Original Article

Glycosaminoglycan Content of the Lateral Compartment Cartilage in Knees Conforming to the Indications for Oxford Medial Unicompartmental Knee Arthroplasty

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Abstract

Background: The quality of the lateral compartment cartilage is important to preoperative evaluation and prognostic prediction of unicompartmental knee arthroplasty (UKA). Delayed gadolinium-enhanced magnetic resonance imaging of cartilage (dGEMRIC) enables noninvasive assessment of glycosaminoglycan (GAG) content in cartilage. This study aimed to determine the GAG content of the lateral compartment cartilage in knees scheduled to undergo Oxford medial UKA.

Methods: From December 2016 to May 2017, twenty patients (20 osteoarthritic knees) conforming to the indications for Oxford medial UKA were included as the osteoarthritis (OA) group, and 20 healthy volunteers (20 knees) paired by sex, knee side, age (±3 years), and body mass index (BMI) (±3 kg/m^2) were included as the control group. The GAG contents of the weight-bearing femoral cartilage (wbFC), the posterior non-weight-bearing femoral cartilage (pFC), the lateral femoral cartilage (FC), and tibial cartilage (TC) were detected using dGEMRIC. The dGEMRIC indices (T1Gd) were calculated in the middle three consecutive slices of the lateral compartment. Paired *t*-tests were used to compare the T1Gd in each region of interest between the OA group and control group.

Results: The average age and BMI in the two groups were similar. In the OA group, T1Gd of FC and TC was 386.7 ± 50.7 ms and 429.6 ± 59.9 ms, respectively. In the control group, T1Gd of FC and TC was 397.5 ± 52.3 ms and 448.6 ± 62.5 ms, respectively. The respective T1Gd of wbFC and pFC was 380.0 ± 47.8 ms and 391.0 ± 66.3 ms in the OA group and 400.3 ± 51.5 ms and 393.6 ± 57.9 ms in the control group. Although the T1Gd of wbFC and TC tended to be lower in the OA group than the control group, there was no significant difference between groups in the T1Gd in any of the analyzed cartilage regions (*P* value of wbFC, pFC, FC, and TC was 0.236, 0.857, 0.465, and 0.324, respectively).

Conclusions: The GAG content of the lateral compartment cartilage in knees conforming to indications for Oxford medial UKA is similar with those of age- and BMI-matched participants without OA.

Key words: Cartilage; Glycosaminoglycan; Unicompartmental Knee Arthroplasty

Introduction

Knee osteoarthritis (OA) is a chronic degenerative joint disease characterized by cartilage degeneration, wear, and loss. OA commonly affects the elderly, causing physical pain and dysfunction, and seriously influencing the quality of patients' lives.[1] Knee OA at a particular stage can be successfully treated with unicompartmental knee arthroplasty (UKA). UKA is less invasive and has a faster recovery than total knee arthroplasty.[2,3] Multiple studies have reported UKA survival rates of more than 90–95% at 10 years.[4,5]

The progression of OA in the lateral compartment of the knee is one of the main failure modes of UKA, accounting

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for approximately 20–40% of UKA failures.[6] An accurate assessment of the quality of the lateral compartment cartilage is therefore essential when determining the indication for UKA. It is currently recommended that the cartilage in the lateral compartment should be full thickness.[7] The most common and useful method to assess the thickness of cartilage is valgus stress radiography.[8,9] The cartilage thickness is defined as normal when the lateral joint space width is >5 mm on valgus stress radiography. However, a radiographically normal lateral compartment may not indicate the normal metabolism of cartilage.[10-12]

Glycosaminoglycans (GAGs) are highly negatively charged sugar chains that are covalently bound to a protein core to form aggrecan, which is one of the primary matrix molecules of cartilage. A few studies have proved that depletion of the GAG content, which is responsible for load distribution and compressive stiffness, is associated with cartilage degeneration and is believed to be an early event in the development of OA.[13,14] Similar to T1 rho, which is sensitive to changes in PG loss of cartilage, delayed gadolinium-enhanced magnetic resonance imaging of cartilage (dGEMRIC) is a molecular imaging technique that is widely used to determine the GAG content in cartilage, especially in the knee joint.[15,16] Owman *et al*.[17] investigated patients with knee pain but normal radiography using dGEMRIC at baseline, and found that the GAG content in cartilage was associated with radiographic OA 6 years later.

The GAG content of the lateral compartment cartilage in knees conforming to the indications for Oxford medial UKA has not yet been clarified. Given the importance of the lateral compartment cartilage in preoperative evaluation and prognostic prediction of UKA, this study aimed to use dGEMRIC to identify the GAG content of the lateral compartment cartilage in knees conforming to the indications for Oxford medial UKA.

Methods

Ethical approval

The Ethics Committee of China-Japan Friendship Hospital approved the study (No. 2016-96). All procedures were in accordance with the *Helsinki Declaration* of 1975, as revised in 2000. All participants signed written informed consent before inclusion.

Participants

From December 2016 to May 2017, twenty patients (20 osteoarthritic knees) scheduled to undergo Oxford medial UKA were included as the OA group. The inclusion criteria were the current indications for Oxford medial UKA:[4,7] isolated anteromedial OA producing pain, preserved full-thickness cartilage in the lateral compartment (joint space width >5 mm on valgus stress radiography), an intact anterior cruciate ligament (ACL), posterior cruciate ligament and medial collateral ligament (MCL), range of motion >90°, and varus and flexion deformity <15°. Age, obesity, and patellofemoral OA were not considered contraindications to surgery. In the same period, twenty healthy volunteers (20 knees without OA) paired with the OA group regarding sex, knee side, age (±3 years), and body mass index (BMI) (±3 kg/m^2) were included as the control group. Controls were excluded if there was any pain or radiographic OA in the knee. All participants were evaluated by careful physical and radiographic examinations of the knee to make sure that they met the inclusion criteria exactly. Radiographic examinations included standard weight-bearing anteroposterior (AP), valgus stress (in 20° flexion), true lateral, skyline, and AP hip-to-ankle radiographs. In the OA group, the ACL was evaluated on the true lateral radiograph (wear in the anterior or middle area of the medial tibial plateau), and the MCL was evaluated on the valgus stress radiograph (medial joint space turn to normal). The integrity of both the ACL and the MCL was finally confirmed intraoperatively. Exclusion criteria for both groups were a history of arthrotomy, history of contrast medium allergy, renal insufficiency (glomerular filtration rate <60 ml/min), and absolute contraindications to magnetic resonance imaging (MRI; metal implants within the body). All participants received dGEMRIC.

Magnetic resonance imaging evaluation

A 3.0 T MRI system (General Electric Healthcare, Milwaukee, WI, USA) with a dedicated knee coil was used for the examinations. Gd-DTPA^{2-} (Magnevist, Schering AG, Berlin, Germany) was injected intravenously at a dose of 0.2 mmol/kg approximately 1.5 h before the dGEMRIC investigation. The injection time of Gd-DTPA^{2-} was <5 min. To increase the Gd-DTPA^{2-} distribution in the articular cartilage, the participants continuously walked for 10 min after the injection. After walking and a delay of 80 min, the dGEMRIC images were acquired. Seven sagittal slices (3-mm-thick) were positioned in the lateral femoral condyle and tibial plateau. The inversion recovery fast spin echo sequence was used in the MRI examination, and the relative parameters were set (inversion times: 100, 300, 500, 800, and 1600 ms; repetition time: 3000 ms; echo time: 14 ms; field of view: 160 mm × 160 mm; and matrix: 256 × 256 pixels).

The selection of the regions of interest (ROIs) was standardized and based on the suggestions by Eckstein *et al*.[18] and van Tiel *et al*.[19] The ROIs were drawn manually on three consecutive slices through the lateral compartment (central slice and one adjacent slice on each side), and consisted of the femoral cartilage (FC), the weight-bearing FC (wbFC), the posterior non-weight-bearing FC (pFC), and the tibial cartilage (TC) [Figure 1a]. The MATLAB 7.1 (Mathworks Inc., Natick, MA, USA) and MRIMapper software packages (2006a R2.2, Beth Israel Deaconess Medical Center, Boston, MA, USA) were used to create T1 maps of the femoral and tibial cartilage in the three consecutive slices, and the mean dGEMRIC indices (T1Gd) were calculated in each ROI [Figure 1]. The measurements were repeated two times by the same researcher in every ROI, and the mean T1Gd was recorded. To ensure the accuracy of outcomes, the

selection of the ROIs and creation of the T1 maps were done by an experienced researcher who had been focused on this field for more than 5 years. The anterior FC belongs to the lateral facet of the trochlea and had worn in some patients. Given patellofemoral OA is not considered an absolute contraindication to UKA, we did not detect the anterior FC and patellar cartilage.[20]

Statistical analysis

All statistical analyses were performed using SPSS 21.0 statistical software (SPSS Inc., Chicago, IL, USA). Chi-squared tests were used to compare the preoperative count data of both groups. Paired *t*-tests were used to compare the T1Gd in each ROI between the OA group and the control group. One-way analysis of variance (ANOVA) and least significant difference (LSD) *t*-tests was used to compare the T1Gd of the wbFC, pFC, FC, and TC within each group. A value of $P < 0.05$ was considered statistically significant.

Results

A total of 40 participants (40 knees) were included, with 20 osteoarthritic knees in the OA group and 20 healthy knees in the control group. There were fourteen females and six males in each group. The demographics of the two groups were similar [all $P > 0.05$; Table 1]. In the OA group, the average time for pain in knees was 8.1 ± 5.6 years. The average range of motion of knee was 119.0 ± 10.5°. All patients had mild varus deformities, which was 7.7 ± 3.5° in average. The lateral joint space width of all patients was >5 mm (mean 6.2 ± 0.7 mm). The average HSS score of patients was 58.4 ± 7.1.

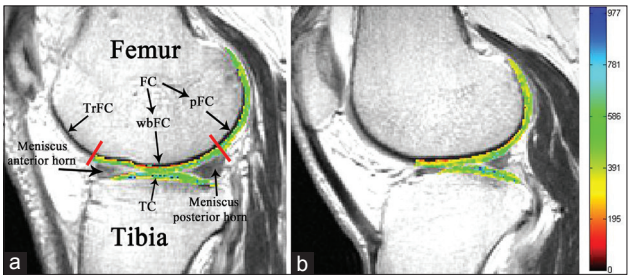

Figure 1: The mean delayed gadolinium-enhanced magnetic resonance imaging of cartilage indices (T1Gd) was shown in the middle slice of lateral compartment. (a) ROIs were shown on the image was form a patient aged 63 years old. (b) Image was from a volunteer aged 65 years old. The blue and red regions represent high and low GAG content, respectively. GAG: Glycosaminoglycan; ROIs: Region of interests; FC: Femoral cartilage; wbFC: Weight-bearing femoral cartilage; pFC: The posterior non-weight-bearing femoral cartilage; TC: Tibial cartilage; TrFC: The trochlear femoral cartilage.

In the OA group, T1Gd of FC and TC was 386.7 ± 50.7 ms and 429.6 ± 59.9 ms, respectively. In the control group, T1Gd of FC and TC was 397.5 ± 52.3 ms and 448.6 ± 62.5 ms, respectively. The respective T1Gd of wbFC and pFC was 380.0 ± 47.8 ms and 391.0 ± 66.3 ms in the OA group and 400.3 ± 51.5 ms and 393.6 ± 57.9 ms in the control group. Although the T1Gd in the wbFC and TC tended to be lower in the OA group than the control group, there was no significant difference between the two groups in wbFC and TC [$t = -1.224$, $P = 0.236$; $t = -1.013$, $P = 0.324$, respectively; Table 2]. As for pFC and FC, similar statistic results were shown [$t = -0.183$, $P = 0.857$; $t = -0.745$, $P = 0.465$, respectively; Table 2].

However, theT1Gd of TC was significantly different from that of wbFC, pFC, and FC in both healthy knees and osteoarthritic knees [$F = 3.103$, $P = 0.032$ in the OA group; $F = 4.242$, $P = 0.008$ in the control group; Table 3]. In the OA group, theT1Gd of TC was significantly higher than that of wbFC, pFC, and FC ($P = 0.007$, $P = 0.034$, and $P = 0.019$, respectively). In the control group, the T1Gd of TC was also significantly higher than that of wbFC, pFC, and FC ($P = 0.008$, $P = 0.003$, $P = 0.005$, respectively). The results demonstrated that TC may have higher GAG content than FC in knee joint.

Discussion

The depletion of GAG is closely associated with cartilage degeneration and is therefore believed to be a specific marker in predicting radiographic OA.[14,21] This study demonstrated that the GAG content of the lateral compartment cartilage in knees conforming to the indications for Oxford medial UKA was not significantly lower than those in healthy controls of the same age. Meanwhile, the results justified modern Oxford medial UKA indications from metabolic aspect.

Isolated medial compartment OA is accepted as an appropriate indication for Oxford medial UKA.[7,22] However, the quality of the lateral compartment cartilage in knees with isolated medial compartment OA has been a subject of debate. Previous research[22] has suggested that in knees with isolated medial compartment OA, the lateral compartments are not usually involved, and the cartilage is even free

Table 1: Demographics of the OA group for Oxford medial unicompartmental knee arthroplasty and healthy control group

Variables	OA group ($n = 20$)	Control group ($n = 20$)	Statistics	*P*
Age (years), mean ± SD	65.5 ± 7.6	64.8 ± 6.9	1.629*	0.120
Gender (female/male), *n*	14/6	14/6	0.119†	0.730
Side (left/right), *n*	8/12	8/12	0.104†	0.747
Height (cm), mean ± SD	160.2 ± 7.5	160.2 ± 6.5	−0.025*	0.981
Weight (kg), mean ± SD	68.4 ± 10.2	68.0 ± 8.1	0.219*	0.829
BMI (kg/m^2), mean ± SD	26.7 ± 3.6	26.2 ± 3.1	1.081*	0.293

*Paired *t*-tests; †Chi-squared tests. BMI: Body mass index; SD: Standard deviation; OA: Osteoarthritis.

of osteoarthritic changes in water content, proteoglycan composition, and GAG synthesis rates.[23] However, it has also been suggested that there is no completely isolated compartmental OA. Even in anteromedial OA, the lateral compartment cartilage may be involved to some degree. Obeid *et al*.[24] found that the apparently unaffected cartilage in knees with unicompartmental OA is mechanically inferior to normal cartilage, even though it appears to be sound radiologically. Moen *et al*.[11] demonstrated that in patients with radiographic evidence of medial OA and a radiographically normal lateral compartment, there is mild OA in the lateral compartment. Sugita *et al*.[25] showed that about 7–15% of varus osteoarthritic knees have bone formation within the articular cartilage of the lateral compartment, which may result in the deterioration of the lateral compartment after UKA. Our results showed that the GAG content of the lateral compartment cartilage in knees conforming to the indications for Oxford medial UKA was not significantly decreased compared with age- and BMI-matched healthy controls. This indicates that OA could be limited to the medial compartment, leaving the lateral compartment unaffected in particular conditions.

Attention should be paid to the inclusion criteria of the present study. Although both biochemical and mechanical factors affect cartilage degeneration, mechanical factors may play a more important role.[26,27] The OA group had approximately normal ACLs, MCLs, and lateral menisci, which ensured good protection of the lateral compartment.[28-30] Furthermore, the varus angles were limited within 15°, with a mean of 7.7 ± 3.5°. Mild varus has little influence on the stability of the joint but could reduce the loading of the lateral compartment to some extent.[31] Mild varus, therefore, could be a protective factor to the lateral compartment and the present results also proved it. If the above conditions were not present, the lateral cartilage could have been less well protected, and there may have been an obvious decline in the GAG content of OA knees compared with age-matched healthy controls. Therefore, the indications for Oxford medial UKA were important to ensure the quality of the lateral cartilage in knees with isolated medial OA.

Our results did not rule out the possible degeneration of the lateral cartilage in knees conforming to the indications for Oxford medial UKA. In fact, several studies have proved that the GAG content in cartilage decreases with increasing age.[32] Even in the present study, there was a slight decline in the GAG content in the wbFC and TC in the OA group compared with healthy controls.

The GAG content was significantly higher in the TC than the wbFC, pFC, and FC in both healthy knees and osteoarthritic knees, which is in line with previous researches.[19,33] We have no proper explanations for this finding yet. The reason may be related to mechanical transmission, as mechanical stress in the lateral compartment is transmitted through a smaller surface area of the TC and dissipated along a broader area of the corresponding FC.[11,27] Another possible explanation could be related to the thickness maps of cartilage, which reveal that cartilage regions are thickest at the lateral facet of the tibia and are thinnest at the medial facet.[34-36] Another point, we would mention is that most patients in the OA group had varying degrees of patellofemoral OA, but the GAG content of the lateral cartilage in these patients was similar to that of healthy knees. Therefore, we hypothesize that patellofemoral OA also had little influence on the lateral compartment. However, further research is needed to confirm this.

There are some limitations to our study. First, most osteoarthritic knees conforming to the indications for Oxford medial UKA underwent UKA in our department. Thus, we could not get lateral cartilage samples and examine them histologically. Second, the sample size in our study was relatively small. A larger cohort of participants is needed in the future. Finally, although many factors could affect the GAG content in the lateral cartilage, risk factors affecting the GAG content in the lateral cartilage were not analyzed in this study because of the limited number of participants.

In conclusion, our study identified the metabolic status of the lateral compartment cartilage in knees conforming to

Table 2: Difference of T1Gd between OA group for Oxford medial unicompartmental knee arthroplasty and healthy control group

ROIs	OA group (n = 20)	Control group (n = 20)	t	P
wbFC (T1Gd, ms)	380.0 ± 47.8	400.3 ± 51.5	−1.224	0.236
pFC (T1Gd, ms)	391.0 ± 66.3	393.6 ± 57.9	−0.183	0.857
FC (T1Gd, ms)	386.7 ± 50.7	397.5 ± 52.3	−0.745	0.465
TC (T1Gd, ms)	429.6 ± 59.9	448.6 ± 62.5	−1.013	0.324

The data were presented by mean ± SD. wbFC: Weight-bearing femoral cartilage; pFC: Posterior nonweight-bearing femoral cartilage; FC: Femoral cartilage; TC: Tibial cartilage; SD: Standard deviation; OA: Osteoarthritis; ROIs: Region of interests.

Table 3: Difference of T1Gd within OA group for Oxford medial unicompartmental knee arthroplasty and that for healthy control group (n = 20)

Groups	T1Gd, ms				F	P
	wbFC	pFC	FC	TC		
OA group	380.0 ± 47.8	391.0 ± 66.3	386.7 ± 50.7	429.6 ± 59.9	3.103	0.032
Control group	400.3 ± 51.5	393.6 ± 57.9	397.5 ± 52.3	448.6 ± 62.5	4.242	0.008

wbFC: Weight-bearing femoral cartilage; pFC: Posterior non-weight-bearing femoral cartilage; FC: Femoral cartilage; TC: Tibial cartilage; OA: Osteoarthritis.

the indications for Oxford medial UKA and demonstrated that the GAG content of the lateral compartment cartilage in these knees was not significantly lower than in age- and BMI-matched healthy controls.

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Conflicts of interest

There are no conflicts of interest.

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