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Relationship of alignment in the lower extremity with early degeneration of articular cartilage after resection of the medial meniscus

Quantitative analysis using T_2 mapping

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Abstract

The objective of this study was to examine the relationship between cartilage degeneration early after partial medial meniscectomy and abnormal alignment in the lower extremity.

The subjects were 34 patients (37 knees) with medial meniscal tear who underwent arthroscopic partial meniscectomy. MRI was performed before and 6 months after surgery. T_2 mapping images in sagittal sections of medial femoral condyle were produced and 10 regions of interest were set at intervals of 10° in the articular cartilage in the femur. Subjects with an increase in T_2 of ≥6% at a flexion angle of 30° were assigned to the degeneration group. Patient background, hip-knee-ankle (HKA) angle, and total resection of meniscal segments were compared between this group and the other patients to identify factors involved in degeneration of articular cartilage.

T_2 values 6 months after surgery in 3 ROIs at flexion angles of 30° to 50° were significantly longer than those before surgery. The preoperative HKA angle was significantly higher in the degeneration group. T_2 values in articular cartilage of the femoral condyle increased earlier after meniscectomy with abnormal alignment in the lower extremity.

Meniscectomy in cases with abnormal alignment may have a risk of early onset of osteoarthritis.

Level of evidence: Level IV

Abbreviations: AUC = area under the curve, BMI = body mass index, HKA = hip-knee-ankle, ICC = interclass correlation coefficient, ICRS = International Cartilage Repair Society, KL = Kellgren and Lawrence, MRI = magnetic resonance imaging, OA = osteoarthritis, ROC = receiver operating characteristic, ROI = region of interest.

Keywords: arthroscopic meniscectomy, articular cartilage, cartilage evaluation, T_2 mapping, varus alignment

1. Introduction

The medial meniscus distributes the load on the knee joint and absorbs shock, indicating that the medial meniscus is involved in stability of the knee joint.[1] Therefore, total meniscectomy frequently induces long-term osteoarthritis (OA).[2] Advanced arthroscopic surgery enables a minimal resection range for a damaged meniscus, leading to good postoperative outcomes. However, partial meniscectomy also weakens the mechanism for shock absorption, resulting in OA in the long term. Therefore, it is necessary to identify factors that influence the articular cartilage early after partial meniscectomy to prevent OA.[3]

Alignment of the knee joint is also an important determinant of load distribution. In normal alignment, 60% to 80% of the load is distributed on the medial compartment and homeostasis is maintained; however, abnormal alignment such as varus knee joint induces onset and progression of OA.[4] Consequently, we proposed the hypothesis that early degeneration of articular cartilage occurs after partial meniscectomy of a knee joint with abnormal alignment.

Minimally invasive qualitative assessment of articular cartilage can be performed using 3T magnetic resonance imaging (MRI). In particular, T_2 mapping is a quantitative MRI method for analysis of collagen alignment and water content in articular cartilage.[5] In this study, we evaluated changes in articular cartilage from before to 6 months after partial meniscectomy

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All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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using T_2 mapping to examine the effect of preoperative abnormal alignment in the lower extremity on the articular cartilage.

2. Materials and methods

This study was approved by our Institutional Review Board of Kyoto Prefectural University of Medicine (ERB-C210-2). Informed written consent was obtained from all participants in the study.

2.1. Subjects

The subjects in this retrospective study were 34 patients (37 knees) with medial meniscal tear in white zones who underwent arthroscopic partial meniscectomy from November 2010 to September 2016 in the Orthopedics Department of Kyoto Prefectural University of Medicine. Diagnosis was made with clinical examination, MRI, and confirmed with arthroscopy. The indication for arthroscopic partial meniscectomy was the presence of symptomatic medial meniscal injury. The exclusion criteria included repair of meniscus, ligament injury, medial femorotibial joints of International Cartilage Repair Society (ICRS) grades III and IV, and patients who could not undergo MRI before and 6 months after surgery. The patients included 26 males (29 knees) and 8 females (8 knees). Partial meniscectomy was performed by two experienced orthopedic specialists under the supervision of a sport orthopedic director. The results of a McMurray test were positive in all subjects before surgery, but negative 6 months after surgery. Pain and reduced mobility disappeared after surgery. During this period, 3 knees with changing of surgical procedure and 12 knees unable to perform MRI were excluded.

2.2. Clinical outcomes and radiological evaluations

Patients were evaluated clinically by determining their American Knee Society Scores before partial meniscectomy and at 6 months after surgery. The hip-knee-ankle (HKA) angle was measured by long-leg full-weight-bearing radiograph to assess the severity of varus deformity. HKA angle of varus knee was defined as negative. Radiographic evaluations were measured twice by the same observer at different times to determine intraobserver reliability, and blindly and independently by two different observers (HI and SN) to determine interobserver reliability.

2.3. T_2 mapping

MRI was performed before and 6 months after arthroscopic partial meniscectomy using an Achieva 3T X-series (Philips Medical Systems, Best, Netherlands) with an 8-channel knee coil. The imaging conditions were designed for T_2 measurement (TSE multi TE, TR: 2000 ms, TE: 15/30/45/60/75/90 (ms), FOV: 160×160 (mm), slice thickness: 2.5 mm, matrix: 384×313).[6] All T_2 mapping images were calculated and generated from multiple TE images using Philips MR console software. T_2 mapping images in sagittal sections of medial femoral condyle were produced and 10 regions of interest (ROI) were set at intervals of 10° from the crossing site of the femoral axis and the articular surface of the femoral condyle to the posterior site bending to the bone axis by approximately 90° (Fig. 1). The depth of the ROI was from the superficial to middle layers of articular cartilage. T_2 changes from before to after surgery were evaluated,

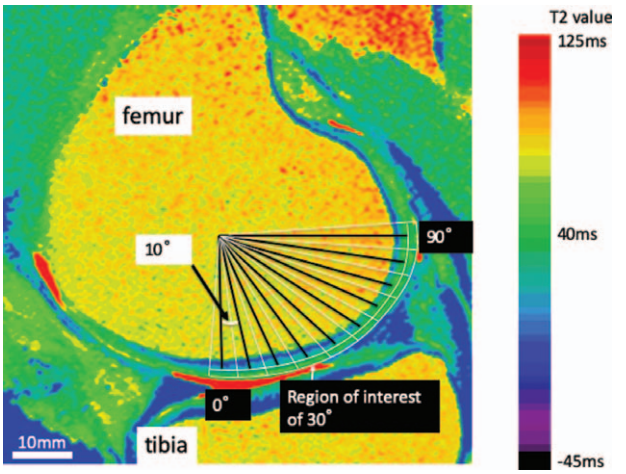

Figure 1. Quantitative assessment of articular cartilage by T_2 mapping. Ten regions of interest (ROIs) were established on the surface of the femoral load from 0° to 90°. The depth of each ROI was from the cortical to middle layers of articular cartilage.

with quantification of T_2 values using OsiriX imaging software (OsiriX Foundation, Switzerland). Two orthopedic specialists belonging to the Japanese Orthopaedic Association determined the ROIs and estimated the mean T_2 value.

2.4. Comparison of survey items in the increase and no increase groups of T_2 value

Subjects with increases in T_2 of ≥6% and <6% at a flexion angle of 30° were defined as the degeneration and non-degeneration groups, respectively.[7] Age, sex, BMI, HKA angle, Tegner activity scale, preoperative knee score, and total resection of meniscal segments were compared between the two groups to identify factors involved in degeneration of articular cartilage. The area of resected meniscus was classified as one-third, two-thirds and total resection according to Hulet et al,[8] and total resection of the anterior, middle or posterior segment was defined as total meniscectomy.

2.5. Statistical analysis

All analyses were performed using EZR (Saitama Medical Center, Jichi Medical University), which is a graphical user interface for R (The R Foundation for Statistical Computing, version 2.13.0).[9] Values of $P < .05$ were considered to be significant. T_2 values before and after surgery were compared by paired t test. Comparison of risk factors between the degeneration and no degeneration groups was performed by Student's *t* test or Fisher Exact test. Single and multivariable regression analyses were used to assess the relationship of increased T_2 values in MRI with risk factors including age, sex, BMI, HKA angle, preoperative Kellgren and Lawrence (KL) grade, total resection of meniscus, and ICRS grade. Receiver operating characteristic (ROC) curves were analyzed to determine HKA angle cut-off values and calculate sensitivity, specificity, and area under the curve (AUC). For comparison of HKA angle between the degeneration group and no degeneration group, a total of 58 patients were required to show a significant difference at an α level of 0.05 and a β level of 80%. Interclass correlation

Table 1

Pre- and intraoperative patient characteristics.

Characteristic	Patients (n = 37)
Demographic data	
Gender (male/female)	29/8
Age at surgery, mean ± SD (yr)	56.7 ± 11.3
Right knee involved, no (%)	21 (56.8)
Height (cm)	168.4 ± 9.1
Weight (kg)	68.3 ± 10.7
Body mass index (kg/m2)	24.1 ± 3.3
Preoperative Tegner activity scale	3.5 ± 1.6
History of trauma, no (%)	5 (13.6)
History of smoking, no (%)	6 (16.2)
Preoperative Knee Score	68.9 ± 7.8
Hip-knee-ankle angle (°)	-2.4 ± 2.6
Duration of surgery (min)	35.6 ± 15.8
Type of meniscal tear, no (%)	
Vertical	8 (21.6)
Horizontal	27 (73.0)
Degenerative/complex7(18.9)	
Radial	8 (21.6)
Postoperative Knee Score	97.6 ± 3.9

coefficients (ICCs) were calculated with a two-way random model

3. Results

The mean age was 56.7 ± 11.3 years old and the mean body mass index (BMI) was 24.1 ± 3.3 kg/m^2. Patient background and preoperative ICRS grades are shown in Tables 1 and 2.

T_2 values before and 6 months after medial meniscectomy increased as the flexion angle to the femoral axis increased from 0° to 70°, resulting in the longest T_2 at a flexion angle of 70° (Fig. 2). T_2 values then decreased as the flexion angle increased from 70° to 90°. In comparison of T_2 values before and after surgery, T_2 values 6 months after surgery in 3 ROIs at flexion angles of 30° to 50° were significantly longer than those before surgery.

T_2 values increased ≥6% in 15 knees (degeneration group), and <6% in 22 knees (no degeneration group) at a flexion angle of 30°. There was no significant difference in age, sex, BMI, preoperative knee score, KL grade, or total resection of meniscus between the degeneration and no degeneration groups (Table 3). The HKA angle was significantly lower in the degeneration group. Simple regression analysis showed that age, BMI and HKA angle were related to cartilage degeneration (Table 4). In multiple regression analysis using these three factors, the HKA angle was the only independent risk factor for cartilage degeneration (Table 5).

Table 2

Joint cartilage changes noted at surgery (number of patients).

Knee compartment /Grading of cartilage damage according to ICRS classification	0	1	2	3	4
Lateral compartment	26	8	3	0	0
Medial compartment	13	20	4	0	0
Patellofemoral compartment	28	4	5	0	0

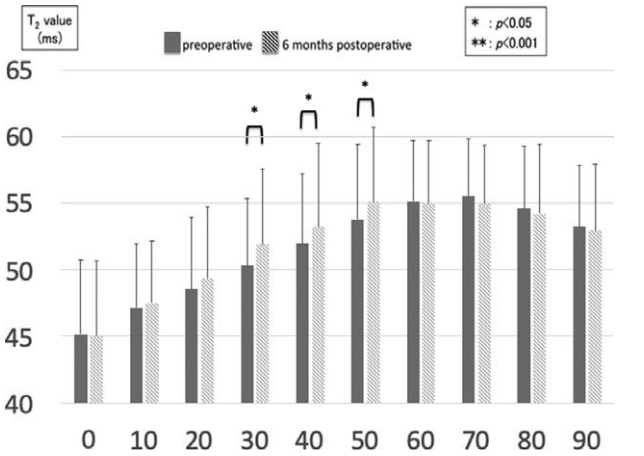

Figure 2. T_2 values before and 6 months after medial meniscectomy increased with an increased flexion angle to the femoral axis from 0° to 70°, with the longest T_2 at a flexion angle of 70°. T_2 values then decreased as the flexion angle increased from 70° to 90°.

ROC curves for the HKA angle as a predictor of cartilage degeneration were constructed to show the relationship between true positives and false positives. A cut-off value of −3° for the HKA angle had an AUC of 0.63 (95% CI 0.46-0.81) and sensitivity of 67% and specificity of 68% for prediction of cartilage degeneration (Fig. 3). Fisher's Exact test demonstrated a statistically significant association between the T_2 value elevation and HKA ≥−3° ($P = .04$) (Table 6).

4. Discussion

The most important finding of the present study was that T_2 values in the femoral condyle increase early after meniscectomy, and that varus knee of HKA angle −3° or less may be a risk factor for knee early OA.

The medial meniscus is involved in load distribution, shock absorption, and stability of the knee joint. However, after meniscectomy, clinical symptoms occur in about 44% of cases in

Table 3

Comparison of patients with and without cartilage degeneration.

	No degeneration group (n = 22)	Degeneration group (n = 15)	*P* value
Age (yr)	59.6 ± 8.8	52.5 ± 13.4	.08
Gender (male/female)	18/4	11/4	.56
BMI (kg/m^2)	24.7 ± 2.7	23.1 ± 2.1	.08
Preoperative HKA (°)	-1.5 ± 2.3	-3.2 ± 2.1	.03*
Preoperative Tegner score	4.2 ± 2.0	3.2 ± 2.2	.59
Preoperative Knee score	69.5 ± 8.8	67.9 ± 6.4	.56
Preoperative KL grade (0/1/2/3)	12/7/2/1	10/4/1/0	.43
Variation of tear (n)			
Vertical	2	6	
Horizontal	17	10	
Degenerative/complex	6	1	
Radial	2	6	
Total resection of any segment (yes/no)	4/18	5/10	.31

* $P < .05$.

Table 4

Single linear regression analysis of factors influencing post-operative T2 value elevation.

	Odds ratio	95% CI	*P* value
Age	0.988	0.973–1.002	.08
Gender	1.128	0.751–1.695	.55
BMI	0.943	0.884–1.006	.07
HKA	1.100	1.006–1.153	.03*
ICRS	0.913	0.701–1.189	.49
KL grade	0.905	0.727–1.128	0.37
Knee Score	0.994	0.972–1.015	.56
Tegner activity scale	1.008	0.904–1.123	.88
Total resection of meniscus	1.219	0.828–1.795	.31

* $P < .05$.

the long term and simple X-ray images show arthropathy-related changes in about 66%.[10] This may be because medial meniscectomy decreases the contact area in the femoral condyle by 50% to 70% and increases the contact pressure by 100%.[11,12] Our results showed that T_2 values of articular cartilage at flexion angles of 30° to 50° to the femoral axis were significantly longer and that the change in T_2 at a flexion angle of 30° was the highest. Consequently, stress on the articular cartilage was increased at flexion angles of 30° to 50° to the femoral axis. Rosenberg et al proposed that abrasion of the articular cartilage in the femur of patients with knee OA occurred at flexion angles of 30° to 60°.[13] Our results confirm that even after partial medial meniscectomy, degeneration of articular cartilage begins in the same region as early knee OA.

An epidemiological study of healthy knees showed that alignment in the lower extremity was related to onset and progression of OA.[14] Sharma et al showed that medial OA in genu varum and genu valgum was approximately 4-fold and 5-fold higher, respectively, than in normal knee alignment.[15] Therefore, abnormal alignment in the lower extremity is a clear risk factor for cartilage degeneration. Meniscectomy in patients with abnormal alignment may promote cartilage generation, but there is no consensus among previous studies. Burks et al showed progression of OA in simple X-ray images in 15-year follow-up after medial meniscectomy in genu varum,[16] but Kruger-Franke et al found no correlation between abnormal alignment in the lower extremity and OA in simple X-ray images in 7-year follow-up after medial and lateral meniscectomy.[17] This difference may be due to qualitative changes in the articular cartilage itself that cannot be detected in simple X-ray images.

T_2 mapping has been used for sensitive detection of change in articular cartilage. Souza reported no overall difference in T_2 relaxation times across all cartilage surfaces when comparing baseline data to 6-month follow-up data, but weight-bearing areas of the medial tibial condyle showed significant increase at 6-month follow-up.[18] In this study, 10 ROIs were set at the

Table 5

Multivariable regression analysis of factors influencing post-operative T2 value elevation.

	Odds ratio	95% CI	*P* value
Age	0.987	0.974–1.001	.05
BMI	0.945	0.891–1.002	.06
HKA	1.088	1.022–1.159	.01*

* $P < .05$.

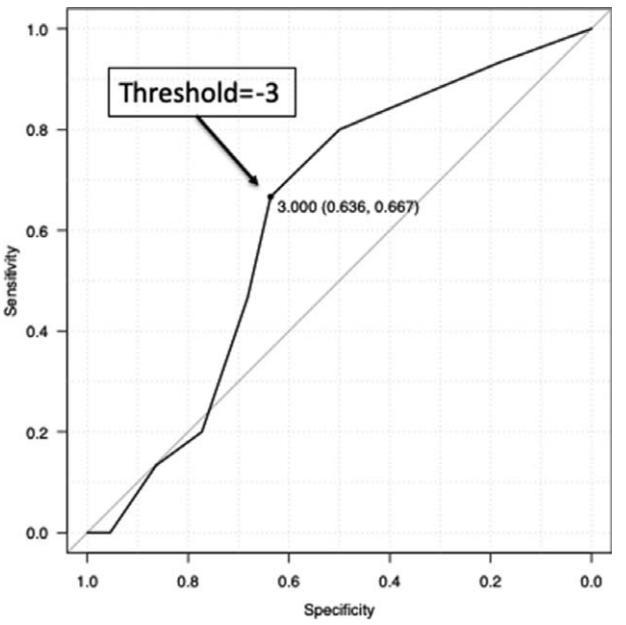

Figure 3. Receiver operating characteristic (ROC) curve for the hip-knee-ankle (HKA) angle. The cut-off value was 3°.

medial femoral condyle, T_2 values in only 3 ROIs at flexion angles of 30° to 50° were significantly increased 6 months after surgery. We found no significant difference in disease site, preoperative KL grade or ICRS grade between patients with and without degeneration of articular cartilage. However, patients with preoperative abnormal alignment in the lower extremity had early degeneration of articular cartilage in the femur, regardless of the site of the resected meniscus or OA changes in simple X-ray images. This is the first study to show the relationship between cartilage degeneration early after medial meniscectomy and abnormal alignment in the lower extremity using T_2 mapping. The results may indicate the need to pay attention to early degeneration of articular cartilage after medial meniscectomy in patients with genu varum $\leqq -3°$. In some cases, around the knee osteotomy such as high tibial osteotomy, should be considered for medial meniscus injuries with varus knee.

The present study had several limitations, including the small number of patients and its retrospective nature. First, the small

Table 6

Comparison between postoperative T_2 value elevation and HKA.

		Degeneration Group	No Degeneration Group
HKA angle	$\leqq$- 3°	10	7
	>-3 °	5	15
			P=.048
Sensitivity		0.67	
Specificity		0.68	
Positive predictive value		0.59	
Negative predictive value		0.75	
Positive likelihood ratio		2.1	
Negative likelihood ratio		0.49	
Area under the ROC curve		0.63	
Diagnostic odds		4.2	
Youden index		0.35	

sample size might have been responsible for the fact that there was a significant difference only in the HKA angle but not in the age or BMI. We would perform the same protocol with a larger number of patients to make the study powerful enough to allow therapeutic recommendation. Second, since T_2 mapping presents the collagen sequence and water content, we were unable to evaluate proteoglycans. Future analyses using T1ρ mapping or T2* values may be useful. Third, it is important to clarify the effect of elevated T2 on risk of osteoarthritis over the long term. Patients with elevated T_2 values should be carefully followed by radiographic imaging, including simple X-rays. In a future study, we will examine whether prophylactic alignment correction is necessary for meniscus injuries associated with varus knee.

5. Conclusions

Degeneration of articular cartilage begins at flexion angles of 30° to 50° to the femoral axis after partial medial meniscectomy. Meniscectomy for patients with genu varum $\leqq -3°$ may be a risk factor for early OA.

Author contributions

Conceptualization: Yuta Fujii.
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Formal analysis: Kenta Kaihara.
Methodology: Yuji Arai.
Supervision: Yasuo Mikami.
Writing – original draft: Shuji Nakagawa.

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