Association Between MRI-Based Tibial Slope Measurements and Mucoid Degeneration of the Anterior Cruciate Ligament

A Propensity Score–Matched Case-Control Study

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Background: The cause of mucoid degeneration (MD) of the anterior cruciate ligament (ACL), which is commonly observed on magnetic resonance imaging (MRI) of patients with knee pain, has yet to be elucidated. Despite the limited evidence on the relationship between ACL lesions (injury and MD) and tibial morphologic features (ie, posterior tibial slope), the potential association between the presence of ACL MD and medial and lateral tibial slope (MTS and LTS) has not been well-established.

Purpose: To investigate whether MTS and LTS measurements are associated with the presence of ACL MD.

Study Design: Cross-sectional study; Level of evidence, 3.

Methods: Consecutive knee MRI examinations of patients referred by an orthopaedic surgeon for potential internal joint derangements were identified within a 4-year period. The presence of ACL MD and the MTS/LTS values were assessed by independent expert observers in consensus in a blinded fashion. From 413 consecutive knee MRI scans, a sample of 80 knees, including 32 knees with ACL MD (cases) and 48 knees with normal ACL (controls), were selected using propensity score matching method for age, sex, body mass index, and presence of severe medial tibiofemoral compartment cartilage damage. The association between ACL MD and MTS/LTS was evaluated using conditional regression models.

Results: Knees with ACL MD had higher values of LTS (mean ± SD, 7.18° ± 3.58°) in comparison with control knees (5.32° ± 3.35°). Conditional regression analysis revealed a significant association between LTS measurements (not MTS) and ACL MD; every 1° increase in LTS was associated with a 17% (95% CI, 1%-35%) higher probability of having ACL MD.

Conclusion: Excessive LTS was associated with the presence of ACL MD, independent of participants' age, sex, BMI, and cartilage damage severity.

Keywords: anterior cruciate ligament; mucoid degeneration; tibial slope; medial tibial slope; lateral tibial slope

Mucoid degeneration (MD) of the anterior cruciate ligament (ACL) is a chronic degenerative condition of unclear origins that can cause posterior knee pain and flexion limitation.[11,15,19] In 1999, Kumar et al[15] described ACL MD as the deterioration of fibrous collagen that can mimic a chronic interstitial ACL tear.[11,19] Despite the high prevalence (9%-12%) of ACL MD among patients who undergo 3.0-T magnetic resonance imaging (MRI), the cause of ACL MD remains unclear,[6,11] as previous studies were unable to illustrate the underlying knee joint structural damages that are associated with the presence of ACL MD.[6,11] In this regard, a growing body of evidence suggests that ACL MD is likely associated with subtle knee instability and/or knee osteoarthritis (OA).[3,10,23]

The posterior tibial slope (PTS) is defined as the inclination of the tibial plateau with respect to the longitudinal axis of the tibial bone, and it can be calculated for both medial and lateral sides (ie, medial tibial slope [MTS] and lateral tibial slope [LTS] measures).[10] Using MRI, recent studies reported a larger LTS and a smaller MTS in patients with ACL rupture in comparison with noninjured participants, highlighting the potential interaction between tibial morphologic characteristics and ACL lesions.[10,23] A recent study using MRI-based measurements demonstrated that increased LTS is associated with a higher risk of ACL rupture as well as reinjury of the

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reconstructed grafts.[3] In addition, prior studies demonstrated that ACL MD is associated with increased PTS (measured by radiographs), confirming that changes in tibial morphologic characteristics may have a role in ACL MD.[13,25] Despite the limited evidence on the possible relationship between ACL lesions and PTS, the potential association between the presence of ACL MD and MTS or LTS has not been well-established.

Drawing on previous studies, we hypothesized that greater MTS or LTS measurements might be associated with increased probability of having ACL MD. As such, we aimed to evaluate the possible association between MRI-based MTS and LTS measurements and the presence of ACL MD using a propensity score (PS)–matched case-control design.

METHODS

Participants: Cases vs Controls

Institutional review board approval was obtained, and patient consent was waived for this retrospective study, which was compliant with the HIPAA (Health Insurance Portability and Accountability Act). Initially, 471 consecutive knee MRI examinations of patients with various knee symptoms were identified (between July 2010 and February 2014). Details of patient recruitments and knee MRI examinations were described previously (Figure 1).[16] In brief, patients with potential internal joint derangement who were referred by an orthopaedic surgeon (working at a tertiary care center) were included in this study. Knee MRI scans of patients with previous surgery (including meniscectomy, ACL and posterior cruciate ligament [PCL] reconstruction, cartilage repair, surgery for maltracking, arthroscopy, iliotibial band surgery, tendon repair, and arthrotomy), multiple follow-up MRI scans of the same knee, and incomplete MRI scans were excluded. After exclusion criteria were applied, remaining knee MRI scans were assessed by musculoskeletal radiologists (described in the next sections), and a diagnosis of ACL MD was made in 36 knees. Meanwhile, 321 knee MRI scans were interpreted as control (ie, no ACL MD or tear).

Next, the PS-matching method was used for the purpose of this matched case-control study.[4] The study groups (those with and without ACL MD) were matched for baseline age, sex, body mass index (BMI), and presence of severe medial tibiofemoral compartment (MTFC) cartilage damage (described in next sections). We used the 1:1 or 1:2 (based on available data and caliper) nearest-neighbor matching method with parallel matched sets and caliper distance of 0.2. Best-matched participants were defined as those with the highest match PS level measured by logistic regression.[1,4] By using this method, we included 32 participants with ACL MD and 48 matched control participants (1 knee in each participant).

MRI Protocol

MRI scanners were used to attain images using 1.5-T (Gyroscan Intera; Philips Medical Systems) or 3.0-T scanners (Magnetom Verio, Magnetom Trio, and Magnetom Skyra, Siemens Healthcare; and Signa HDxt 3-T, GE Healthcare). Standardized knee coils were used. All protocols for MRI in the axial, coronal, and sagittal planes comprised proton density (PD)–weighted images both with and without fat saturation (repetition time/echo time, 3000-3100/27-35 ms). For 1.5-T MRI, the matrix size was 256×256 with a field of view of 16 cm; for 3.0-T scanning, the matrix size was 320×320 and the field of view 16 cm.

MRI Assessment: ACL Morphologic Characteristics and MTFC Cartilage Damage

Details of the image analysis, protocols, and reading consensus were as described in our previous study.[16] Initially, 3 independent, fellowship-trained musculoskeletal radiologists (S.D., S.A., and J.N.M., with 6, 4, and 3 years of experience, respectively) inspected all knee MRI scans in a blinded fashion for clinical information and available radiology reports. Cases with a discrepancy in interpretations were reviewed by a senior radiologist (L.M.F., 15 years of experience), and final determination of ACL status was established by consensus. The remaining knee MRI scans with discrepancy were excluded from further analyses (Figure 1). The ACL was examined in various planes (sagittal, axial, and coronal) and grouped into 1 of 3 categories: (A) normal, (B) ruptured, or (C) with MD.[16] (A) Ligaments with low signal intensity and continuous fibers on all sequences from origin to insertion that ran parallel to the intercondylar line of Blumensaat were defined as normal ACL. (B) An ACL was classified as ruptured when there was a disruption on 1 or both ACL bundles (a nonparallel course of the ACL bundles to the intercondylar line of Blumensaat) and no visibility of 1 or both bundles of the ACL on all sequences. (C) ACL MD was diagnosed when anteromedial and posterolateral bundles of ACL were easily distinguishable on fat-saturated, PD-weighted images but indistinguishable on PD-weighted images. The ACL bundles were

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Ethical approval for this study was obtained from Johns Hopkins School of Medicine.

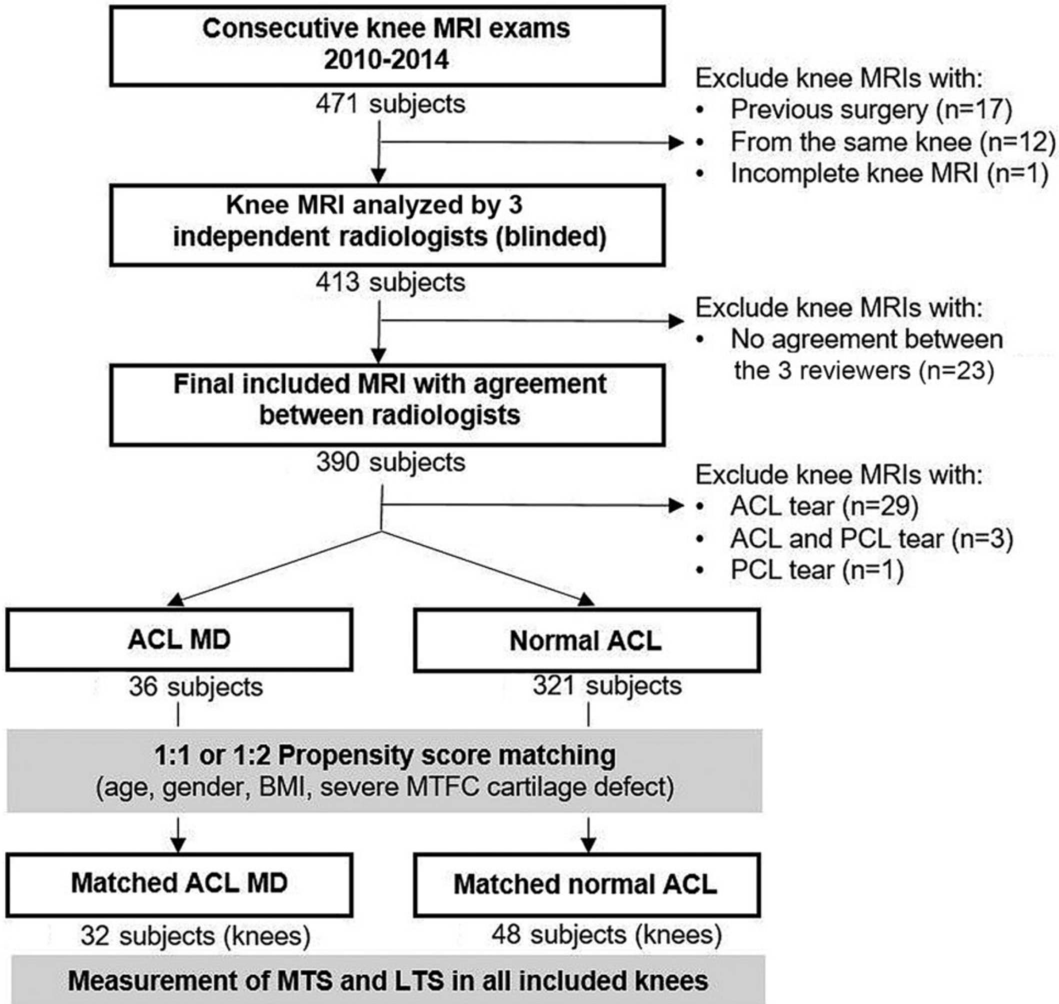

Figure 1. Flowchart of anterior cruciate ligament (ACL) evaluation and study design. BMI, body mass index; LTS, lateral tibial slope; MD, mucoid degeneration; MRI, magnetic resonance imaging; MTFC, medial tibiofemoral compartment; MTS, medial tibial slope; PCL, posterior cruciate ligament.

confirmed as intact from origin to insertion by eliminating any possibility of misdiagnosing a partial tear if secondary signs of a tear were absent (Figure 2).

The Whole-Organ Magnetic Resonance Imaging Score (WORMS) was calculated by 1 radiologist (A.J.K.) to evaluate the severity of cartilage damage[8,21] in 5 subregions of the MTFC (central and posterior femur; anterior, central, and posterior tibia) separately (from 0 to 6 points). WORMS values $\geq$5 showed the presence of full-thickness cartilage damage.[7] Knees with full-thickness cartilage damage (scores of $\geq$5) in at least 1 subregion were considered positive for MTFC cartilage damage (vs knees without full-thickness cartilage damage in any subregions).

MRI Assessment: MTS and LTS Measurements

MTS and LTS were measured according to the technique described by Hudek et al[12] using conventional MRI examinations. This method has to be repeatable and appropriate when using a proximal tibial MRI scan.[18] First, measurements were started by defining the tibial proximal anatomic axis (TPAA) (Figure 3A). This axis was determined by drawing a circle within the most proximal portion of the tibia touching the anterior, posterior, and cranial tibial cortices. The circle was drawn on the central sagittal MRI scan, which was the best image to demonstrate the tibial attachment of the PCL, the intercondylar eminence, and a concave appearance to the anterior and posterior tibial cortices. A second circle was drawn on the same image using the center of the more cranial circle as its most proximal extent while also touching the anterior and posterior cortices. A line was drawn through the center of these circles to define the TPAA. This axis was physically marked on the computer screen using an adhesive note. The images representing the widest portions of the medial tibial plateau and lateral tibial plateau were selected. Tangent lines were drawn on MRI scans to the medial and lateral tibial plateaus. Angles were measured between the marked TPAA and the medial and lateral

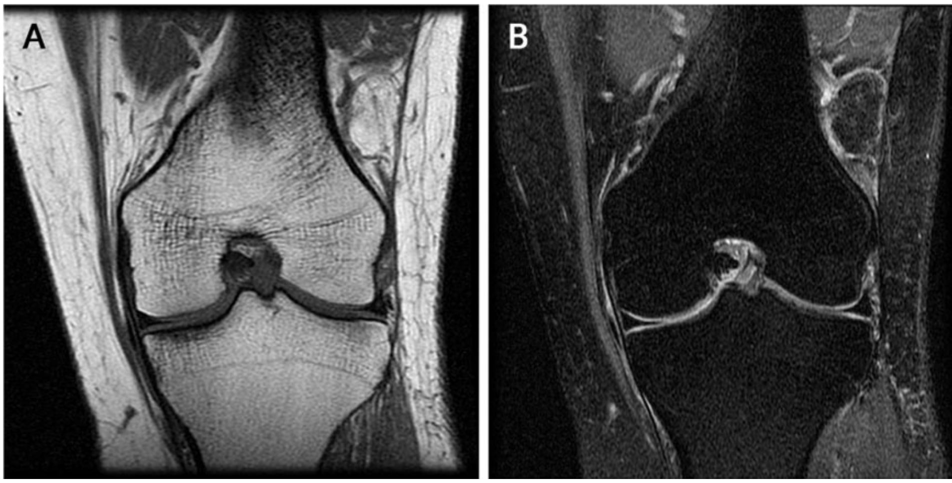

Figure 2. Anterior cruciate ligament (ACL) mucoid degeneration in a 45-year-old male. (A) A thickened ACL with mildly increased signal intensity with its anteromedial and posterolateral bundles is distinct on coronal, fat-saturated, proton density (PD)–weighted images but (B) is not clearly delineated on the corresponding coronal PD-weighted images.

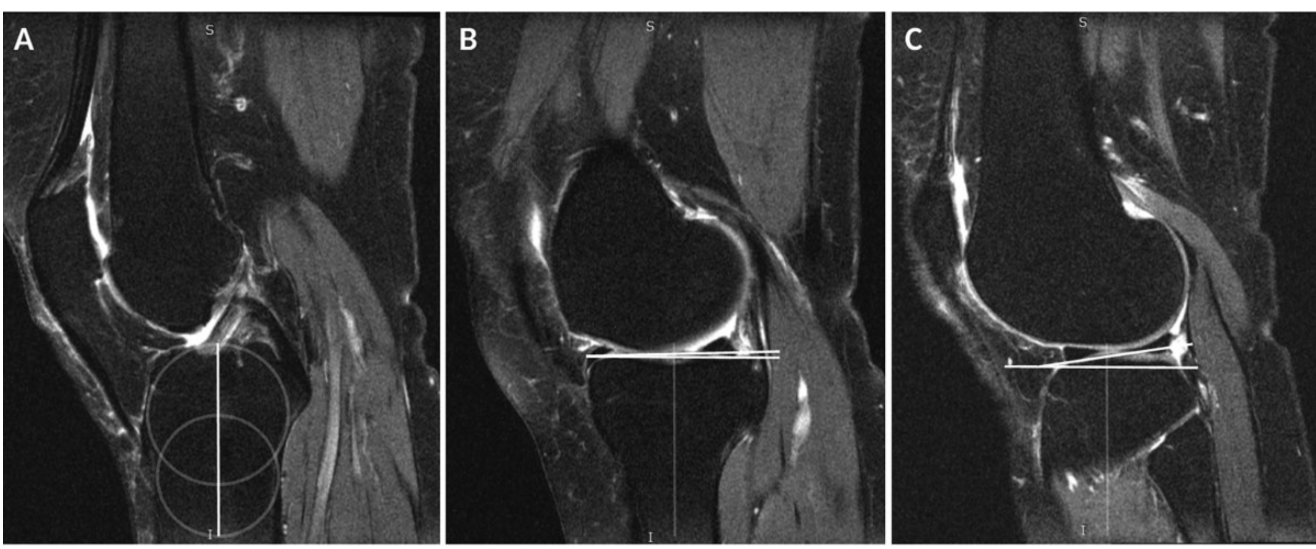

Figure 3. Sagittal, non–fat-saturated, proton density–weighted MRI scan. (A) To determine the tibial proximal anatomic axis (TPAA), a line was drawn through the center of 2 circles, *upper circle:* within the most proximal portion of the tibia touching the anterior, posterior, and cranial tibial cortices; *lower circle:* touching the anterior and posterior cortices) to define the TPAA in midsagittal magnetic resonance imaging. (B) The medial tibial slope is the angle between the TPAA and medial tibial plateau. (C) The lateral tibial slope is the angle between the TPAA and lateral tibial plateau.

tibial plateaus to give the MTS and LTS measurements (Figure 3, B and C). All measurements were performed on the fat-saturated PD images by an orthopaedic surgery resident (A.J.) in a blinded fashion.

Statistical Analysis

Baseline characteristics (including age, sex, BMI, WORMS, MTFC cartilage damage, and MRI-derived MTS/LTS) were compared among the cases and controls using independent-samples *t* test or chi-square test. The distribution of data was evaluated using Kolmogorov-Smirnov normality tests. The association between MTS/LTS and ACL MD was assessed using conditional logistic regression, which is the preferred regression model for matched participants.[14] A *P* value of .05 was considered the significance threshold. The statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) software, Version 25.0 (IBM).

RESULTS

As presented in the diagram of study population selection, ACL MD was detected in 36 of 390 knees with consensus

TABLE 1
Baseline Characteristics of the Propensity Score–Matched Study Population[a]

	Cases (n = 32)	Controls (n = 48)	P Value
Propensity score	0.37 ± 0.11	0.35 ± 0.11	.300
Age, y[b]	54.4 ± 13.7	51.6 ± 13.9	.372
% Female[b]	62.5	60.4	>.999
Body mass index, kg/m^2 [b]	32.7 ± 8.1	32.3 ± 8.2	.826
Presence of severe MTFC cartilage damage (WORMS ≥5 vs <5), %[b]	31.3	18.8	.284

[a]Data are presented as mean ± SD or percentage. Cases were knees with anterior cruciate ligament mucoid degeneration (ACL MD); controls were knees without ACL MD. Data were compared using the independent-samples *t* test and chi-square test with Fisher exact test whenever applicable. MTFC, medial tibiofemoral compartment; WORMS, Whole-Organ Magnetic Resonance Imaging Score.

[b]Propensity score matching was performed for these variables.

TABLE 2
Association of Medial Tibial Slope and Lateral Tibial Slope With ACL Mucoid Degeneration Using Conditional Logistic Regression Model[a]

	Cases	Controls	Odds Ratio	95% CI	P Value
MTS	5.23 ± 3.25	4.51 ± 2.57	1.11	0.93-1.33	.252
LTS	7.18 ± 3.58	5.32 ± 3.35	1.17	1.01-1.35	.034

[a]The association between MTS/LTS and ACL MD was analyzed using a conditional logistic regression model. Odds ratios were reported by comparing cases (knees with ACL MD) and controls (knees without ACL MD) for the values of MTS and LTS. Data for cases and controls are presented in degrees as mean ± SD. ACL, anterior cruciate ligament; LTS, lateral tibial slope; MTS, medial tibial slope.

agreement regarding radiology reports (overall prevalence of 9% for ACL MD).

The baseline characteristics of the study populations, including cases (32 knees) and controls (48 knees), are presented in Table 1. The study groups were completely matched for all available potential confounding variables using the PS matching method. In this regard, 62.5% and 60.4% of cases and controls were female, respectively. The mean age of participants in the case group was 54.4 years, which was similar to the control group, 51.6 years. Furthermore, 31.3% of participants with ACL MD and 18.8% of controls showed severe WORMS MTFC cartilage damage; however, the analysis showed no significant difference between the study groups regarding the presence of severe cartilage damage (Table 1).

Knees with ACL MD had significantly larger LTS measures (mean ± SD, 7.18° ± 3.58°) in comparison with controls (5.32° ± 3.35°; $P = .034$) (Table 2). However, no significant difference was observed between cases and controls regarding MTS measures (Table 2). Results of the conditional logistic regression analysis demonstrated that the presence of ACL MD was significantly associated with the greater LTS measures (odds ratio, 1.17; 95% CI, 1.01-1.35; $P = .034$). In other words, every 1° increase in LTS values was associated with a 17% higher probability of having ACL MD (Table 2). However, no significant association was found between MTS measurement and ACL MD (Table 2).

DISCUSSION

In this study, we found that LTS measurement was associated with the presence of ACL MD, independent of the potential confounding/mediating roles of age, sex, BMI, and presence of severe MTFC cartilage damage. ACL MD is a commonly observed entity in MRI images of older female participants with obesity and early degenerative knee changes, although its origin has yet to be elucidated. Several hypotheses have been suggested for the cause of ACL MD, including synovial (synovial fluid accumulation inside the ACL), traumatic (injury-induced cellular responses and fibroblast glycosaminoglycan secretion), degenerative (due to aging), and joint kinematic theories.[17,20] Among all these hypotheses, it has been suggested that altered joint mechanics due to the subtle changes in the joint morphologic characteristics leads to multiple microtraumas that may result in ACL stretching, microcyst formation, and thereby ACL MD and OA. In this regard, the potential associations between ACL MD and knee instability, OA, meniscal tear, and other degenerative changes have been suggested by several reports.[3,10,23]

Regarding the prevalence of ACL MD, studies using 1.5-T MRI initially reported that <2% of patients had ACL MD.[2,16] A recent study using 3.0-T MRI performed on randomly sampled elderly patients found that ACL MD occurred in 9% of patients,[11,16] suggesting that the type of MRI could affect the interpretation of whether ACL MD is present in the knee. In contrast, histologic analysis reported a prevalence of 62% for ACL MD using autopsy specimens; however, results from these autopsy studies may have been confounded by the higher ages of participants.[9] In our study, we observed a 9% prevalence of ACL MD in our initial population.

Previous research studies have attempted to evaluate the possible association between ACL MD, ACL injury, and tibial slope measurements.[10,13,23] The potential association of MTS/LTS with ACL injury was reported in prior studies.[22,23] It has been suggested that other measures such as medial tibial plateau depth could be associated with ACL damage as well.[10] Most of these studies found an increased LTS and shallow MTS measurement in patients with ACL injury.[10,24] In a recent study, researchers found an association between ACL MD and increased overall PTS using a random matching method.[13] Another study, conducted on nonmatched participants, found that knees with the shallower medial tibial depth of concavity and increased PTS were more prone to ACL injuries (not MD).[10] In line with previous reports, we presented a similar association for

ACL MD and tibial slope in our study. Various studies have attempted to clarify the tibiofemoral geometry and determine the association of various factors that help to detect ACL injury. Although other studies found an association between tibial slopes and ACL defects, to the best of our knowledge, most of them did not eliminate the potential impact of confounding covariates. Based on the previous investigations, it is difficult to assess which anatomic measurement will determine ACL MD, as each research study has various interpretations and even inconsistencies with measurement.

Unlike ACL tears, MD of this ligament is a chronic and presumably degenerative process; however, we hypothesize that ACL MD and tears may share a common biomechanical derangement as a predisposing factor. Previous work showed that during flexion, anterior translation of the tibia was slightly greater on the lateral tibial plateau; these investigators cited the greater LTS as a potential factor that may aggravate the stress on the ACL and cause an ACL tear.[23] Our cross-sectional results raise the possibility that such morphological abnormality and associated biomechanical derangement are also associated with the presence of ACL MD.

Although ACL MD can be effectively managed by surgical interventions (ie, arthroscopic debridement), young and active participants may experience joint instability postsurgically that requires further reconstruction. Given this background, identifying the potential risk factors associated with ACL MD is of the utmost importance to better characterize this subset of participants at risk of joint instability after corrective surgery. Herein, we found a pattern of association between LTS and the presence of ACL MD. However, further research is needed to verify the causal relationship of MTS/LTS and ACL MD as well as to study the clinical implications of this finding (whether participants with higher LTS are at greater risk of joint instability after reconstruction).

Our study has limitations. The diagnosis of ACL MD was not confirmed via histological biopsy. Because ACL MD has similar characteristics to partial interstitial tears, we cannot exclude the possibility that some MRI scans could have been misdiagnosed. However, we tried to maximize our precision in MRI assessments by having the images evaluated by multiple radiologists. Our MRI evaluation method and criteria for ACL MD diagnosis were strictly followed, as previously used as a standard for reference for consistent interpretation.[16] Our retrospective study was limited in that we included images from 1.5-T and 3.0-T MRI, knowing that higher sensitivity of 3.0-T MRI may be associated with altered results.[5] Also, the cause and effect relationship or temporal causality of MTS/LTS in relation to ACL MD cannot be directly established, because of the nature of this study. Moreover, quasi-experimental PS matching designs, per definition, control for only the effects of known and available confounders. There may still remain confounding effects from unknown or unavailable confounders (eg, a participant's activity, data on which were not available for this study). A long-term study would be required to test the possibility of acute and chronic damage and would require a longer time frame to better understand chronicity and the degeneration process. The current study aimed to assess only ACL MD and not PCL MD. We could not deduce that all knees with ACL MD (using MRI) also had an ACL deficiency on physical evaluation. In a future prospective study, tests should be used to assess for ACL MD in physical examinations, including but not limited to pivot-shift tests, instrumental measurements, and stress radiography. Further, limited information was available regarding the patellofemoral joint and its pathology.

CONCLUSION

In this analysis, we showed that LTS (but not MTS) was associated with a higher prevalence of ACL MD in the MRI assessments, independent of effects of known confounders (age, sex, BMI, and degenerative cartilage damage). Future studies are required to confirm the potential cause-and-effect link between LTS and ACL MD and to furthermore assess the clinical implications of LTS in assessing the risk of patients for experiencing joint instability after ACL MD reconstruction surgery.

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