Lateral Meniscal Allograft Transplantation Shows a Long-Term Chondroprotective Effect on Quantitative Magnetic Resonance Imaging T2 Mapping at 7-Year Minimum Follow-Up

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Purpose: To assess the long-term chondroprotective effect of lateral meniscal allograft transplantation (MAT) using quantitative magnetic resonance imaging (MRI) T2 mapping. **Methods:** In patients who underwent isolated lateral MAT, quantitative MRI T2 mapping was conducted preoperatively and postoperatively with at minimum follow-up of 7 years to assess the articular cartilage status. On the sagittal section image bisecting the lateral femoral condyle, the weight-bearing portions of the femoral and tibial articular cartilage were divided into 3 segments each—6 segments in total—based on the meniscal coverage area. The regions-of-interest analyses were performed on the 6 segments to measure the mean T2 value. Then the whole layer was divided into deep and superficial layers for further zonal analysis. The longitudinal change in T2 values was statistically analyzed using paired *t*-tests. Clinical outcome was evaluated using the Lysholm score. **Results:** A total of 31 patients were included in the study, with the MRI follow-up period of a minimum of 7 years (mean: 8.9 ± 1.3 years; range: 7.0-11.2 years). The mean T2 value of the whole layer showed significant improvement in all segments of the femoral cartilage and the posterior segment of tibial cartilage. In the zonal analysis, the mean T2 value of the tibial cartilage showed significant improvement in the superficial layer of the mid to posterior portion, while the deep layer remained stable. In contrast, the mean T2 value of the femoral cartilage showed significant improvement in the superficial and deep layers in all segments. The mean Lysholm score significantly improved from 62.6 ± 12.8 to 90.9 ± 10.5 ($P < .001$). **Conclusions:** This study suggests that MAT appears to have a long-term chondroprotective effect on the articular cartilage as judged by quantitative T2 mapping. **Level of Evidence:** Level IV, case series.

See commentary on page 1575

Meniscal allograft transplantation (MAT) is an effective treatment option for meniscus-deficient patients who suffer persistent symptoms.[1,2] MAT was reported to have superior pain relief compared with conservative treatments.[3] Similarly, long-term pain relief following MAT was found in other studies.[4-7] In contrast to sufficient evidence regarding pain relief, previous studies lack research on the chondroprotective effect of MAT. In contrast to the sufficient evidence regarding pain relief, the small number of previous studies on the chondroprotective effect of MAT makes it difficult to draw a conclusion. This has led to contradictory clinical practice in that MAT is performed only after the appearance of symptoms caused by chondral wear, which may lead to an inferior prognosis.[8,9] Considering that meniscus deficiency leads to early-onset knee osteoarthritis (OA),[4,10-12] early intervention might be desirable to avoid degenerative

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change if there is evidence supporting the chondroprotective effect of MAT. Although previous studies reported that MAT might have a chondroprotective effect, most were performed on the basis of conventional methods, such as plain radiography, second-look arthroscopy, and conventional magnetic resonance imaging (MRI).[9,13,14] Adequate evaluation of the articular cartilage presents challenges when relying solely on conventional methods.

Quantitative MRI T2 mapping is a validated tool to detect cartilage tissue properties. The articular hyaline cartilage is composed of chondrocytes and a surrounding extracellular matrix, primarily water, making up between 65% and 80% of the total mass of the cartilage.[15] Since the T2 value (T2 relaxation time) reflects interactions between water protons and the macromolecules of the extracellular matrix, T2 mapping allows for the identification of slight changes in water content and variations in the structural integrity of collagen and proteoglycans.[16] A previous study utilizing T2 mapping discovered that the articular cartilage status, as determined by T2 values, improved following isolated MAT, with a mean follow-up of 3.2 years.[17] However, long-term change in the T2 value following MAT has not been reported.

The purpose of this study was to assess the long-term chondroprotective effect of lateral MAT using quantitative MRI T2 mapping. We hypothesized that the cartilage's T2 value would not worsen at the long-term follow-up.

Methods

This retrospective study received ethical approval from Asan Medical Center Institutional Review Board (receipt no. S2021-1648-0001). Patient credentials were anonymously collected and assessed by the first author (H.Y.L.).

Patients

Among patients who underwent lateral MAT between August 2010 and August 2015, 35 patients were assessed by quantitative MRI preoperatively and postoperatively at minimum follow-up of 7 years (Fig 1). Lateral MAT was indicated in patients who had persistent discomfort or pain in the lateral compartment due to meniscus deficiency, well-aligned mechanical axis within 5°, and no instability. Osteotomy or ligament reconstruction or repair was performed to address malalignment and uncorrected instability prior to or during MAT. Articular cartilage status same or lesser than International Cartilage Repair Society grade 2 was regarded as the ideal indication for MAT, whereas a localized cartilage lesion exceeding International Cartilage Repair Society grade 2 was considered permissible and taken into consideration for concomitant cartilage restoration procedures. In general, the cartilage repair procedures, such as microfracture and osteochondral autograft transfers, were preferred for high-grade cartilage lesions with size smaller than 4 cm^2, whereas no procedure was performed for lesions smaller than 0.1 cm^2.

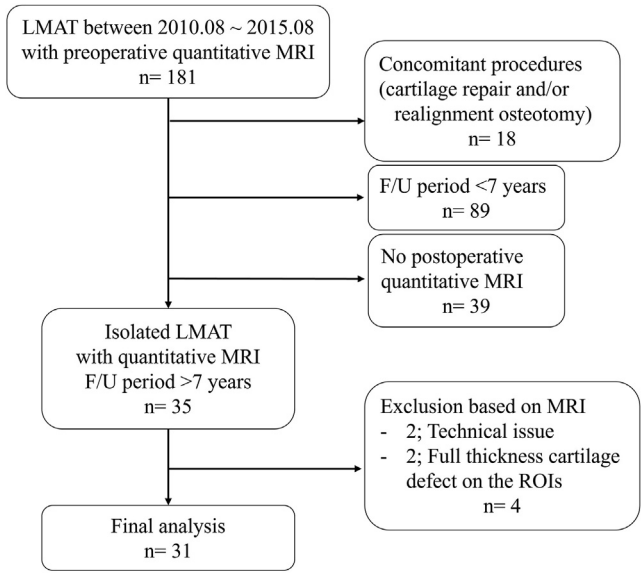

Fig 1. Flowchart of patient selection for this study. (F/U, follow-up; LMAT, lateral meniscal allograft transplantation; MRI, magnetic resonance imaging; ROI, region of interest.)

The inclusion criteria for this study were (1) patients who underwent isolated lateral MAT, (2) patients in whom both preoperative and postoperative quantitative MRIs were assessed, and (3) a minimum of 7-year follow-up. The exclusion criteria were (1) patients who underwent concomitant procedures, such as cartilage repair, ligament reconstruction, or realignment osteotomies (so that the chondroprotective effect of lateral MAT alone may be investigated), and (2) patients with uninterpretable MRIs due to technical issues (e.g., motion artifacts and corrupt spectroscopic data).[17-19] Two patients with full-thickness localized chondral defects in the ROI were excluded, and 2 other patients were excluded because of technical issues with the MRI. Thus, 31 patients who underwent lateral MAT were retrospectively reviewed.

Surgical Technique and Postoperative Management

The lateral MAT was performed by 2 surgeons (J-M.K. and S-I.B.) using the same keyhole technique and a size-matched fresh-frozen allograft. The procedure began with an arthroscopic examination to assess the condition of the meniscus, cartilage, and ligaments. The remaining meniscus was surgically removed, while preserving 2 mm of rim of meniscus at the periphery. Then a tunnel was created in the tibia, referring to the native meniscus position. A guide pin was inserted below the lateral tibial spine parallel to the

anteroposterior axis of the tibia, followed by drilling using a 10-mm keyhole drill. Then the meniscal allograft was anteriorly inserted into the knee through a small incision of ~4 cm. During the arthroscopic meniscal repair procedure, either the outside-in or inside-out techniques were employed after the allograft position was determined as optimal. Adequate tensioning was confirmed under arthroscopic inspection. Following the surgery, patients were instructed to immediately begin quadriceps sets and straight leg raises. Emphasis was placed on achieving full knee extension and a range of motion of 90° and 120° flexion within 4 and 6 to 8 weeks, respectively. The use of crutches and partial weight bearing on the affected foot was recommended in the immediate postoperative period. The weight-bearing amount was gradually increased over 2 weeks to achieve full weight bearing by 6 to 8 weeks. As a precautionary measure, patients were advised to limit their physical activity to light sports only, including cycling and swimming. Strenuous exercise and heavy labor were not recommended for all patients without time limits to avoid potential complications related to the healing of the transplanted meniscus. For postoperative surveillance, patients were advised to undergo MRI at 3 months after achieving full weight bearing and range of motion, 1 year postoperatively for short-term follow-up, and at intervals of 2 to 3 years for regular follow-up thereafter.

Quantitative Sequencing Protocol

In the medical center of the current study, quantitative sequence has been additionally performed after 30 minutes of conventional MRI. Patients underwent scanning in a supine position using an Achieva or Ingenia 3.0-T MR scanner (manufactured by Philips Medical Systems in Best, The Netherlands) and a dedicated 16-channel knee coil. The scan acquired a sagittal, multiecho spin echo, T2-weighted sequence for quantitative T2 mapping analysis with the following parameters: 6 echo times at 13, 26, 39, 52, 65, and 78 ms; repetition time of 3,500 ms; slice thickness of 3 mm; field of view of 160 × 160 mm; pixel matrix of 304 × 304; and total acquisition time of 7.93 min. The T2 values (measured in milliseconds) were obtained from T2 maps reconstructed using a multiecho measurement. Then T2 mapping images were generated using an advanced cartilage assessment application (IntelliSpace Portal, developed by Philips Healthcare, Amsterdam, The Netherlands). The program used a least-squares regression method weighted by the variance of the signal intensity estimates. The color T2 maps of the articular cartilage were generated from the T2 mapping source data, with a color scale ranging from 1 to 81 ms.

Cartilage segmentation for T2 mapping assessment

Regions-of-interest (ROI) analysis was conducted at the center of the lateral femoral condyle, according to a previously described method.[9,17,20] On the sagittal section image, the weight-bearing area of each femoral and tibial articular cartilage was divided into 3 portions: the anterior and posterior meniscal coverage areas and the central weight-bearing portion. The segments of the femoral articular cartilage covered by the anterior and posterior horn of the lateral meniscus were designated as F1 and F3, respectively. The cartilage between these 2 segments was referred to as the F2 segment. Therefore, the F1, F2, and F3 segments were arranged on the femoral cartilage in the anterior-to-posterior direction. Similarly, the articular cartilage on the tibia plateau was divided into 3 portions defined as the TP1, TP2, and TP3 segments in the anterior-to-posterior direction. ROI curves were drawn for each of the 6 segments. The software automatically calculated the mean T2 value of the ROI. In addition, the ROIs were automatically divided into 2 layers of equal thickness: the deep and superficial layers. A zonal assessment was performed to evaluate the variation of the T2 value across different zones, in accordance with previous studies.[19,21,22] (Fig 2) The intraclass correlation coefficient was assessed to evaluate the validity of the measurement method. One month after the initial assessment, the first author (H.Y.L.) randomly selected 5 patients for assessing intraobserver reliability, and a distinct set of 5 patients was chosen for evaluating interobserver agreement by 2 other authors (S-M.K. and S-J.L.). The intraobserver reliability and interobserver agreement were both high, with values of 0.962 (95% confidence interval [CI], 0.943-0.975; $P < .001$) and 0.911 (95% CI, 0.865-0.941; $P < .001$), respectively, indicating excellent reliability for T2 value measurements.[23]

Clinical Outcome

Clinical outcomes were assessed using the Lysholm knee scores, which were evaluated both preoperatively and during the final follow-up visit.

Data Analysis

T2 values for 18 ROIs, divided into whole, superficial, and deep layers for the 6 segments, were evaluated using paired Student's *t*-test to determine the difference between preoperative and last follow-up values. Lysholm score was also evaluated using paired Student's *t*-test. A *P* value of less than .05 was considered statistically significant. The statistical analysis for this study was conducted using IBM SPSS 25.0 software.

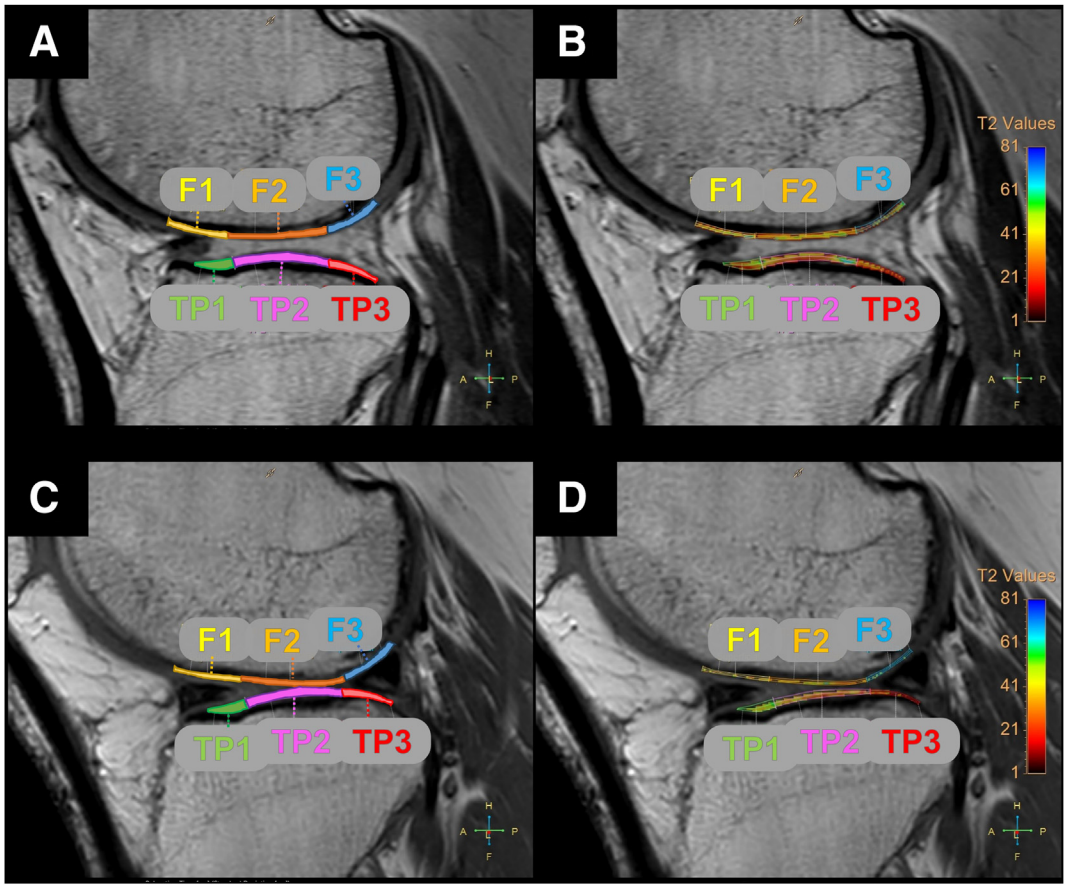

Fig 2. Color-scaled T2 mapping of a 34-year-old woman who underwent lateral meniscal allograft transplantation on her left knee. (A) On the preoperative magnetic resonance image, region-of-interest segmentation was performed according to the meniscal coverage area. From the anterior-to-posterior direction, the femoral articular cartilage was segmented as F1, F2, and F3; likewise, the tibial plateau articular cartilage was segmented as TP1, TP2, and TP3. (B) The color T2 maps of the articular cartilage were generated from the T2 mapping source data, with a color scale ranging from 1 to 81 ms. (C) Postoperative image after 10 years of lateral meniscal allograft transplantation. Region-of-interest segmentation was performed. (D) The cartilage T2 value shows significant improvement at postoperative 10 years.

Results

A total of 31 patients were included in the study, with the MRI follow-up period of a minimum of 7 years (mean: 8.9 ± 1.3 years; range: 7.0-11.2 years). None of the included patients were professional athletes. A summary of patient characteristics can be found in Table 1.

Table 2 shows the longitudinal change in the mean T2 value of the femoral articular cartilage. For the whole layer, the mean T2 value showed statistically significant improvement in F1 segment from 46.0 ± 9.1 to 40.2 ± 7.0 ($P < .001$), F2 segment from 52.1 ± 12.4 to 40.5 ± 7.4 ($P < .001$), and F3 segment from 52.3 ± 12.6 to 43.5 ± 6.3 ($P < .001$). When further dividing the ROIs into deep and superficial layers for zonal assessment, the mean T2 value of the deep layer exhibited statistically significant improvement in F1 segment from 43.7 ± 9.7 to 38.0 ± 7.2 ($P < .001$), F2 segment from 48.6 ± 12.6 to 38.6 ± 7.7 ($P < .001$), and F3 segment from 49.3 ± 13.0 to 42.4 ± 6.4 ($P = .005$). Similarly, the superficial layer demonstrated significant improvement in F1 segment from 48.5 ± 8.4 to 43.0 ± 7.0 ($P = .002$), F2 segment from 55.3 ± 11.9 to 43.0 ± 7.3 ($P < .001$), and F3 segment from 55.0 ± 11.8 to 44.5 ± 6.5 ($P < .001$), respectively. Table 3 displays the longitudinal change in the mean T2 value of the tibial plateau articular cartilage. For the whole layer, the mean T2 value showed statistically significant improvement only in TP3 segment from 36.9 ± 7.7 to 32.9 ± 5.3 ($P = .006$). When further dividing the ROIs into deep and superficial layers, the mean T2 value of superficial layer exhibited statistically significant improvement in TP2 segment from 35.6 ± 9.9 to 32.5 ± 5.2 ($P = .046$) and TP3 segment from 41.2 ± 9.4 to 35.6 ± 5.8 ($P = .001$), whereas the deep layers of TP3 segments did not show significant change. The mean Lysholm score showed significant improvement from 62.6 ± 12.8 to 90.9 ± 10.5 ($P < .001$).

Table 1. Patients' Characteristics*

Lateral Meniscal Allograft Transplantation (n = 31)	
Age, year	30.2 ± 10.8 (15-51)
Sex, male/female, n	18/13
Side, right/left, n	16/15
Body mass index	23.0 ± 2.6
Mechanical axis (varus), °	2.1 ± 3.0°
Time from meniscectomy, year	5.7 ± 6.9
MRI follow-up period, year	8.9 ± 1.3 (7.0-11.2)
Preoperative ICRS grade assessed by arthroscopy	
LFC: 0, I, II, II + III (focal), II + IV (focal), n	2, 7, 16, 2, 4
LTP: 0, I, II, II + III (focal), II + IV (focal), n	0, 3, 18, 8, 2

ICRS, International Cartilage Repair Society; LFC, lateral femoral condyle; LTP, lateral tibial plateau; MRI, magnetic resonance imaging.
*Data are shown as mean ± standard deviation (range) unless otherwise indicated. ICRS grade was recorded based on the most severe lesion regardless of size.

Discussion

The most important finding of this study is that the cartilage property judged by quantitative MRI T2 mapping showed an improvement at a minimal follow-up of 7 years. This result suggests that MAT may have a long-term chondroprotective effect on the articular cartilage.

Quantitative MRI T2 mapping is increasingly applied in orthopedic surgery and related research to assess the cartilage status because T2 relaxation time (T2 value) reflects the biochemical composition of the tissue.[24-26] Moreover, Casula et al. reported that the severity of cartilage degeneration might not be revealed solely by diagnostic arthroscopy; thus, quantitative MRI can have a role in the investigation of cartilage degeneration, enabling the assessment of the whole-thickness articular cartilage tissue.[21] Previous studies have consistently shown that MAT has good-to-excellent patient-reported outcomes,[5,27,28] but the chondroprotective effect of MAT was uncertain through limited investigation using conventional methods.

Table 2. Change in T2 Values of the Femoral Cartilage After Lateral MAT†

Segments	Layer	Preoperative	Postoperative	*P* Value‡
F1	Whole	46.0 ± 9.1	40.2 ± 7.0	<.001*
	Deep	43.7 ± 9.7	38.0 ± 7.2	<.001*
	Superficial	48.5 ± 8.4	43.0 ± 7.0	.002*
F2	Whole	52.1 ± 12.4	40.5 ± 7.4	<.001*
	Deep	48.6 ± 12.6	38.6 ± 7.7	<.001*
	Superficial	55.3 ± 11.9	43.0 ± 7.3	<.001*
F3	Whole	52.3 ± 12.6	43.5 ± 6.3	<.001*
	Deep	49.3 ± 13.0	42.4 ± 6.4	.005*
	Superficial	55.0 ± 11.8	44.5 ± 6.5	<.001*

F, Femur; MAT, meniscal allograft transplantation; TP, Tibia plateau.
†Lower T2 value indicates better cartilage bio-composition quality. Data are shown as mean ± standard deviation.
‡Paired Student's *t*-test.*P* < .05.
*Statistically significant difference.

Table 3. Change in T2 Values of the Tibial Plateau Cartilage After Lateral MAT†

Segment	Layer	Preoperative	Postoperative	*P* Value‡
TP1	Whole	33.7 ± 11.3	31.4 ± 6.7	.205
	Deep	29.2 ± 10.8	26.9 ± 7.0	.187
	Superficial	38.4 ± 11.5	36.1 ± 7.0	.204
TP2	Whole	30.9 ± 9.7	29.1 ± 4.5	.190
	Deep	26.3 ± 9.7	25.6 ± 4.4	.607
	Superficial	35.6 ± 9.9	32.5 ± 5.2	.046*
TP3	Whole	36.9 ± 7.7	32.9 ± 5.3	.006*
	Deep	32.9 ± 7.7	30.3 ± 5.4	.086
	Superficial	41.2 ± 9.4	35.6 ± 5.8	.001*

F, femur; MAT, meniscal allograft transplantation; TP, tibia plateau.
†Lower T2 value indicates better cartilage biocomposition quality. Data are shown as mean ± standard deviation.
‡Paired Student's *t*-test.
*Statistically significant difference, *P* < .05.

Surgeons have been seeking the chondroprotective effect of MAT beyond symptom relief, but it has not been fully understood.[29,30] In this context, T2 mapping could be a useful tool to investigate the cartilage tissue property following MAT.

Recent literature has reported that MAT may have a chondroprotective effect using T2 mapping. Lee et al.[17] conducted preoperative and postoperative T2 mapping to investigate the longitudinal change in T2 value at mean follow-up of 3.2 years. They found that cartilage T2 values improved or remained stable after MAT at the midterm follow-up period without performing cartilage treatment procedures. This study suggests that the transplanted meniscus has a chondroprotective effect. However, the data in this study are not long term and the study does not have any group comparison. Wang et al.[14] found that patients who underwent MAT had moderate advantages over those who underwent meniscectomy in terms of long-term chondroprotection using preoperative and postoperative analysis of arthroscopy findings. They also used a T2 mapping study at the final follow-up and found that the T2 value dispersion of the MAT group was comparable to that of the healthy control group, and the meniscectomized group had increased T2 values, suggesting early OA status. However, these results should be interpreted with caution as the normative T2 values for healthy individuals vary widely and are influenced by temporary loading conditions.[15,31,32] Moreover, this study included a relatively small number of 21 cases that were divided into 7 medial and 14 lateral MATs. Compared with previous studies, the present study demonstrates longitudinal changes in the cartilage T2 values for 31 patients with lateral MAT. The study's results indicate that cartilage T2 values improved or remained stable after MAT at minimum follow-up of 7 years in weight-bearing portions of the cartilage.

Another significant finding in this study is that cartilage T2 values of the articular cartilage improved in

all portions of femoral cartilage but only improved in the superficial layer of the mid- to posterior portion of tibial cartilage. Some previous literature has reported findings similar to this result. A study by Lee et al.[17] reported that the cartilage T2 value of the weight-bearing portion of the articular cartilage improved mainly in the mid- to posterior femoral cartilage and posterior tibial cartilage after MAT, with a mean follow-up of 3.2 years. Since the present study is also conducted in the same institute, it includes an overlap of 21 patients between the 2 studies. On the other hand, some studies have shown that the posterior part of the tibia articular cartilage is particularly susceptible to damage, with cartilage degeneration observed in patients who underwent meniscal surgery[33] and in competitive athletes.[19] Verschueren et al. reported an increase in T2 relaxation time in the weight-bearing lateral tibial plateau following 10 minutes of cycling in healthy adults.[34] Thus, it could be assumed that the repetitive mechanical load affects the flexion weight-bearing area of knee cartilage that is vulnerable when the meniscus is damaged, and the transplanted meniscus would provide chondroprotection in the weight-bearing portion of the articular cartilage, particularly in the flexion weight-bearing area.

This study has strength in that it conducted investigation with T2 value, a well-established indicator that quantifies the quality of articular cartilage with objective data. If the T2 values remain consistent over time without deterioration, it can be inferred that MAT offers a chondroprotective effect in postmeniscectomized knees. Besides, this study result suggests that MAT might partially reverse cartilage damage to some degree depending on the portion of the articular cartilage, as evidenced by improved cartilage T2 values. Conducting future studies to compare the longitudinal changes in cartilage between knees treated with MAT and those that are meniscus deficient would provide more information to daily clinical practice.

Limitations

The present study had some limitations. First, this study included a relatively small number of participants, which hindered subgroup analyses. Despite graft extrusion consistently being reported as a factor contributing to the deterioration of surgical outcomes, assessing its impact could not be performed since only 7 patients showed graft extrusion of more than 3 mm in this study.[10,22] Second, this was a retrospective case series, which could potentially introduce selection bias. Third, only the Lysholm score was assessed both preoperatively and postoperatively as a patient-reported outcome measure. Fourth, this study excluded patients who underwent concomitant procedures to prevent an overestimation of the chondroprotective effect of lateral MAT; however, this approach could potentially introduce selection bias. Finally, a number of patients were excluded due to technical limitations. T2 mapping of articular cartilage can only be conducted when the cartilage thickness is adequate; therefore, 2 patients with focal full-thickness chondral defects precisely within the location corresponding to the ROI were excluded. These limitations might have introduced selection bias.

Conclusions

This study suggests that MAT appears to have a long-term chondroprotective effect on the articular cartilage as judged by quantitative T2 mapping.

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