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Impact of Chronic Lateral Ankle Instability with Lateral Collateral Ligament Injuries on Biochemical Alterations in the Cartilage of the Subtalar and Midtarsal Joints Based on MRI T2 Mapping

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Objective: To quantitatively assess biochemical alterations in the cartilage of the subtalar and midtarsal joints in chronic lateral ankle instability (CLAI) patients with isolated anterior talofibular ligament (ATFL) injuries and combined calcaneofibular ligament (CFL) injuries using MRI T2 mapping.
Materials and Methods: This study was performed according to regulations of the Committee for Human Research at our institution, and written informed consent was obtained from all participants. Forty CLAI patients (26 with isolated ATFL injuries and 14 with combined ATFL and CFL injuries) and 25 healthy subjects were recruited for this study. All participants underwent MRI scans with T2 mapping. Patients were assessed with the American Orthopedic Foot and Ankle Society (AOFAS) rating system. The subtalar and midtarsal joints were segmented into 14 cartilage subregions. The T2 value of each subregion was measured from T2 mapping images. Data were analyzed with ANOVA, the Student's *t* test, and Pearson's correlation coefficient.
Results: T2 values of most subregions of the subtalar joint and the calcaneal facet of the calcaneocuboid joint in CLAI patients with combined CFL injuries were higher than those in healthy controls (all $p < 0.05$). However, there were no significant differences in T2 values in subtalar and midtarsal joints between patients with isolated ATFL injuries and healthy controls (all $p > 0.05$). Moreover, T2 values of the medial talar subregions of the posterior subtalar joint in patients with combined CFL injuries showed negative correlations with the AOFAS scores ($r = -0.687$, $p = 0.007$; $r = -0.609$, $p = 0.021$, respectively).
Conclusion: CLAI with combined CFL injuries can lead to cartilage degeneration in subtalar and calcaneocuboid joints, while an isolated ATFL injury might not have a significant impact on the cartilage in these joints.
Keywords: *Magnetic resonance imaging; Chronic lateral ankle instability; Subtalar joint; Midtarsal joint; Cartilage*

INTRODUCTION

Injuries to the lateral collateral ligaments of the ankle are frequently observed in sports and recreational activities (1). Injury to the anterior talofibular ligament (ATFL) is the most common injury, followed by injury to both the ATFL and calcaneofibular ligament (CFL) (2-4). Approximately 10–30% of patients with inadequate healing of ligaments and

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repeated ankle sprains may develop chronic lateral ankle instability (CLAI) (5). Persistently altered ankle kinematics caused by CLAI have been suggested to contribute to the development of cartilage degeneration and the progression of osteoarthritis (OA) (6, 7), the prevalence of which is expected to be as high as 77% in 10 years (8-10).

The subtalar joint consists of anterior, middle, and posterior facets of the talocalcaneal joint and acts synchronously with midtarsal joints to coordinate the ankle and foot during gait. The midtarsal joints consist of talonavicular and calcaneocuboid joints. The subtalar and midtarsal joints play a critical role in transmitting the body's weight and forces to the distal foot (11, 12). A previous study suggested that cartilage degeneration in subtalar and midtarsal joints may be associated with CLAI (7). However, cartilage degeneration is difficult to detect using physical examinations and routine imaging options and is thus usually missed in the clinic. If left undiagnosed, it will lead to pain, impaired mobility, and potentially OA of these joints over time (13-15). Since the early degeneration of cartilage preceding morphological deterioration may be reversible if an intervention is performed in a timely manner (16), it is clinically important to detect early biochemical alterations in the cartilage matrix of these joints.

Magnetic resonance imaging (MRI) is a reliable method for the quantitative assessment of articular cartilage (17). MRI relaxation time measurements are very powerful tools for the noninvasive assessment of biochemical changes in cartilage matrices (17-19). The T2 value was shown to be associated with the orientation and integrity of collagen as well as free water content in the cartilage matrix (20). An increased T2 value is thought to be closely associated with disorganized arrangement of collagen and increased free water, which suggests cartilage degeneration (21). T2-mapping has been confirmed to be sensitive to cartilage biochemical alterations in knees, hips, and ankles in previous publications (17, 22, 23). In addition, the application of 3T scanner and dedicated multichannel coils make T2-mapping a high-resolution imaging technique for the thin cartilages in small joints.

Recent studies have reported that there is elevated cartilage contact pressure on the talus in CLAI patients compared to healthy controls, and cartilage degeneration in the talar dome, distal tibia, and subtalar joint has been found using quantitative T2-mapping, T2*-mapping, or T1rho-mapping (24-28). Biomechanical and anatomic studies have shown that ATFL and CFL play different roles in maintaining the stability of hindfoot joints (29-31). However, few studies have specifically assessed the different biochemical effects of isolated ATFL injury and combined CFL injury on the cartilage of subtalar and midtarsal joints in CLAI patients and the correlations between these alterations and clinical scores. Therefore, the objectives of the current study were (1) to quantitatively assess the biochemical alterations in the cartilage of subtalar and midtarsal joints in CLAI patients with ATFL injuries and combined CFL injuries using MRI T2-mapping and (2) to analyze the correlations between T2 values and American Orthopedic Foot and Ankle Society (AOFAS) scores.

MATERIALS AND METHODS

This study was performed according to the regulations of the Committee for Human Research at our institution, and written informed consent was obtained from all participants.

Patient Population

From September 2015 to August 2018, we randomly recruited 50 patients who were diagnosed with symptomatic CLAI in the Sports Medicine Department of our hospital. The patients underwent ankle MRI scans. The inclusion criteria were as follows: unilateral repetitive lateral ankle sprain for more than six months; clinically diagnosed CLAI based on physical examinations and ankle radiographs by a surgeon from the Sports Medicine Department (Yinghui Hua, 15 years of experience in foot and ankle surgery); ATFL injury or combined CFL injury evident in morphological MR images and confirmed by arthroscopy during surgical procedure; no history of contralateral ankle injury; age at initial sprain between 18 and 50 years old; and body mass index (BMI) less than 24 kg/m^2. The exclusion criteria were as follows: osteochondral lesion (OCL) in subtalar and midtarsal joints; previous history of ankle fracture; diagnosis of OA or infective arthritis; bony malalignment; injury to the ligaments in the subtalar joint; injury to the medial deltoid ligament or peroneal tendon; and prior surgery on either ankle. In addition, we recruited 30 healthy subjects who were matched with CLAI patients according to age, sex, and BMI. The subjects were mainly comprised of office workers, teachers, technicians, and engineers. Professional athletes and ballet dancers were not included in the cohorts. Two musculoskeletal radiologists (18 years of experience in musculoskeletal radiology and five years of experience

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in musculoskeletal radiology) who were blinded to the clinical diagnoses reviewed the MR images in consensus to determine the status of ATFL and CFL and other pathologic conditions. On fat saturation-proton density images, the MRI findings of ligament injury included laxity, waviness, thickening and irregularity with abnormal signal intensity, nonvisualization, and discontinuity (32, 33). The ligament was considered to be normal if it had intact continuity and uniform low signal intensity (34, 35).

The subjects' enrollment process is shown in Figure 1. Finally, a total of 40 CLAI patients and 25 healthy controls were included in our study. The CLAI patients were divided into two groups according to the status of ATFL and CFL: the isolated ATFL injury group was composed of 26 patients and the combined CFL injury group was composed of 14 patients. Grade III-IV OCLs in the talar dome were observed in seven patients. They were not excluded because the OCL in the talar dome was found to have no significant effect on the cartilage of the subtalar joint in a previous study (28). There were no significant differences in demographic data among the three groups (Table 1).

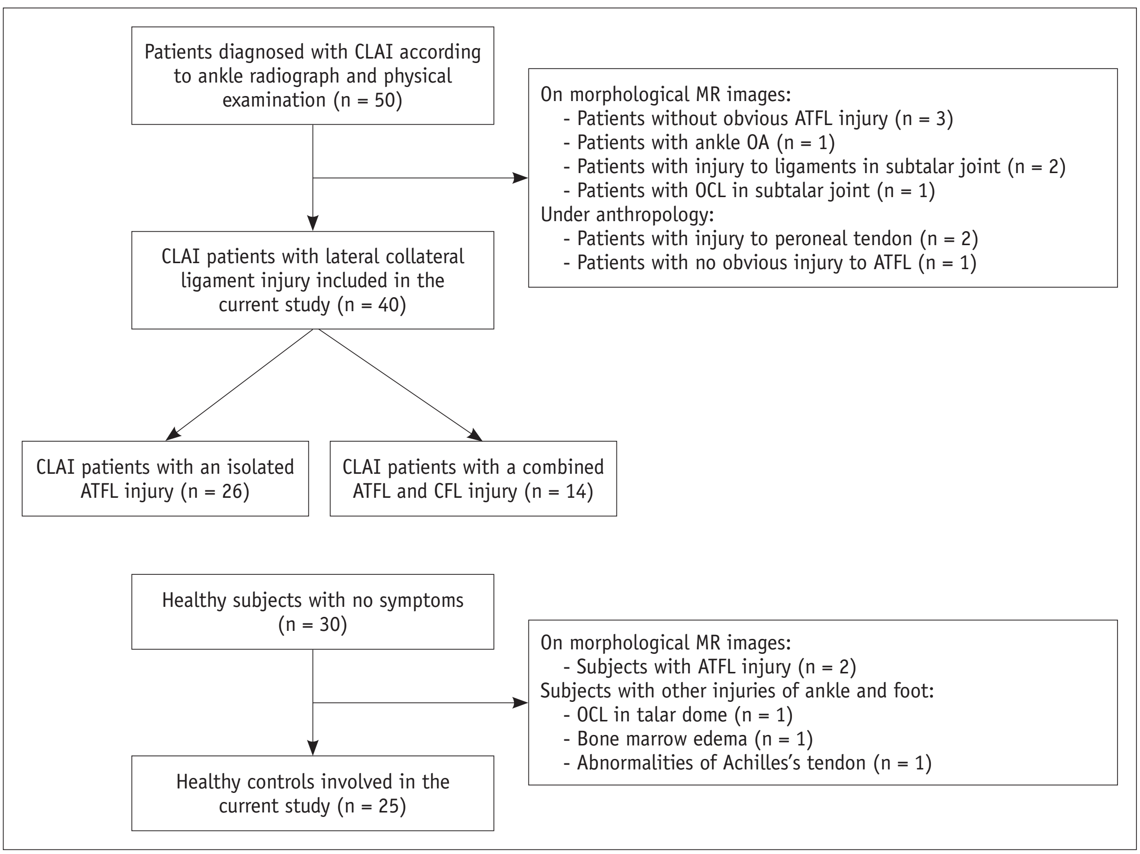

Fig. 1. Flow chart of the subject enrollment process. ATFL = anterior talofibular ligament, CFL = calcaneofibular ligament, CLAI = chronic lateral ankle instability, OA = osteoarthritis, OCL = osteochondral lesion

Table 1. Demographic Data of Participants in the Three Groups

Demographics	Healthy Controls	CLAI with ATFL Injury	CLAI with Combined CFL Injury	*P*
Sex, male/female, n	20/5	18/8	10/4	0.664
Age, mean ± SD, y	28.5 ± 4.4	28.8 ± 6.3	29.4 ± 7.8	0.903
BMI, mean ± SD, kg/m^2	22.7 ± 2.0	23.2 ± 2.3	23.0 ± 2.5	0.668
left/right ankle, n	13/12	13/13	8/6	0.910
Symptom duration, mean ± SD, mo	-	31.6 (6–108)	32.3 (6–120)	0.677
Combined OCL in talar dome (grade III–IV), n	-	4	3	0.631

ATFL = anterior talofibular ligament, BMI = body mass index, CFL = calcaneofibular ligament, CLAI = chronic lateral ankle instability, OCL = osteochondral lesion, SD = standard deviation

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Imaging Acquisition

A 3T MRI scanner (MAGNETOM Verio, Siemens Healthineers) with 45 mT/m gradient strength and an 8-channel phased array coil were used. The MRI sequences and parameters are displayed in Table 2. The T2 relaxation times were measured from T2-mapping images. Only the subtalar cartilage in posterior and middle facets of the talocalcaneal joint was selected for T2 measurements because of the frequent anatomical variant of the anterior facet, which may be missing or fused with middle facets (25). The talar facet of the posterior subtalar joint was divided into medial and lateral regions equally. The curve talar and calcaneal facets on sagittal images were further divided into two equal segments respectively: the anterior and posterior regions. In total, regions of interest (ROIs) were drawn in 14 cartilage subregions in the subtalar and midtarsal joints: 1) middle subtalar joint including the talar facet (mSTJ-T) and calcaneus facet (mSTJ-Cal); 2) posterior subtalar joint containing the medial anterior talar facet (pSTJ-MAT), medial posterior talar facet (pSTJ-MPT), lateral anterior talar facet (pSTJ-LAT), lateral posterior talar facet (pSTJ-LPT), medial anterior calcaneal facet (pSTJ-MAC), medial posterior calcaneal facet (pSTJ-MPC), lateral anterior calcaneal facet (pSTJ-LAC), and lateral posterior calcaneal facet (pSTJ-LPC); and 3) midtarsal joints comprising of the talar facet of talonavicular joint, navicular facet of talonavicular joint, calcaneal facet of calcaneocuboid joint (CCJ-Cal), and cuboidal facet of calcaneocuboid joint (as illustrated in Fig. 2). The ROIs were drawn by using a custom-made semiautomatic software and carefully adjusted by observers. The synovial fluid and subchondral bone were not included when drawing ROIs. Subsequently, color-scale T2-mapping images were generated to show the detailed topographic distribution of T2 values.

Clinical Assessment

The patients underwent AOFAS assessments on the day after MRI examination by the same observer from the Department of Sports Medicine. The 100-point AOFAS scoring system assesses three aspects: function (45 points), pain (40 points), and alignment (15 points).

Statistical Analysis

Statistical analysis was performed using SPSS version 23.0 software (IBM Corp.). The descriptive statistics for the continuous variables are reported as the arithmetic mean value and standard deviation.

In 10 randomly selected subjects, each T2 measurement was performed by the main musculoskeletal radiologist and another observer (3rd-year radiology resident). The main observer reanalyzed these subjects after two months. Both interobserver reliability and intraobserver reproducibility were analyzed using interclass correlation coefficients (ICCs). The ICCs were interpreted as follows: less than 0.40, poor agreement; between 0.40 and 0.75, fair to good agreement; and greater than 0.75, excellent agreement (28).

ANOVA was used to compare the differences in T2 values among the three groups. Multiple comparisons were performed using the least-significant difference. An independent Student's *t* test was used to compare the difference in AOFAS scores between the two patient groups, and Pearson's correlation analysis was performed to assess the correlations between T2 values and AOFAS scores. The chi-squared test was used to compare categorical variables.

Table 2. MR Imaging Sequences and Parameters

Sequences	Cor-FS-PD	Ax-FS-PD	Sag-FS-PD	Ax-T1WI	T2-Mapping
TR (ms)	843	650	737	600	1220
TE (ms)	9.9	15.0	18.0	18.0	13.8, 27.6, 41.4, 55.2, 69.0
Field of view (mm)	150 x 150	150 x 150	150 x 150	150 x 150	160 x 160
Matrix	256 x 187	256 x 205	256 x 192	256 x 205	384 x 384
Matrix phase (%)	73	80	75	80	100
Pixel size (mm)	0.8 x 0.6 x 2.0	0.7 x 0.6 x 2.0	0.8 x 0.6 x 2.0	0.7 x 0.6 x 2.0	0.4 x 0.4 x 2.0
Slice thickness (mm)	2.0	2.0	2.0	2.0	2.0
Number of excitations	1	1	1	1	2
Flip angle (degrees)	150	90	140	90	180
Bandwidth (Hz/pixel)	250	250	260	250	228
Scan time (min)	2:32	2:17	1:17	1:57	8:22

Ax = axial, Cor = coronal, Sag = sagittal, FS-PD = fat saturation-proton density, TE = echo time, TR = repetition time, T1WI = T1-weighted imaging

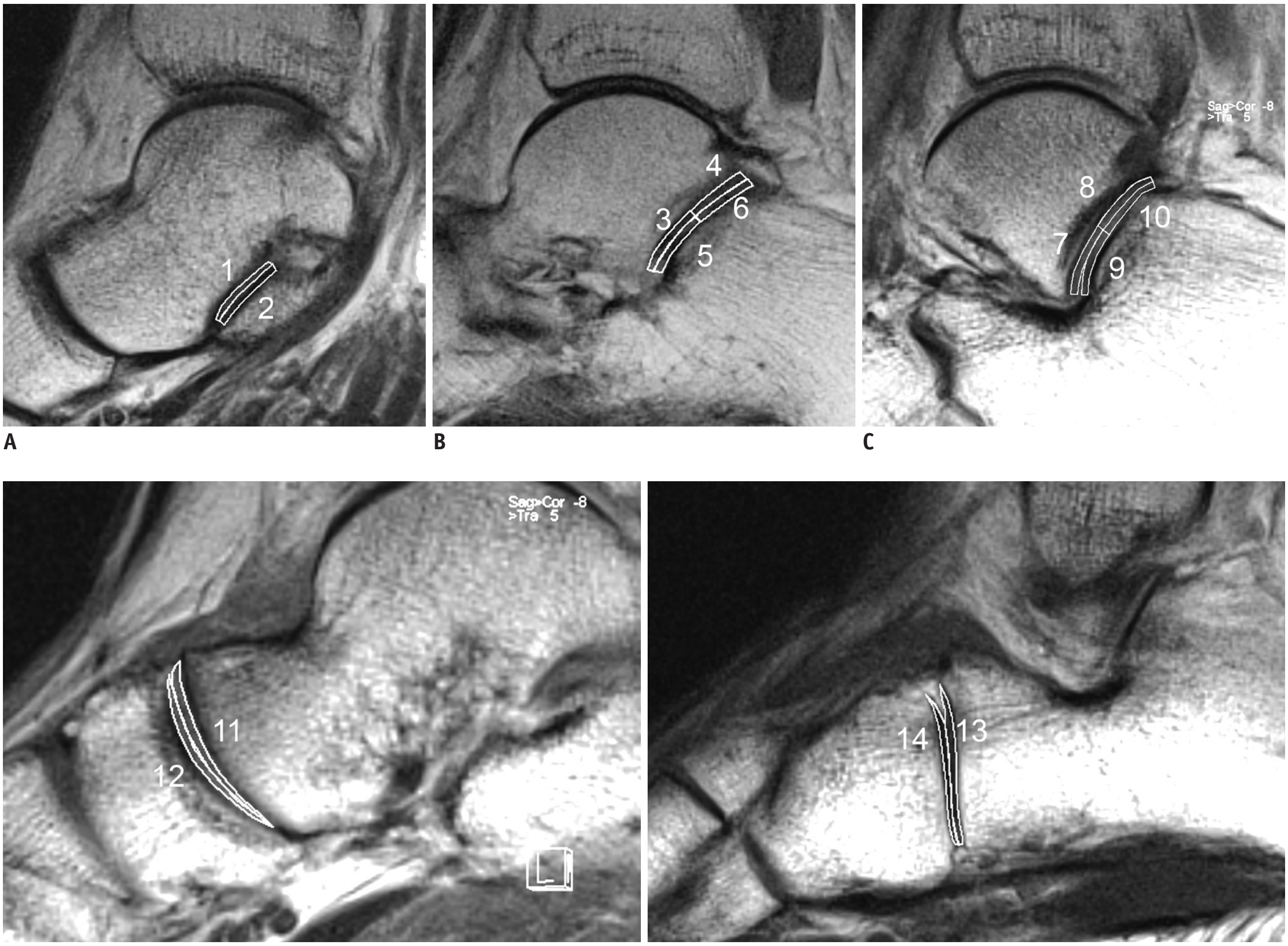

Fig. 2. Regions of interest were drawn in 14 cartilage subregions in the subtalar and midtarsal joints.
A. Middle subtalar joint, including the mSTJ-T (1) and mSTJ-Cal (2). **B.** Medial posterior subtalar joint, containing the pSTJ-MAT (3), pSTJ-MPT (4), pSTJ-MAC (5), and pSTJ-MPC (6). **C.** Lateral posterior subtalar joint, containing the pSTJ-LAT (7), pSTJ-LPT (8), pSTJ-LAC (9), and pSTJ-LPC (10). **D.** Talonavicular joint, comprising of the TNJ-T (11) and TNJ-N (12). **E.** Calcaneocuboid joint, comprising of the CCJ-Cal (13) and CCJ-Cu (14). CCJ-Cal = calcaneal facet of calcaneocuboid joint, CCJ-Cu = cuboidal facet of calcaneocuboid joint, mSTJ-Cal = calcaneus facet middle subtalar joint, mSTJ-T = talar facet of middle subtalar joint, pSTJ-LAC = lateral anterior calcaneal facet of posterior subtalar joint, pSTJ-LAT = lateral anterior talar facet of posterior subtalar joint, pSTJ-LPC = lateral posterior calcaneal facet of posterior subtalar joint, pSTJ-LPT = lateral posterior talar facet of posterior subtalar joint, pSTJ-MAC = medial anterior calcaneal facet of posterior subtalar joint, pSTJ-MAT = medial anterior talar facet of posterior subtalar joint, pSTJ-MPC = medial posterior calcaneal facet of posterior subtalar joint, pSTJ-MPT = medial posterior talar facet of posterior subtalar joint, TNJ-N = navicular facet of talonavicular joint, TNJ-T = talar facet of talonavicular joint

Results corresponding to $p < 0.05$ were considered statistically significant.

RESULTS

The ICC indexes of intraobserver reproducibility and interobserver reliability regarding T2 measurements of each defined cartilage subregion were all greater than 0.75 (range, 0.785–0.964), indicating excellent interobserver reliability and intraobserver reproducibility (Table 3).

The T2 values of all cartilage subregions in the three groups are displayed in Table 4 and Figure 3, and the color-scale T2-mapping images are shown in Figure 4. The T2 values of cartilage subregions were significantly different among the three groups in the middle subtalar joint and most posterior subtalar joint, except for the posterior calcaneus facet (pSTJ-MPC, $p = 0.390$ and pSTJ-LPC, $p = 0.080$). For the midtarsal joints, only the T2 value of the CCJ-Cal was significantly different among the three groups ($p = 0.032$). A post hoc comparison showed that CLAI patients with combined CFL injuries had significantly higher T2 values in the middle subtalar joint and most posterior subtalar joint, except for two posterior calcaneus facets (pSTJ-MPC, $p = 0.226$; pSTJ-LPC, $p = 0.069$), and CCJ-Cal

(p = 0.011) compared to healthy controls. There were no significant differences in T2 values in either the subtalar joint or midtarsal joint between CLAI patients with isolated ATFL injuries and healthy controls (all p > 0.05). Moreover, the T2 values of the mSTJ-T, anterior pSTJ (pSTJ-MAT, pSTJ-LAT, pSTJ-MAC, pSTJ-LAC), pSTJ-LPC, and CCJ-Cal in CLAI patients with combined CFL injuries were higher than those in patients with isolated ATFL injuries (p < 0.05).

The mean AOFAS score of CLAI patients with combined CFL injuries was significantly lower than that of patients

Table 3. The ICC Indexes of Intraobserver Reproducibility and Interobserver Reliability for T2 Value Measurement of Each Defined Cartilage Subregion in the Subtalar and Midtarsal Joints

Cartilage Subregions	Observer 1 T2 Values (ms)	Observer 2 T2 Values (ms)	Observer 1 (after Two Months) T2 Values (ms)	Intraobserver ICC	95% CI	Interobserver ICC	95% CI
mSTJ-T	45.82 ± 3.86	46.09 ± 4.60	46.79 ± 4.08	0.932	0.742–0.983	0.921	0.681–0.980
mSTJ-Cal	44.08 ± 5.16	44.64 ± 6.06	44.86 ± 5.91	0.920	0.728–0.979	0.859	0.532–0.963
pSTJ-MAT	43.54 ± 7.28	43.80 ± 6.13	44.64 ± 6.15	0.920	0.727–0.979	0.883	0.601–0.970
pSTJ-MPT	40.30 ± 8.65	42.54 ± 9.40	42.77 ± 8.10	0.941	0.794–0.985	0.917	0.703–0.979
pSTJ-LAT	46.93 ± 10.97	46.19 ± 8.09	46.71 ± 9.20	0.946	0.810–0.986	0.906	0.668–0.976
pSTJ-LPT	43.76 ± 10.43	45.91 ± 8.21	44.36 ± 11.04	0.928	0.752–0.981	0.908	0.676–0.976
pSTJ-MAC	42.14 ± 6.03	43.00 ± 5.85	42.91 ± 6.70	0.855	0.544–0.961	0.813	0.459–0.955
pSTJ-MPC	42.50 ± 6.84	43.76 ± 5.72	42.96 ± 5.71	0.928	0.753–0.981	0.861	0.539–0.964
pSTJ-LAC	37.19 ± 9.17	40.42 ± 8.51	38.44 ± 9.64	0.927	0.751–0.981	0.939	0.777–0.985
pSTJ-LPC	43.41 ± 8.89	44.86 ± 7.15	44.14 ± 7.98	0.913	0.708–0.977	0.867	0.554–0.965
TNJ-T	36.99 ± 7.33	37.19 ± 4.57	36.62 ± 6.62	0.862	0.554–0.963	0.883	0.600–0.970
TNJ-N	31.14 ± 4.95	33.93 ± 3.24	33.70 ± 4.77	0.841	0.507–0.957	0.785	0.346–0.942
CCJ-Cal	40.71 ± 10.01	41.01 ± 9.13	41.19 ± 9.67	0.964	0.869–0.991	0.896	0.638–0.973
CCJ-Cu	35.33 ± 7.83	36.98 ± 5.24	36.91 ± 7.20	0.946	0.811–0.986	0.856	0.524–0.962

CCJ-Cal = calcaneal facet of calcaneocuboid joint, CCJ-Cu = cuboidal facet of calcaneocuboid joint, CI = confidence interval, ICC = interclass correlation coefficient, mSTJ-Cal = calcaneus facet middle subtalar joint, mSTJ-T = talar facet of middle subtalar joint, pSTJ-LAC = lateral anterior calcaneal facet of posterior subtalar joint, pSTJ-LAT = lateral anterior talar facet of posterior subtalar joint, pSTJ-LPC = lateral posterior calcaneal facet of posterior subtalar joint, pSTJ-LPT = lateral posterior talar facet of posterior subtalar joint, pSTJ-MAC = medial anterior calcaneal facet of posterior subtalar joint, pSTJ-MAT = medial anterior talar facet of posterior subtalar joint, pSTJ-MPC = medial posterior calcaneal facet of posterior subtalar joint, pSTJ-MPT = medial posterior talar facet of posterior subtalar joint, TNJ-N = navicular facet of talonavicular joint, TNJ-T = talar facet of talonavicular joint

Table 4. The T2 Values of All Cartilage Subregions in the Three Groups

Cartilage Subregions	Healthy Controls (1) T2 Values (ms)	CLAI with ATFL Injury (2) T2 Values (ms)	CLAI with Combined CFL Injury (3) T2 Values (ms)	*P*	(2) vs. (1) *P*	(3) vs. (1) *P*	(2) vs. (3) *P*
mSTJ-T	43.12 ± 6.02	44.49 ± 6.20	50.11 ± 7.45	0.006*	0.446	0.002*	0.010*
mSTJ-Cal	39.72 ± 6.41	41.87 ± 6.61	46.05 ± 8.10	0.028*	0.268	0.008*	0.072
pSTJ-MAT	40.27 ± 5.87	43.32 ± 6.97	47.78 ± 6.03	0.003*	0.092	0.001*	0.039*
pSTJ-MPT	42.60 ± 10.15	46.23 ± 8.57	50.42 ± 7.58	0.039*	0.157	0.012*	0.167
pSTJ-LAT	41.37 ± 5.77	43.39 ± 7.51	50.28 ± 9.53	0.002*	0.332	0.001*	0.007*
pSTJ-LPT	39.52 ± 6.51	42.26 ± 5.81	45.81 ± 10.36	0.039*	0.182	0.012*	0.145
pSTJ-MAC	37.64 ± 5.88	36.88 ± 6.32	43.41 ± 6.84	0.007*	0.668	0.008*	0.003*
pSTJ-MPC	40.81 ± 7.32	40.70 ± 6.30	43.49 ± 5.58	0.390	0.953	0.226	0.205
pSTJ-LAC	33.74 ± 4.57	34.01 ± 7.14	40.52 ± 7.12	0.004*	0.880	0.002*	0.003*
pSTJ-LPC	41.99 ± 7.23	40.24 ± 6.92	46.32 ± 6.70	0.080	0.375	0.069	0.011*
TNJ-T	36.40 ± 4.74	36.78 ± 5.18	38.06 ± 5.04	0.598	0.783	0.320	0.440
TNJ-N	31.64 ± 3.73	32.12 ± 5.56	31.51 ± 3.32	0.893	0.702	0.930	0.681
CCJ-Cal	39.54 ± 7.09	40.68 ± 6.71	45.69 ± 7.31	0.032*	0.564	0.011*	0.034*
CCJ-Cu	36.78 ± 7.33	36.91 ± 8.55	40.19 ± 6.25	0.358	0.958	0.189	0.201

*The mean difference is significantly different at p < 0.05.

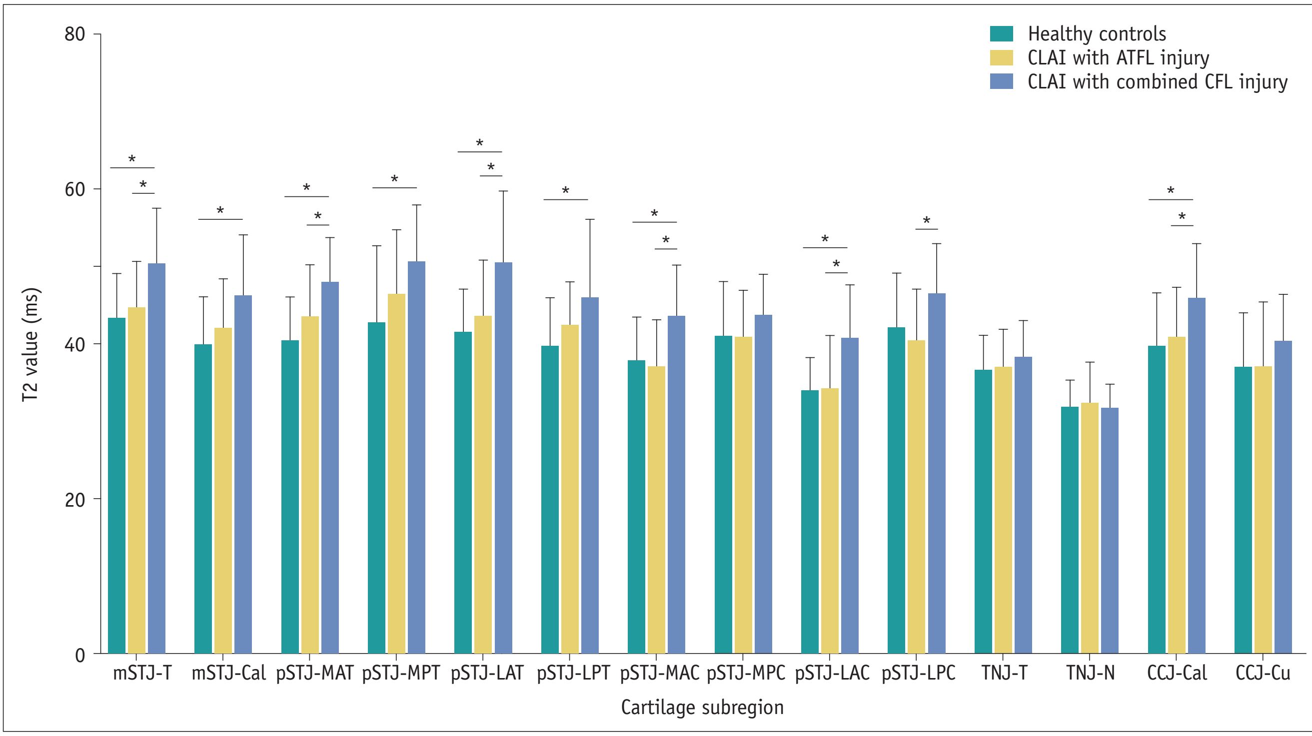

Fig. 3. The histogram of the T2 values in the subtalar and midtarsal joints for the three groups. *A significant difference between the two groups ($p < 0.05$).

with isolated ATFL injuries (59.79 ± 5.92 vs. 70.96 ± 6.17, $p < 0.001$), which indicated a worse clinical symptom for patients with combined CFL injuries.

The correlation analysis results are displayed in Table 5. The T2 values of the medial talar cartilage of the posterior subtalar joint (pSTJ-MAT and pSTJ-MPT) in CLAI patients with combined CFL injuries showed negative correlations with AOFAS scores ($r = -0.687$, $p = 0.007$; $r = -0.609$, $p = 0.021$, respectively), while the T2 values of other cartilage subregions showed no significant correlations with AOFAS scores. Regarding CLAI patients with isolated ATFL injuries, there was no statistically significant correlation between the T2 value of any cartilage subregion in subtalar or midtarsal joints and the AOFAS score (all $p > 0.05$).

DISCUSSION

The most important finding of this study was that CLAI patients with combined CFL injuries can develop biochemical alterations in the cartilage of the subtalar and calcaneocuboid joints before morphological changes occur, while patients with isolated ATFL injuries might not develop changes in the cartilage of the subtalar and midtarsal joints. Additionally, the T2 values of the medial talar cartilage of the posterior subtalar joint in CLAI patients with combined CFL injuries were negatively correlated with the AOFAS scores, which suggests that the biochemical alteration of the cartilage in this subregion may affect the patients' clinical symptoms.

We demonstrated excellent intraobserver reproducibility and interobserver reliability for quantitative T2 measurements of cartilage subregions in the subtalar and midtarsal joints. This result is in accordance with those of previous studies that reported excellent intraobserver and interobserver agreement for T2-mapping of the subtalar joint and good to excellent reproducibility for T2- mapping of the hindfoot joints, respectively (12, 28).

In our study, we found higher T2 values in the middle subtalar joint, most posterior subtalar joint, and calcaneocuboid joint in CLAI patients with combined CFL injuries compared to healthy controls. However, there were no significant differences in the T2 values of these joints between CLAI patients with isolated ATFL injuries and healthy controls. Previous studies have demonstrated that T2 quantification is sensitive to biochemical changes in the cartilage matrix. Higher T2 values reflect increased free water and irregular collagen arrangement in the cartilage matrix (17, 20, 23). Similarly, our result showing a significant T2 elevation in the aforementioned cartilage subregions can be explained by the loss of structural anisotropy in

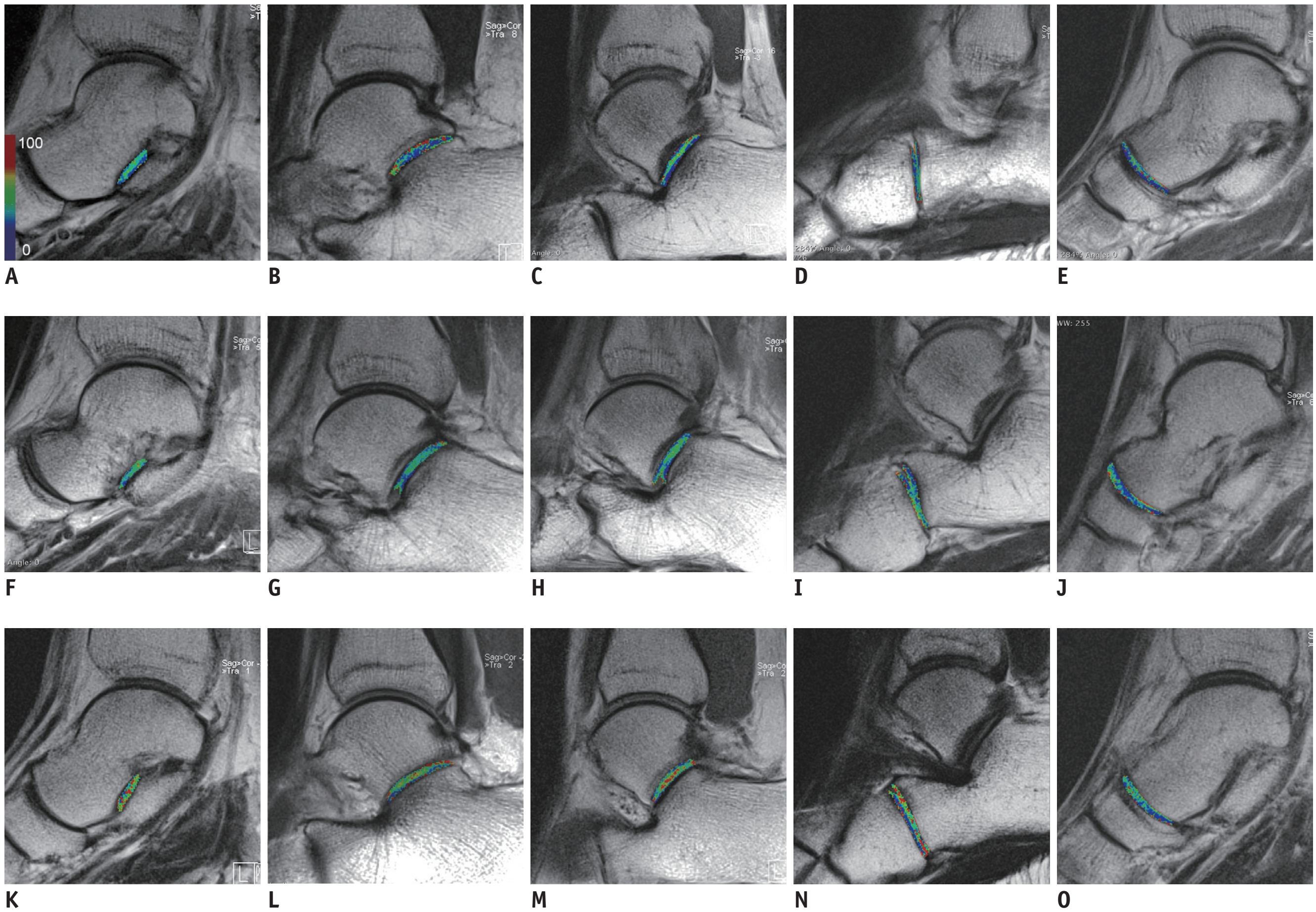

Fig. 4. The color scale T2 mapping images of the cartilage in the middle subtalar joints (A, F, K), medial posterior subtalar joint (B, G, L), lateral posterior subtalar joint (C, H, M), talonavicular joint (D, I, N), and calcaneocuboid joint (E, J, O) of a healthy control (upper row), a CLAI patient with an ATFL injury (middle row), and a CLAI patient with a combined CFL injury (bottom row). The T2 values of the middle subtalar joint, most posterior subtalar joint, and CCJ-Cal of CLAI patients with combined CFL injuries were higher than those of CLAI patients with ATFL injuries and the healthy controls, according to the corresponding color bar, while the T2 values for these joints in CLAI patients with ATFL injuries were comparable to those of healthy controls.

the collagen matrix and a concomitant increase in free water, which indicates cartilage degeneration. Therefore, our results demonstrated that combined CFL injuries can lead to the occurrence of cartilage degeneration in the subtalar joint and calcaneocuboid joint in CLAI patients, while isolated ATFL injuries have no significant impact on cartilage in these joints. A recent study reported that T2 values of all posterior subtalar cartilage compartments were significantly higher in lateral ankle instability (LAI) patients with lateral collateral ligament injuries compared to healthy controls (28). The result was partially consistent with ours. However, the study did not differentiate LAI patients with isolated ATFL injuries from those with combined ATFL and CFL injuries. It is possible that patients with combined CFL injuries had a high weighted impact on the results.

In addition, our findings are supported by previous anatomic and biomechanical studies. It is known that the ATFL and CFL provide lateral anatomical stability for the ankle. With anterior drawer loading, sequentially sectioning the ATFL and CFL has been shown to result in increased anterior displacement (36). On the other hand, the CFL is a major contributor to subtalar joint stability. The main stabilizers of the subtalar joint include the CFL, interosseous talocalcaneal ligament, and cervical ligament (37, 38). The CFL is more important for resisting inversion of the subtalar joint than the interosseous talocalcaneal ligament (39). With inversion loading, the sectioning of the ATFL and CFL has been shown to increase rotation by 29% compared to an intact ankle, while isolated sectioning of the ATFL has been shown to increase rotation by only 2% (36). Thus, an injury to the CFL increases anterior displacement and inversion rotation of the subtalar joint, which may lead to elevated abutment and stress distribution on the medial and anterior cartilage facets

Table 5. The Correlations between T2 Values of Each Cartilage Subregion and AOFAS Scores in CLAI with ATFL Injury and CLAI with Combined CFL Injury

Cartilage Subregions	CLAI with ATFL Injury		CLAI with Combined CFL Injury	
	r	*P*	*r*	*P*
mSTJ-T	-0.183	0.371	-0.213	0.464
mSTJ-Cal	-0.124	0.547	-0.069	0.814
pSTJ-MAT	-0.043	0.835	-0.687	0.007*
pSTJ-MPT	-0.136	0.509	-0.609	0.021*
pSTJ-LAT	-0.203	0.320	-0.302	0.295
pSTJ-LPT	-0.069	0.736	-0.455	0.102
pSTJ-MAC	-0.114	0.578	-0.148	0.613
pSTJ-MPC	-0.018	0.932	-0.190	0.514
pSTJ-LAC	-0.067	0.743	-0.258	0.374
pSTJ-LPC	-0.111	0.689	-0.376	0.186
TNJ-T	-0.157	0.445	-0.070	0.812
TNJ-N	-0.008	0.968	-0.203	0.486
CCJ-Cal	-0.129	0.346	-0.079	0.789
CCJ-Cu	-0.035	0.865	-0.096	0.744

*The mean difference is significantly different at $p < 0.05$. AOFAS = American Orthopaedic Foot and Ankle Society

of the subtalar joint, which may then be transferred to the adjacent midtarsal joints. The subtalar and midtarsal joints are linked anatomically and functionally when a gait cycle is completed (11, 40). The calcaneocuboid joint had higher T2 values on the calcaneal site, which might suggest that the CCJ-Cal facet experiences more stress contact and is more likely to suffer from cartilage degeneration than other facets of the midtarsal joints in CLAI patients with combined CFL injuries (39). However, additional biomechanical studies are needed to investigate this mechanism.

The T2 values of the medial talar cartilage of the posterior subtalar joint in combined CFL injury patients were negatively correlated with their AOFAS scores. This finding suggested that the medial talar cartilage of the posterior subtalar joint is the main subregion that might affect the clinical symptoms and function of patients.

The findings in this study may have clinical implications for the management of CLAI patients with combined CFL injuries. Currently, most arthroscopic procedures are used to treat ATFL injuries only. These procedures may not be sufficient for patients with combined CFL injuries. Early ligament repair or anatomic reconstruction of the CFL is needed to restore the normal kinematics of the subtalar and midtarsal joints, which can be beneficial in preventing the cartilage in these joints from degenerating.

There are several limitations in the present study. First, the study included a relatively small cohort of patients. Second, we identified injuries to the subtalar and midtarsal joints based on clinical examinations and morphological MRI. They were not confirmed by arthroscopy. Arthroscopy, which is an invasive procedure, was not performed if surgery was not needed in these joints. Third, due to the magic angle effect, the T2 value will physiologically increase when the orientation of the collagen approaches 55^0 with the orientation of B_0 (41). This effect was addressed by positioning the hindfoot joints of all participants in the same orientation during MRI scan and subdividing the subtalar and midtarsal cartilage into different subregions to compare the same cartilage subregion among the groups. Finally, we did not follow up these patients over different time intervals. Additional studies with more patients and different follow-up times are needed.

In conclusion, T2 measurements of the articular cartilage can be accurately performed in the subtalar and midtarsal joints. CLAI with combined CFL injuries can lead to the occurrence of cartilage degeneration in most subtalar joints and CCJ-Cal, while isolated ATFL injuries may have no significant impact on cartilage in subtalar and midtarsal joints. The medial talar facets of the posterior subtalar joint are the main cartilage subregions that might contribute to the clinical symptoms and function of patients. MRI T2-mapping may serve as a quantitative tool to detect early biochemical alterations in the cartilage of subtalar and midtarsal joints before morphological deterioration occurs, which can aid treatment planning and cartilage condition monitoring in CLAI patients.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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