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● *Original Contribution*

FEMORAL CARTILAGE ULTRASOUND ECHO INTENSITY ASSOCIATES WITH ARTHROSCOPIC CARTILAGE DAMAGE

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Abstract—This study compared quantitative cartilage ultrasound metrics between people with ($n = 12$) and without ($n = 12$) arthroscopic cartilage damage after anterior cruciate ligament injury (age, 24.9 ± 3.7 y; sex, 33% female, 67% male; days since injury = 50 ± 52). A transverse suprapatellar ultrasound assessment imaged the femoral cartilage in participants' injured knees before a clinical arthroscopy. A custom program automatically separated a manual cartilage segmentation into standardized medial and lateral femoral regions and calculated mean thickness (*i.e.,* cross-sectional area/length of cartilage-bone interface), mean echo intensity and echo-intensity heterogeneity. An orthopedic surgeon assessed arthroscopic cartilage damage in the medial and lateral femoral condyles using the Outerbridge grading system (cartilage damage = Outerbridge ≥ 1). Separate logistic regressions for medial and lateral femoral cartilage were used to determine the association between each ultrasound metric and arthroscopic cartilage damage. In medial femoral cartilage, for every 1 standard deviation decrease in echo-intensity mean and heterogeneity, there is, respectively, a 91% (adjusted odds ratio, 0.09; 95% confidence interval, 0.01−0.69) and 97% (adjusted odds ratio, 0.03; 95% confidence interval, 0.002−0.50) increase in the odds of having arthroscopic cartilage damage. Lateral cartilage ultrasound metrics are not associated with lateral arthroscopic cartilage damage. This study provides preliminary evidence that femoral cartilage ultrasound echo intensity is a non-invasive measure associated with medial femoral cartilage health after anterior cruciate ligament injury. (E-mail: harkeym1@msu.edu) © 2020 World Federation for Ultrasound in Medicine & Biology. All rights reserved.

Key Words: **Knee, Cartilage thickness, Ultrasonography, Arthroscopy, Outerbridge.**

INTRODUCTION

Acute knee injuries are a key risk factor for the development of knee osteoarthritis (OA) (Lohmander et al. 2007). Specifically, 33% of people develop radiographic knee OA within the first decade after anterior cruciate ligament (ACL) injury (Luc et al. 2014). The initial injury is considered an inciting event that leads to sequelae of biomechanical, biochemical and structural changes that eventually lead to a decline in articular cartilage health (*e.g.,* morphologic or composition alterations) and radiographic knee OA changes (Andriacchi et al. 2015; Chu and Andriacchi 2015). Monitoring for early changes in cartilage health after an ACL injury could provide insight into early disease mechanisms (Chu et al. 2011). Using imaging modalities to detect subtle declines in cartilage health is a needed first step to identify people early in the disease process to effectively target disease-modifying or preventive interventions (Chu et al. 2012).

Altered cartilage health, especially in the patellofemoral joint, can be detected within the first 12 mo after an ACL injury or reconstruction (Frobell 2011; Theologis et al. 2014) and may be prognostic of poor outcomes (Culvenor et al. 2016; Su et al. 2016). While most studies focus on tibiofemoral cartilage after an ACL injury, compositional and morphologic cartilage abnormalities are more common and likely to change in the patellofemoral joint than the tibiofemoral joint (Frobell 2011; Culvenor et al. 2013, 2015, 2016, 2019; Li et al. 2013a; Su et al. 2016; Kim et al. 2018). Diagnostic ultrasound is a valid and reliable method for assessing the femoral trochlear articular cartilage in the

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patellofemoral joint and represents a more accessible, inexpensive and clinically oriented alternative to magnetic resonance (MR) imaging (Naredo et al. 2009). Quantitative assessments of femoral trochlear cartilage using ultrasound have mainly focused on assessing measures related to cartilage size (*e.g.,* cartilage thickness or cross-sectional area) (Harkey et al. 2018; Roberts et al. 2019). However, investigators have disagreed about whether femoral trochlear cartilage is thicker, thinner or not different in an ACL-reconstructed knee compared with the contralateral knee or a healthy control knee (Akkaya et al. 2016; Harkey et al. 2018; Pamukoff et al. 2018). The discrepancies between prior studies may be owing to differences in the time since ACL reconstruction among participants (Harkey et al. 2018; Pamukoff et al. 2018). Yet there is evidence that early cartilage degradation may result in either cartilage thickening or thinning (Buck et al. 2010a). In addition to measuring cartilage size, an assessment of the cartilage ultrasound echo intensity (*i.e.,* brightness of the image) quantifies the integrity of the superficial cartilage collagen matrix (Kuroki et al. 2008). While cartilage breakdown appears on ultrasound as a loss of a sharp contour and alterations in the cartilage echo intensity (Möller et al. 2008), previous qualitative assessments indicate that it may lead to either a decrease or an increase of the ultrasound echo intensity (Finucci et al. 2015; Podlipská et al. 2017). This highlights the need for assessments that directly quantify the magnitude and heterogeneity of the cartilage echo intensity. Since disrupted cartilage integrity (*e.g.,* altered cartilage composition) may occur before cartilage thickness changes (Li and Majumdar, 2013b), quantitative assessment of cartilage ultrasound echo intensity may be an early indicator of altered cartilage composition (Kuroki et al. 2008; Saarakkala et al. 2012; Gupta et al. 2014; Pamukoff et al. 2020).

One method to determine if ultrasound echo intensity is associated with cartilage health is to compare its characteristics between people with and without arthroscopic-based cartilage damage (Kuroki et al. 2008; Saarakkala et al. 2012; Gupta et al. 2014). After ACL injury, cartilage with arthroscopic damage has worse composition than cartilage regions without arthroscopic damage based on compositional MR imaging (*i.e.,* greater $T1\rho$ relaxation times = less proteoglycan density) (Gupta et al. 2014). Additionally, an invasive arthroscopic quantitative assessment of cartilage ultrasound echo intensity indicating lesser signal intensity has been associated with a clinical assessment of greater arthroscopic cartilage damage (Kuroki et al. 2008). Thus, arthroscopic cartilage damage in people after ACL injury is related to poor cartilage composition, and an assessment of femoral cartilage ultrasound echo intensity may be able to detect these early alterations. However, it is unclear whether a non-invasive quantitative assessment of ultrasound echo intensity is related to arthroscopic cartilage damage in people who have had an ACL injury.

A transverse cartilage ultrasound technique assesses the femoral trochlea within the patellofemoral joint, while the arthroscopic assessment used in this study assesses the femoral condyle in the tibiofemoral joint. The intent of this study was not to specifically detect the arthroscopic lesion with ultrasound assessment, but to determine if ultrasound cartilage characteristics of the femoral trochlea are associated with any cartilage damage within the same femoral region (*i.e.,* medial or lateral). Therefore, our purpose was to determine the association between quantitative femoral cartilage ultrasound metrics (*i.e.,* mean thickness, mean echo intensity and echo-intensity heterogeneity in the medial and lateral trochlea) and arthroscopic femoral cartilage damage after an ACL injury. We hypothesized that thinner ultrasound-assessed cartilage would be associated with arthroscopic femoral cartilage damage because the presence of cartilage defects may be detected as cartilage thinning. Since there is qualitative evidence that a decline in cartilage health may result in lesser or greater cartilage echo intensity (Möller et al. 2008; Finucci et al. 2015; Podlipská et al. 2017), we hypothesized that altered quantitative ultrasound metrics of echo-intensity mean and heterogeneity would be associated with arthroscopic femoral cartilage damage. This study would provide preliminary evidence of which non-invasive quantitative cartilage ultrasound metrics may detect a decline in cartilage health.

MATERIALS AND METHODS

Participants

We recruited participants between 18 and 35 y of age with a primary unilateral ACL injury who had not yet undergone an ACL reconstruction. A single orthopedic surgeon with a sub-specialty in sports medicine confirmed ACL injury with a clinical knee exam and MR imaging. Participants were excluded if they had a history of lower-extremity surgery, injury in either knee within the prior 6 mo (other than ACL injury), multiligament knee injuries, locked bucket handle meniscal tears, knee or lower-extremity surgery on the contralateral leg or previous diagnosis of any form of arthritis. Written informed consent was obtained from all participants before data collection, and the university's institutional review board approved the study.

Ultrasound assessment of femoral articular cartilage

A pre-operative knee ultrasound assessment was completed before the arthroscopy. A single examiner with 6 y of femoral cartilage ultrasound experience, who has demonstrated excellent intra-session reliability using this technique (Lisee et al. 2020), used a LOGIQ e ultrasound machine with a 12 L-RS linear probe (GE Healthcare, Chicago, IL, USA) to acquire the ultrasound images.

Participant positioning, probe positioning and imaging acquisition. After 30 min of sitting, participants were positioned with their ACL-injured limb in maximal knee flexion (≥110˚) to allow for visualization of the femoral articular cartilage (Finucci et al. 2015). The use of maximal knee flexion is recommended for assessing femoral articular cartilage, especially in individuals who may have limited range of motion (Finucci et al. 2015). The knee flexion angle was recorded for all participants. The ultrasound probe was placed in a transverse suprapatellar approach and positioned such that it was perpendicular to the femoral cartilage surface, similar to previous methods (Naredo et al. 2009; Harkey et al. 2017; Lisee et al. 2020). During image acquisition, a transparency grid was placed over the ultrasound monitor to ensure consistent probe positioning between successive images (Lisee et al. 2020). Three images were recorded using the same procedures, removing the probe from the knee after each image.

Ultrasound image processing. Ultrasound images were manually segmented using publicly available ImageJ software (https://imagej.nih.gov/) (Schneider et al. 2012). A single reader, who was unaware of the grade of arthroscopic cartilage damage, manually segmented the total femoral cartilage cross-sectional area of each ultrasound image (Fig. 1a) (Harkey et al. 2018). After the initial segmentation, the central point of the intercondylar notch was identified on each image at the deepest point of the synovial-cartilage border (Fig. 1a). Next, the segmented cartilage image was exported to a custom MATLAB program (version 9.2, The MathWorks, Natick, MA, USA) that completed the following steps to automatically determine the mean cartilage thickness and echo-intensity characteristics (*i. e.,* mean and heterogeneity) in standardized cartilage regions. First, it separated the total cartilage cross-sectional area into standardized medial, intercondylar and lateral regions: (i) the intercondylar region was centered around the manually identified central point of the intercondylar notch, which represented the middle 25% of the cartilage based on the overall image width (Fig. 1b); (ii) the medial and lateral regions of the image were defined as the areas medial or lateral to the intercondylar region (Fig. 1b). We used the middle 25% of image, which represents 4.8 mm on either side of the central point of the intercondylar notch, to define the

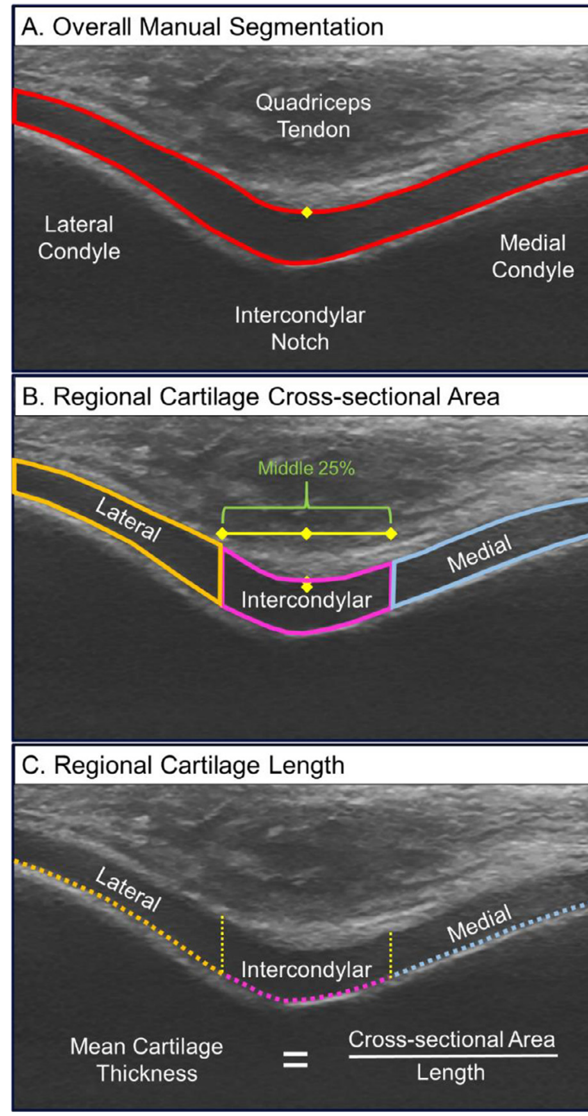

Fig. 1. Standardized femoral cartilage segmentation. First, a single reader manually segmented the total cartilage cross-sectional area and marked the lowest point of the intercondylar notch (*yellow diamond*; a). Next, a custom program automatically separated the manual segmentation into standardized cartilage regions (*i.e.,* medial, intercondylar, lateral; b). Last, the custom program calculated the mean cartilage thickness by dividing the regional cartilage cross-sectional area (b) by the regional cartilage length (c).

intercondylar cartilage region to ensure assessment of the intercondylar notch and to allow the medial and lateral regions to include the upslope of the femoral condyles (Fig. 1) (Lisee et al. 2020). Despite potential variability in the femoral condyle shape, previous studies have used a standardized distance of 10 mm from the midpoint of the intercondylar notch when assessing medial and lateral cartilage thickness (Roberts et al. 2016, 2019). Therefore, this technique creates standardized medial and lateral cartilage regions that include the cartilage locations commonly assessed in prior work. We did not include the intercondylar region in the analysis, because we specifically associated the medial and lateral ultrasound cartilage outcomes with the medial and lateral arthroscopic femoral cartilage damage, respectively. The program then determined the length of the cartilage-bone interface for each region (Fig. 1c). For this study, the program calculated the following cartilage outcomes in the medial and lateral regions and averaged over the three images: (i) mean cartilage thickness—cartilage cross-sectional area by the length of the cartilage-bone interface; (ii) mean echo intensity—average grayscale pixel value ranging from black (0) to white (255); (iii) echo-intensity heterogeneity—standard deviation of the grayscale pixel value within the region (Lisee et al. 2020). All ultrasound cartilage outcomes were averaged across the three images acquired during the assessment. The same reader in this study also performed the readings in our prior study that demonstrated excellent intra-rater (*i.e.,* comparing segmentations on the same images that were completed 2 wk apart; intraclass correlation coefficient $(ICC)_{2,k} > 0.99$) and inter-rater (*i.e.,* comparing segmentations between a novice and a more experienced reader; $ICC_{2,k} > 0.94$) reliability, as well as acceptable measurement sensitivity (*i.e.,* minimal detectable change and standard error of the measurement) for medial and lateral mean cartilage thickness, mean echo intensity and echo-intensity heterogeneity (Lisee et al. 2020). This method of calculating mean cartilage thickness within the imaged region (*i.e.,* cartilage cross-sectional area divided by the length of the cartilage-bone interface) replicates the approach of MR imaging studies that calculate mean cartilage as the cartilage volume divided by the subchondral bone area (Eckstein et al. 2006; Buck et al. 2010b). This novel technique for assessing ultrasound femoral cartilage thickness used manual segmentation of the entire cartilage cross-sectional area and then used an automated program to standardize the medial and lateral cartilage regions and calculate an average cartilage thickness throughout the region (Lisee et al. 2020). The increased standardization and automation may remove some of the reader error and improve upon some of the inconsistencies observed when using traditional ultrasound thickness assessment (Roberts et al. 2019).

Arthroscopic assessment of femoral articular cartilage

A single orthopedic surgeon with a sub-specialty in sports medicine graded the medial and lateral femoral condyle using the Outerbridge grading system during the initial diagnostic arthroscopy at the time of ACL reconstruction (Cameron et al. 2003): 0 = normal cartilage, 1 = cartilage with softening and swelling, 2 = a partial-thickness defect with fissures on the surface that do not reach subchondral bone or exceed 1.5 cm in diameter, 3 = fissuring to the level of subchondral bone in an area with a diameter more than 1.5 cm and 4 = exposed subchondral bone. Based on previous studies, we created a dichotomous cartilage damage variable for both the medial and lateral femoral condyle based on the Outerbridge grade: (1) normal cartilage, Outerbridge = 0, or (2) cartilage damage, Outerbridge ≥1.

Statistical analysis

We used separate logistic regression analyses to determine the association between each cartilage ultrasound characteristic (*i.e.,* mean cartilage thickness, mean echo intensity and echo-intensity heterogeneity) and arthroscopic evidence of medial femoral cartilage damage. These analyses were repeated for participants with and without arthroscopic evidence of lateral cartilage damage. We report adjusted odds ratios (aORs) with 95% confidence intervals (CIs) to control for body mass index (BMI), knee angle during the ultrasound assessment and age in all models. An aOR with a 95% CI that did not cross 0 was considered statistically significant. All statistical analyses were performed using SAS Enterprise software, version 7.15 (SAS Institute).

This study was stopped early owing to research restrictions imposed by the coronavirus disease 2019 (COVID-19) pandemic, and this report is an interim analysis using the available sample. There was no formal power analysis to determine the minimum sample size needed to detect an association between cartilage ultrasound metrics and arthroscopic cartilage damage.

RESULTS

Table 1 highlights the demographic characteristics of the overall cohort of 24 participants, as well as separated into those with and without arthroscopic medial and lateral femoral cartilage damage. Twelve of the 24 participants presented with arthroscopic medial femoral cartilage damage, while a different 12 of the 24 total presented with arthroscopic lateral femoral cartilage damage. All demographic characteristics were similar between participants with and without femoral cartilage damage, except for a smaller BMI in participants with lateral cartilage damage than those without. Additionally, Table 1 highlights the frequency of the individual Outerbridge scores for those with medial and lateral femoral cartilage damage. Specifically, five of the 12 participants with medial femoral cartilage damage had an Outerbridge score = 1, while 11 of the 12 participants with lateral femoral cartilage damage had an Outerbridge score = 1.

Table 2 highlights the means and standard deviations for the cartilage ultrasound characteristics between

Table 1. Participant demographic characteristics

Demographic characteristics		Overall	Medial cartilage		Lateral cartilage	
			Damaged*	Healthy	Damaged*	Healthy
n		24	12	12	12	12
Sex (% female/male)		33/67	33/67	33/67	33/67	33/67
Body mass index (kg/m^2)		24.9 ± 3.7	25.6 ± 4.2	24.1 ± 3.1	**23.4 ± 3.2**	**26.4 ± 3.7**
Age (y)		24.0 ± 4.6	22.8 ± 4.6	25.3 ± 4.4	25.0 ± 5.2	23.0 ± 3.8
IKDC (0−100)		57.4 ± 14.6	54.3 ± 17.2	61.0 ± 10.4	59.1 ± 15.1	55.7 ± 14.7
Injury to surgery (d)		49.8 ± 51.9	50.6 ± 68.9	49.0 ± 29.7	53.9 ± 66.9	45.7 ± 33.5
Knee angle during ultrasound (°)		128 ± 12	125 ± 14	130 ± 10	131 ± 11	124 ± 12
Outerbridge Score (*n*)	0	—	0	12	0	12
	I	—	5	0	11	0
	II	—	5	0	1	0
	III	—	2	0	0	0
	IV	—	0	0	0	0

Data are given as mean ± standard deviation unless otherwise noted. Bold text indicates statistically significant differences between participants with and without cartilage damage ($p < 0.05$).

IDKC = International Knee Documentation Committee.

* Dichotomous cartilage damage variable based on the Outerbridge grade: 1) normal cartilage: Outerbridge = 0; 2) cartilage damage: Outerbridge ≥1.

Table 2. Comparison of femoral cartilage ultrasound outcomes between people with and without arthroscopic cartilage damage

Cartilage outcome	Healthy	Damaged	OR (95% CI)	aOR (95% CI)
Medial femoral condyle				
Mean thickness (mm)	2.02 ± 0.34	2.22 ± 0.38	1.83 (0.75−4.45)	1.77 (0.68−4.64)
Echo-intensity mean (0−255)	79.37 ± 6.85	71.64 ± 4.64	**0.19 (0.05−0.75)**	**0.09 (0.01−0.69)**
Echo-intensity SD (0−255)	10.47 ± 2.08	8.08 ± 0.97	**0.11 (0.02−0.63)**	**0.03 (0.002−0.50)**
Lateral femoral condyle				
Mean thickness (mm)	1.94 ± 0.31	1.84 ± 0.28	0.71 (0.31−1.65)	1.11 (0.39−3.16)
Echo-intensity mean (0−255)	72.85 ± 7.81	76.62 ± 5.00	1.88 (0.76−4.69)	1.29 (0.40−4.20)
Echo-intensity SD (0−255)	8.48 ± 0.98	8.83 ± 1.49	1.35 (0.58−3.18)	0.83 (0.30−2.26)

aOR = adjusted odds ratio, controlling for age, body mass index, and knee angle during ultrasound assessment; CI = confidence interval; OR = odds ratio; SD = standard deviation.

Odds ratios are reported as increased odds for having arthroscopic femoral cartilage damage per 1 SD difference in cartilage ultrasound outcomes. Bold text indicates statistically significant association between cartilage ultrasound outcomes and arthroscopic cartilage damage.

people with and without arthroscopic cartilage damage. In medial femoral cartilage, for every 1 standard deviation decrease in echo-intensity mean and heterogeneity, there is a respective 91% (aOR, 0.09; 95% CI, 0.01−0.69) and 97% (aOR, 0.03; 95% CI, 0.002−0.50) increase in the odds of having arthroscopic cartilage damage, controlling for age, BMI and knee angle during the ultrasound assessment. However, there was no statistically significant association between mean cartilage thickness and the presence of arthroscopic medial femoral cartilage damage (aOR, 1.77; 95% CI, 0.68−4.64).

In lateral femoral cartilage, there were no statistically significant associations between mean cartilage thickness, echo-intensity mean or echo-intensity heterogeneity and lateral arthroscopic cartilage damage after ACL injury (Table 2).

DISCUSSION

After ACL injury, altered cartilage ultrasound echo-intensity characteristics in the medial femoral trochlea are associated with arthroscopic femoral cartilage damage. Specifically, the medial femoral trochlear cartilage appears darker (*i.e.,* lower mean echo intensity) and more homogeneous (*i.e.,* lower echo-intensity heterogeneity) on ultrasound in knees with arthroscopic medial femoral cartilage damage. However, echo-intensity mean and heterogeneity were not statistically significantly associated with arthroscopic lateral femoral cartilage damage. Additionally, mean cartilage thickness was not statistically significantly associated with either medial or lateral arthroscopic femoral cartilage damage. This study provides evidence that femoral cartilage ultrasound echo-intensity characteristics represent non-invasive outcomes that associate with arthroscopic medial femoral cartilage damage in people after ACL injury.

We hypothesized that thinner cartilage on ultrasound would be associated with arthroscopic cartilage damage because cartilage defects may lead to cartilage thinning. Despite a rejection of our hypothesis, our findings complement prior MR imaging work that identified compositional cartilage differences but not morphologic differences in ACL-injured knees with arthroscopically defined cartilage damage compared with those without cartilage damage (Gupta et al. 2014). This may be because alterations in cartilage composition are theorized to occur before declines in cartilage thickness (Li and Majumdar, 2013b). Since arthroscopic medial femoral cartilage damage is associated with ultrasound echo intensity but not cartilage thickness, alterations in ultrasound echo intensity may offer an earlier marker of declining cartilage composition. Cartilage damage is common in knees after ACL injury, and the presence of this initial damage is related to longitudinal cartilage degradation that is accelerated at 5−7 y after injury (Potter et al. 2012). Therefore, the results of this study justify future studies to determine the utility of assessing ultrasound echo-intensity characteristics as a non-invasive and clinically accessible alternative to detect early declines in cartilage composition after ACL injury.

Additionally, our results complement prior studies indicating that early declines in cartilage health are detectable with ultrasound echo intensity (Kuroki et al. 2008; Saarakkala et al. 2006, 2012). In a qualitative assessment of echo intensity, degenerated cartilage samples presented with lower ultrasound echo intensity at the cartilage surface compared with healthy, intact cartilage samples (Saarakkala et al. 2006). Similarly, the presence of cartilage damage defined by a semi-quantitative ultrasound grading scale is related to both histologic and arthroscopic cartilage damage in people with knee OA or knee pain (Lee et al. 2008; Saarakkala et al. 2012).

While qualitative and semi-quantitative grading scales offer a quick and simple way to describe overall cartilage alterations, they fail to quantify subtle changes in cartilage echo intensity. However, a quantitative ultrasound image analysis of degenerative cartilage samples has provided initial evidence that less ultrasound reflection occurred at the cartilage surface in samples with histologic signs of OA (Saarakkala et al. 2006). Additionally, an invasive arthroscopic ultrasound evaluation performed on people at the time of knee replacement has found that lower ultrasound signal intensity was associated with greater arthroscopic cartilage damage (Kuroki et al. 2008). While these studies used different outcomes to quantify the signal intensity of cartilage, our findings complement them in indicating that lower cartilage echo intensity relates to greater cartilage damage using a non-invasive ultrasound technique in people after an acute knee injury. Before structural changes in cartilage occur, early stages of cartilage damage result in a breakdown of collagen and proteoglycans that leads to a concomitant increase in cartilage water content (Eckstein et al. 2001; Liess et al. 2002; Chou et al. 2009). Because increased water content alters the speed of sound within the cartilage (Töyräs et al. 2003), this may be a potential mechanism for the altered ultrasound echo-intensity characteristics observed in this study, but further work is needed to validate the pathophysiologic implications of the *in vivo* ultrasound echo-intensity outcomes used in this study. Therefore, ultrasound echo-intensity characteristics, specifically lower mean and heterogeneity, appear to be pathologic signs related to early indications of medial femoral cartilage damage.

Ultrasound echo intensity in the lateral femoral cartilage was not associated with the presence of lateral arthroscopic cartilage damage. A previous study observed a similar non-significant association between ultrasound outcomes and arthroscopic lateral femoral cartilage damage, even though there was a significant association between ultrasound and arthroscopic medial femoral cartilage damage (Saarakkala et al. 2012). The lack of relationship between ultrasound and arthroscopy when assessing the lateral femur may be owing to different locations of cartilage being assessed by the two techniques. Since there are region-specific changes in cartilage composition after ACL injury that may be owing to alterations in location-specific joint loading throughout the knee (Chen et al. 2018; Pfeiffer et al. 2019), further work is needed to ensure similar locations in comparing ultrasound and other examination methods (*e.g.,* MR imaging), to confirm that the same cartilage is being evaluated between techniques.

Another reason for the lack of association between cartilage ultrasound outcomes and arthroscopic lateral femoral cartilage damage may be owing to the severity of arthroscopic cartilage damage. Most of the participants in this study with lateral femoral cartilage damage (11 of 12) presented with only "softening or swelling with no visible defect" (*i.e.,* Outerbridge = 1), while 7 of the 12 participants with arthroscopic medial femoral cartilage damage scored had an Outerbridge score of 2 or 3. While a previous study indicated that an invasive ultrasound echo-intensity assessment could discriminate between cartilage graded as 0 and 1 on an arthroscopic grading scale (Kuroki et al. 2008), future studies with larger sample sizes need to determine whether a non-invasive ultrasound echo-intensity assessment can discriminate between the different grades of arthroscopic cartilage damage.

While this study provides preliminary evidence that ultrasound echo-intensity characteristics offer a non-invasive and clinically accessible tool associated with arthroscopic medial femoral cartilage damage, there are some limitations and ideas for future direction that should be taken into consideration. Transverse ultrasound cartilage assessment is limited to assessing the femoral trochlea, and likely not at the same location on the femoral condyle where the arthroscopic cartilage damage was detected. The intent of this study was not to specifically detect arthroscopic lesions with ultrasound assessment but to determine if cartilage ultrasound characteristics in the same femoral region (*i.e.,* medial or lateral) are different between people with and without cartilage damage. Thus, one possibility for the significant association between ultrasound and arthroscopy is that a person with medial compartment cartilage damage may have altered cartilage throughout the entire medial femur, but further studies are needed to confirm this. Quantifying ultrasound echo intensity may provide more sensitive information for early cartilage damage than more traditional semi-quantitative grading scales, but quantitative analysis of non-invasive ultrasound has other challenges (*e.g.,* attenuation effects of overlying soft tissue, affected by different settings of ultrasound equipment) (Saarakkala et al. 2012). Previous muscle ultrasound investigations have corrected for echo intensity using subcutaneous fat thickness to estimate intramuscular fat (Young et al. 2015). While a recent ultrasound article corrected cartilage echo intensity by subcutaneous fat thickness (Pamukoff et al. 2020), further studies are needed to determine the need and to establish the most effective way to correct cartilage ultrasound echo-intensity using subcutaneous fat thickness to estimate cartilage composition. This study highlights a preliminary cross-sectional association between cartilage ultrasound echo intensity and arthroscopic cartilage damage but does not provide an indication of the prognostic value of assessing cartilage ultrasound echo intensity or the natural history of longitudinal changes in cartilage ultrasound echo intensity after injury. Future prospective studies are needed to determine if an initial assessment of cartilage ultrasound echo intensity is related to poor clinical outcomes or the early onset of knee OA, as well as to determine the longitudinal progression of ultrasound-assessed cartilage echo intensity and thickness after ACL injury and surgery.

Participants were positioned in maximal knee flexion during the ultrasound scanning protocol, as this is the recommended positioning for the assessment of femoral cartilage. Future studies may consider attempting to standardize the knee flexion angle across all participants; however, this may be difficult owing to limitations in range of motion among some participants after injury. The small sample size of this study was owing to a research stoppage caused by the COVID-19 pandemic. The results of this study are based on an interim analysis of the available data, but they provide intriguing findings regarding the association between non-invasive cartilage ultrasound metrics and arthroscopic cartilage damage. Future studies are needed to confirm and build upon the results from this study. Due to our small sample size and the use of three covariates, there is a potential for overfitting our model. However, this is unlikely because the unadjusted ORs highlight a similar association between lower cartilage ultrasound echo intensity and increased odds of arthroscopic medial femoral cartilage damage (Table 2).

In conclusion, lower cartilage ultrasound echo-intensity mean and heterogeneity are associated with arthroscopic medial femoral cartilage damage after ACL injury. This study provides preliminary evidence that ultrasound echo-intensity mean and heterogeneity are non-invasive and clinically accessible imaging outcomes associated with medial femoral cartilage damage in people after ACL injury.

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Conflict of interest disclosure—The authors declare no competing interests.

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