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Degeneration of patellar cartilage in patients with recurrent patellar dislocation following conservative treatment: evaluation with delayed gadolinium-enhanced magnetic resonance imaging of cartilage

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Summary

Objective: To examine the characteristics of cartilage degeneration in patients with recurrent patellar dislocation (RPD) following conservative treatment using delayed gadolinium-enhanced magnetic resonance imaging (MRI) of cartilage (dGEMRIC).

Design: This study evaluated three groups of knees: group I, 35 knees from both knees of patients with bilateral RPD and dislocated side knees of patients with unilateral RPD; group II, 15 non-dislocated side knees of patients with unilateral RPD; and group III, 20 knees from both knees of healthy volunteers. Differences in post-contrast T1 [T1(Gd)] of cartilage at both medial and lateral facets between groups I, II and III were analyzed. For group I, possible relationships were evaluated between T1(Gd) of cartilage and patient age, length of time between the initial dislocation and MRI and the total number of dislocations between the initial dislocation and MRI for both medial and lateral facets.

Results: The mean T1(Gd) of cartilage at medial facets for groups I, II and III were 411 ± 46 ms, 465 ± 38 ms and 490 ± 29 ms, respectively; there were significant differences between these means ($P < 0.05$). The mean T1(Gd) of cartilage at lateral facets for groups I, II and III were 426 ± 53 ms, 466 ± 45 ms and 510 ± 36 ms, respectively; there were also significant differences between these means ($P < 0.05$). Significant correlations were observed between T1(Gd) of cartilage for both medial and lateral facets and length of time between the initial dislocation and MRI ($P < 0.05$). No other correlations were significant.

Conclusion: dGEMRIC may be a useful method to monitor glycosaminoglycan concentration in patients with RPD following conservative treatment.

Key words: Magnetic resonance imaging, Glycosaminoglycan, Recurrent patellar dislocation, Cartilage degeneration.

Introduction

Degeneration of the patellar cartilage is often observed in patients with recurrent patellar dislocation (RPD)[1–3]. Several causes of cartilage degeneration related to RPD have been suggested, such as repeated shearing stress at the time of dislocation and relocation and increased mechanical stress caused by an anatomical abnormality or malalignment of the patellofemoral joint[4–6]. Until now, observation of patellar cartilage in patients with RPD was performed at the time of arthroscopic or open surgery[1–3]. Thus, the characteristics of cartilage degeneration in patients with RPD following conservative treatment without need for further surgical treatments are still not well understood.

Although magnetic resonance imaging (MRI) is a useful non-invasive method for evaluating cartilage degeneration, conventional MRI sequences can only provide semi-quantitative assessments of cartilage lesions using classification systems for cartilage lesions[7]. They have a limited potential for detecting a cartilage matrix abnormality in the earliest stages of cartilage degeneration[8].

Recently, an MRI technique called delayed gadolinium-enhanced MRI of cartilage (dGEMRIC) has been developed that is a sensitive, specific method for monitoring glycosaminoglycan (GAG) concentrations in articular cartilage[9,10]. The basis for dGEMRIC is that GAG is negatively charged in the cartilage matrix due to abundant carboxyl and sulfate groups. Given sufficient time following injection to penetrate cartilage, a negatively charged contrast agent, gadopentetate dimeglumine (Gd-DTPA^{2-}; Magnevist; Schering, Berlin, Germany), will be distributed in inverse proportion to the concentration of negatively charged cartilaginous GAG. GAG is a constituent of articular cartilage that is critical to its mechanical strength, and GAG concentrations decrease as cartilage degeneration progresses. Thus, as a non-invasive method for indirectly monitoring GAG concentrations within cartilage, dGEMRIC may be a useful method for quantitatively assessing cartilage degeneration.

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The ability of dGEMRIC to assess GAG concentrations of degenerative cartilages has been validated in basic studies[9,11,12], and dGEMRIC has been used for clinical evaluations of cartilage degeneration[13,14].

The objective of the present study was to examine the characteristics of cartilage degeneration in patients with RPD following conservative treatment using dGEMRIC.

Materials and methods

This study comprised 20 knees from 10 patients with bilateral RPDs, 30 knees from 15 patients with unilateral RPD and 20 knees from 10 healthy volunteers. RPD diagnosis was based on history, physical examination and findings of radiography and MRI. A patient with more than two complete patellar dislocations was diagnosed with RDP[15]. Patients were not included in this study if they had a follow-up period less than 6 months, permanent dislocation of the patella, habitual dislocation of the patella, acute transient dislocation of the patella, medial dislocation of the patella, history of previous medical treatment on the knee or known knee abnormality in the femoro-tibial joint. All patients were conservatively treated by a combination of rest, quadriceps strengthening, a patellar stabilizing brace and anti-inflammatory agents.

Body mass index (BMI) should be taken into account for cross-sectional dGEMRIC studies, as circulating plasma volume does not linearly correlate to the body weight[16]. In this study, no significant differences in BMI were observed between patients with bilateral RDP, patients with unilateral RDP or normal volunteers.

Based on physical activity, all subjects were divided into two groups: a no exercise group that included individuals without regular physical activities and a moderate exercise group that included individuals with regular physical activities, less than three times a week. There was no obvious difference in the activity level at the time of MRI between patients with bilateral RPDs, patients with unilateral RPD and healthy volunteers. Gender, age, BMI and physical activity level of all subjects are listed in Table I.

All knees were divided into three groups. Group I included both knees of patients with bilateral RPD and dislocated side knees of patients with unilateral RPD (35 knees total). Group II included non-dislocated side knees of patients with unilateral RPD (15 knees total). Group III included both knees of healthy volunteers (20 knees total). In group I, the mean length of time between the initial dislocation and MRI was 25.2 ± 13 months, and the mean total number of dislocations between the initial dislocation and MRI was 17.7 ± 6.9.

The study was approved by the ethics review committee of the National Institute of Radiological Sciences, and informed consent was obtained from all patients and volunteers.

MRI

Our dGEMRIC protocol followed the clinical protocol reported by Burstein *et al.*[17]. Gd-DTPA2$^-$ at a dose of 0.2 mmol/kg body weight was intravenously injected in a single bolus 2 h prior to MRI. The subjects walked up and down stairs for 10 min just after the administration of contrast agent. Then, MRI was performed at 1.5 Tesla (Gyroscan Intera; Phillips, Holland) with a dedicated knee coil. A set of T1-weighted axial images, termed morphological image, was acquired and used to select an image which passed through the center of the patella. The T1-weighted scanning parameters were as follows: 500 ms repetition time, 17 ms echo time, 150×150 mm field of view, 3.0 mm section thickness, 16 slices, 512×512 matrix, two excitations and six turbo spin-echo factor. T1 measurement was performed on the selected slice using the single-slice fast-spin-echo inversion-recovery (FSE-IR) sequence.

The FSE-IR scanning parameters were as follows: 1800 ms repetition time, 28 ms echo time, 50, 100, 200, 400, 800, and 1600 ms inversion times, 130×130 mm field of view, 3.0 mm section thickness, 512×512 matrix, one excitations, and six turbo spin-echo factor. Total scanning time for a series of inversion-recovery images was about 17 min. MRI was performed for the right knee and then the left knee for all subjects. The time interval between MRI of the right knee and the left knee was about 25 min.

Table I
Baseline characteristics of the subjects

	Patients with bilateral RDP	Patients with unilateral RDP	Healthy volunteer
Number of patients	10	15	10
Gender (male/female)	0/10	7/8	3/7
Age* (years, mean ± SD)	26.5 ± 7.6	25.3 ± 10.1	26.2 ± 3.4
BMI* (mean ± SD)	22.3 ± 2.7	21.6 ± 2.4	22.1 ± 2.2
Physical activity level* (no exercise/moderate exercise)	8/2	11/4	7/3

There were no significant differences with regard to age or BMI between the patient groups.

*At the time of MR imaging.

IMAGE ANALYSIS

T1 calculated maps of entire images were generated for all knees from FSE-IR images using the commercial software Dr. View (Asahikasei; Tokyo, Japan) with a three-parameter exponential curve fit [$SI = Mo (1 - 2Ae^{-TI/T1} + e^{-TR/T1})$].

For T1 measurement, the patellar cartilage was divided into two parts by the central ridge: medial and lateral facets. A region of interest (ROI) was drawn over the entire cartilage for the medial facet and the lateral facet. Areas with focal chondral defects or with bone sclerosis after osteochondral fractures, which were defined on the morphological image, were not included in the ROI. To standardize the procedure, all image analyses were performed by a single investigator using Dr. View.

To highlight areas of interest in the cartilage, a color-coded T1 calculated map of the cartilage, overlaid on the inversion-recovery image that had the longest inversion time, was created using MATLAB (The Mathworks, Natick, MA, USA). On the color scale, blue represented areas of long T1, indicating cartilage with higher GAG concentrations, and red represented areas of short T1, indicating cartilage with lower GAG concentrations.

DATA ANALYSIS FOR T1 MEASUREMENTS

Post-contrast T1 was referred to as the T1(Gd). Differences in T1(Gd) of cartilage at both medial and lateral facets between groups I, II and III were analyzed to evaluate the characteristics of cartilage degeneration.

For group I, relationships were evaluated between T1(Gd) of cartilage and (1) patient age, (2) length of time between the initial dislocation and MRI and (3) total number of dislocations between the initial dislocation and MRI for both medial and lateral facets to determine possible effects of these factors on the progression of cartilage degeneration.

The relationship between the grading of cartilage using the modified Outerbridge classification system[7], which is one of the most widely used methods for classifying cartilage lesions with conventional MRI, and T1(Gd) with dGEMRIC was evaluated for all knees in groups I, II and III. The cartilage at both the medial and lateral facets was graded on the morphological image using the modified Outerbridge classification system. Representative morphological images of patellar cartilage graded using modified Outerbridge classification system are shown in Fig. 1. For statistical analysis, medial and lateral facets were not separately assessed, as our aim was to evaluate the relationship between the grading of cartilage using the modified Outerbridge classification system and T1(Gd) with dGEMRIC.

There might be a possible effect of the difference in penetration of contrast agent into cartilage on T1(Gd) due to the difference of cartilage thickness between medial and lateral facets. The difference in cartilage thickness between medial and lateral facets and the relationship between thickness of cartilage and T1(Gd) of cartilage for all knees in group III were analyzed.

Cartilage thickness was measured as the minimal distance from the bone−cartilage interface to the cartilage surface over the central ridge. From there, measuring points were defined every 5 mm toward the medial and lateral edges. The mean thickness of all the measuring points at each medial and lateral facet was used for evaluation. For statistical analysis, medial and lateral facets were not separately assessed, as our aim was to evaluate the relationship between cartilage thickness and T1(Gd).

INTER- AND INTRA-OBSERVER VARIABILITIES FOR T1 MEASUREMENTS

Reproducibility studies were performed to assess the precision of the image segmentation technique. The intra-observer variability was assessed for a single investigator who twice measured the T1(Gd) of cartilage at medial facets, lateral facets and both medial and lateral facets for all knees in group I during a 4-week period. The inter-observer variability was assessed for two independent observers who measured the T1(Gd) of cartilage at medial facets, lateral facets and both medial and lateral facets for all knees in group I. Intra- and inter-observer variabilities were calculated as the coefficients of variation [CoV: standard deviation (SD)/mean $\times$ 100(%)], and mean variability was calculated as the root mean square average for each part of cartilage.

ASSESSMENT OF ABNORMALITIES IN MORPHOLOGY AND ALIGNMENT OF THE PATELLOFEMORAL JOINT

The sulcus angle was measured to determine any anatomical abnormality of the patellofemoral joint. *Q* angle, congruence angle, lateral patella angle and patellar lateralization were measured to determine any malalignment