Introduction:

dGEMRIC is a non-invasive technique that reflects cartilage GAG content. The negatively charged contrast medium (Gd-DTPA) is injected intravenously and distributes in the cartilage by diffusion in an inverse relationship to the cartilage GAG content (1). A high GAG content results in a low Gd-DTPA concentration in the cartilage and, consequently, a long T1 relaxation time.

It is well known that an ACL deficient knee is at risk for future osteoarthritis (OA) but the underlying mechanisms are not understood (2). Previous studies have shown increased levels of GAG and proteoglycan fragments in joint fluid during the first weeks after an ACL injury (3). However, it has remained unclear whether that reflects a net loss of GAG from the cartilage or only represents an increased metabolic activity with a preserved tissue homeostasis. Numerous MRI studies have shown that an ACL injury is associated with a subchondral bone bruise in the lateral femoral condyle, although future OA most commonly occurs in the medial femoral compartment (4). This study combines intraarticular GAG analysis, using dGEMRIC, with synovial fluid (SF) GAG analysis in order to increase the knowledge on early cartilage damage following an ACL-injury.

Patients and methods

Twenty-four patients (mean age 27, range 17-40) with an MRI verified acute anterior cruciate ligament rupture in a previously uninjured knee and 24 age and exercise matched healthy volunteers were included in the study. A routine diagnostic MRI as well as dGEMRIC was performed 2-5 weeks after the injury (mean 3 weeks). At the day for the MRI, the joint was aspirated and the joint fluid GAG content was examined by dye-precipitation of chondroitin- and keratan sulphate with Alcian blue according to Björnsson (5).

A 1.5 T system with a dedicated knee coil was used for the MR examinations. Initially, a routine diagnostic series was performed to verify the ACL rupture and to diagnose concomitant subchondral bone bruises. After the diagnostic series, the contrast medium, Gd-DTPA2- (Magnevist®) was injected intravenously at the triple dose, 0.3 mmol/kg body weight. Two hours post-contrast, quantitative T1 relaxation time calculations were made in 3 mm thick sagittal slices using sets of six turbo inversion recovery images with different inversion times. TR=2000 ms, TE=15 ms, turbofactor 11, FoV 120 x 120 mm2, matrix 256 x 256, T1 = 50-2800. One slice was positioned in the central lateral femoral condyle and one slice in the medial femoral condyle according to our previous protocol (6). In the slices, T1 was calculated in regions of interest covering the full cartilage thickness, from the center of the tibial plateau to the rear insertion of the meniscus (weight-bearing area). T-test and regression analyses were used for the statistical evaluation.

Results

MRI revealed subchondral bone bruises in all patients except one, most frequently involving the lateral compartment (22/24). Post-contrast T1 relaxation time was shorter in the ACL injured patients compared with the healthy volunteers, both in the lateral (14%) and the medial (12 %) femoral cartilage, p=0.002 and p=0.004, respectively (Figure 1). There was no difference between compartments in the ACL group, whereas the healthy volunteers had higher T1 laterally than medially (Figure 1).

SF aggrecan concentration: The mean aggrecan fragment concentration in SF was 157±86 µg/ml (mean±SD). There was a positive correlation between T1 and SF aggrecan concentration, R=0.25, p=0.25) or time from injury. (R=-0.18, p=0.41).

Discussion

This study provides the first evidence that an ACL injury results in a global GAG loss from the knee cartilage within the first weeks after trauma. This is supported by a more than ten percent shorter T1 in both medial and lateral femoral cartilage compared with healthy volunteers.

The vast majority of patients had a bone bruise involving the lateral compartment. However, despite this impact to the lateral femoral compartment, the decrease in T1 was highly significant also in the medial femoral cartilage (Figure 1). From these results, we hypothesize that the GAG loss that occurs after an ACL injury does not solely originate from the slices of cartilage impact, but is the result of a generalized degradative enzymatic activity within the joint that could not be fully compensated for by increased synthesis.

No correlation was found between the amount of SF and T1. This indicates that the various degree of post traumatic synovial inflammation that was present at the time for MRI has not influenced the results.

In the present study we observed a positive correlation between SF proteoglycan content and T1. This indicates that the amount of GAG that is released to the joint fluid after an ACL injury depends on the total cartilage GAG content. This information may be important for the evaluation of biomarkers, such as aggrecan, in joint fluid. Follow-up of these patients will provide information about longitudinal compositional matrix changes that may predict future OA development.

Figure 1. Post-contrast T1 (ms, mean±SD) in lateral and medial femoral cartilage, respectively in ACL injured (*, n=24) and reference (●, n=24) groups.

Figure 2. Post-contrast T1 (ms, mean of medial and lateral femoral cartilage) in 23/24 ACL-injured patients in relationship to the synovial fluid aggrecan concentration.

References


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