the combination of KAM impulse and loading frequency encountered in daily activity may better reflect cartilage morphology. Accounting for both KAM impulse and loading frequency together explained variance in pain among adults with knee OA (Robbins et al., 2011a, 2011b) and was superior to the peak KAM in distinguishing between adults with and without knee OA (Maly et al., 2012). KAM impulse reflects the total duration and magnitude of medial knee loading during one stride. KAM impulse was associated with pain intensity in knee OA (Thorp et al., 2007; Robbins et al., 2011a, 2011b). In radiographic knee OA, this moment-time

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integral distinguished between moderate and mild radiographic disease; whereas the peak KAM was not different between groups (Thorp et al., 2006). A higher KAM impulse, but not peak KAM, was associated with greater loss of medial tibial cartilage volume over 12 months in knee OA (Bennell et al., 2011).

Loading frequency is also important in cartilage degradation. Epidemiological studies of sport and occupation show a dose–response relationship between loading frequency and knee OA incidence (Coggon et al., 2000; Vignon et al., 2006; Stehling et al., 2010). A 10-year follow-up of 16,961 patients demonstrated that high loading frequency, noted by distance of a walk or run, had an odds ratio of 2.4 (95%CI 1.5–3.9) for symptomatic knee OA in men (Cheng et al., 2000). Greater steps/day increased cartilage loss over 2.7 years in those with low cartilage volume at baseline; but interestingly protected against cartilage loss in those with greater cartilage volume at baseline ($p=0.046$) (Dore et al., 2013). High loading frequency ($>10{,}000$ steps/day) was associated with a greater severity of cartilage defects in this sample (Dore et al., 2013).

The purpose of this study was to determine the extent to which the peak KAM, and cumulative knee adductor load (KAM impulse, loading frequency) explained variation in medial tibial and femoral cartilage morphology in knee OA. We hypothesized that peak KAM would relate inversely with the 5th percentile of cartilage thickness; while elements of cumulative load would show stronger relationships with morphology. Specifically, we hypothesized that KAM impulse would relate inversely with cartilage volume and thickness, and positively with surface area of the bone–cartilage interface; while loading frequency would relate inversely with cartilage volume.

2. Methods

This cross-sectional study was approved by the Institutional Human Research Ethics Board.

2.1. Participants

Community-dwelling adults between 40 and 70 years who met the American College of Rheumatology (ACR) clinical criteria for knee OA were recruited from rheumatologist's and orthopaedic surgeon's offices. These guidelines include having knee pain on most days of the month and at least three of the following: ≥ 50 years of age; stiffness <30 min; crepitus; bony tenderness; bony enlargement; no palpable warmth (Altman et al., 1986). Exclusion criteria included other forms of arthritis; non-arthritic disease; intra-articular therapies; or previous knee surgeries (e.g. osteotomy, replacement, partial/complete menisectomy, ligament reconstruction). Potential participants were excluded if they required an adaptive walking aid; sustained leg trauma within the past 3 months; had ipsilateral hip or ankle conditions; or had contraindications to MRI. In those with bilateral knee OA, the knee with more severe symptoms was designated as the study knee. All participants provided written, informed consent.

2.2. Cartilage morphometry

Each participant underwent an MRI scan of the study knee using a 1.0 T peripheral MRI scanner (GE Healthcare, USA). Participants were seated with the knee fully extended and centered in the iso-center of the 180 mm removable quadrature volume transmit-receive coil. Padding around the knee, thigh, and leg limited movement. Sagittal gradient-echo and axial fast spin-echo localizer scans were performed (2–3 min). A coronal fat-saturated spoiled gradient recalled acquisition in the steady-state (SPGR) was acquired: TR 60 ms; TE 12.4 ms (or minimum); flip angle 40°; bandwidth 30 kHz; matrix 512 × 256 (frequency × phase); 1 excitation; field of view 150 mm; slice thickness 1.5 mm; 56–64 partitions depending on patient size. Scan time was 15–16 min. MRI fat-saturated sequences (i.e., SPGR) from similar lower level magnets quantify cartilage morphology with accuracy of -13% to 3% and precision around 4.0% (Eckstein et al., 1998; Stammberger et al., 1999; Burgkart et al. 2001; Eckstein and Glaser, 2004).

Medial tibial and femoral cartilage morphology was segmented from these images using a highly automated, atlas-based method (Qmetrics, Rochester, NY, USA) (Tamez-Pena et al., 2012). This method yielded test–retest precision of cartilage thickness values between 0.014 mm (0.6%) at the femur and 0.038 mm (1.6%) at the femoral trochlea in images of OA knees obtained with a 3.0 T MRI (Tamez-Pena et al., 2012) and has evaluated cartilage repair (Shive et al., 2014) and bone morphology (Hunter et al., 2014). The accuracy of segmentation from scans acquired with a 1.5 T magnet produced data within 4–6% of values from a 3.0 T (Schneider et al., 2012). No statistical differences in cartilage measurements existed between 1.5 T and 1.0 T magnets (Inglis et al., 2007). Briefly, eight atlases were used to segment each scan. Each atlas was morphed to match anatomy using a spline deformation with a mutual information similarity metric. After spline morphing, the edges of the segmented image were deformed using a free-form registration algorithm. The morphed cartilage segmentation was then corrected by outlier detection: voxels whose signal was three standard deviations higher than average were classified as outliers. Segmentations from the eight atlases were fused using a fuzzy voting algorithm, and statistically relaxed to create the final segmentation (Tamez-Pena et al., 2012). All segmentations were reviewed by an experienced radiologist (ST) for quality. The following were calculated from the medial tibia and femur: volume (VCtAB; mm^3), surface area of the bone–cartilage interface (cAB; mm^2), mean thickness (ThCtAB; mm) and mean of the 5th percentile thickness (mm). These acronyms (Table 1) are consistent with established nomenclature (Eckstein et al., 2006a, 2006b).

Table 1
Nomenclature for measures of cartilage morphology are consistent with published norms (Eckstein et al., 2006a). The medial tibia and medial femur were represented by the prefixes MT and MF respectively. VC refers to volume of cartilage. tAB refers to total area of subchondral bone. cAB refers to area of subchondral bone covered in cartilage. Finally, ThCtAB refers to cartilage thickness over total subchondral bone area. All measures represent mean values from the medial compartment of the knee.

	Tibial	Femoral
Cartilage volume (mm^3)	MT.VCtAB	MF.VCtAB
Surface area of bone–cartilage interface (mm^2)	MT.cAB	MF.cAB
Cartilage thickness (mm)	MT.ThCtAB	MF.ThCtAB

Coronal weight-bearing knee radiographs were obtained in a standardized fixed-flexion position using a Synaflexer$^{\text{TM}}$ (Kothari et al., 2004). This frame places the feet in 5° of external rotation and ~20° of knee flexion. Each digital radiograph was evaluated by one experienced radiologist (ST) to yield Kellgren and Lawrence (K–L) scores (Kellgren and Lawrence, 1957) and frontal plane alignment (anatomical axis).

2.3. Biomechanical Assessment

Within one week of the MRI, a laboratory visit was conducted. To calculate the peak and impulse of the external KAM, gait analyses were conducted during barefoot walking at a self-selected speed. Kinetics were collected using a synchronized floor-mounted force plate (OR6-7, Advanced Mechanical Technology Inc., Watertown, MA, USA) sampled at 1000 Hz. Concurrently, kinematics were collected using three Optotrak Certus banks (nine cameras) (Northern Digital Inc., Waterloo, ON, Canada) sampled at 100 Hz. Infrared emitting diodes, arranged on rigid bodies in clusters of three, were secured to the lateral sacrum, thigh, shank and foot. The pelvis was digitized using six landmarks (bilateral anterior and posterior superior iliac spines, greater trochanters). Virtual markers were also created for the greater trochanter, medial and lateral femoral and tibial condyles, tibial tuberosity, fibular head, medial and lateral malleoli, calcaneus, and first, second and fifth metatarsal heads. A static reference trial was recorded to determine neutral pelvic and lower-limb joint angles. Participants ambulated until five trials were captured where the participant struck the force plate cleanly with the study leg.

Using commercial software (Visual 3D, C-Motion, Inc., Germantown, MD, USA), marker data were dual-passed through a low-pass Butterworth filter with a 6 Hz cut-off frequency (Robertson and Dowling 2003). Inverse dynamics was used to calculate external knee moments (Winter 1990) in a three-dimensional floating axis coordinate system where flexion/extension occurred about the lateral-medial axis of the thigh, internal/external rotation occurred about the distal-proximal axis of the shank, and adduction/abduction occurred about a floating axis (intermediate axis perpendicular to both lateral-medial and distal-proximal axes) (Cole et al. 1993; Wu and Cavanagh 1995; Schache and Baker 2007). The rotation sequence was consistent with a Cardan XYZ rotation (Wu and Cavanagh 1995).

The KAM peak and impulse are highly reliable, stable measures in knee OA (Birmingham et al. 2007; Robbins et al. 2009). Peak KAM was reported in Nm/kg (Winter 1990). Mean KAM impulse of five trials was calculated using the trapezoid rule, which integrated only positive values from stance (Matlab 7.0.1, Natick, MA, USA). Our interest focused on the medial knee; thus negative (abduction) values were not subtracted from the adduction impulse because these values do not subtract from the loading experienced by the medial knee. To reflect the theoretical underpinnings of cumulative load, which represents the total load exposure experienced by tissues for a given time period, KAM impulse values were in non-normalized units of Nm•s. Non-normalization ensures that the impulse

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