Determinants of Change in Patella Cartilage Volume in Healthy Subjects

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ABSTRACT. ***Objective.*** To examine whether the amount of patella cartilage in healthy, middle-aged subjects is stable or changes over time, and what factors may influence the changes.

Methods. Eighty-five subjects (28 men and 57 women, mean age 55.5 yrs) had magnetic resonance imaging of their dominant knee at baseline and 2 years later. Patella and tibial cartilage volume was measured at baseline and followup. Risk factors assessed at baseline were tested for their association with change in patella cartilage volume over time.

Results. Mean annual percentage loss of patella cartilage was 2.1 (95% confidence interval: 1.1-3.2; $p < 0.001$). Age, gender, body mass index, and initial cartilage volume did not affect rate of change of patellar cartilage volume. There was a weak association between change in patellar cartilage volume and change in lateral tibial cartilage volume ($R = 0.23$, $p = 0.03$) but not medial tibial cartilage volume ($R = 0.09$, $p = 0.43$).

Conclusion. In healthy subjects, a significant amount of patella cartilage is lost annually. The poor correlation between patella and tibial cartilage loss suggests that pathogenetic mechanisms for osteoarthritis in the patellofemoral and tibiofemoral joint may differ. Further work will be required to determine whether the rate of patella cartilage loss in healthy subjects is steady or phasic, and to determine which factors can be modified to reduce cartilage loss. (J Rheumatol 2006;33:1658–61)

Key Indexing Terms:
PROSPECTIVE COHORT CARTILAGE VOLUME HEALTHY WOMEN

Osteoarthritis (OA) is a common cause of disability in people aged over 65 years[1]. It is a disease of joints, involving both cartilage and bone in the disease process. With increasing disease severity, articular cartilage is lost. However, although much is known about what happens after disease onset, at the level of the joint, little is known about initiating factors, and the pre-disease state in healthy humans.

The knee joint consists of 3 compartments: medial and lateral tibiofemoral and patellofemoral. Tibiofemoral disease is predominant, especially in the medial compartment. However, patellofemoral OA is also commonly present, either in combination with tibiofemoral disease, but also in isolation. Patellofemoral disease has been implicated as the cause of significant symptoms and disability[2-4]. Despite this, little is known about the healthy patellofemoral compartment, prior to disease onset.

Cartilage loss occurs as a significant component of OA. Cartilage loss has recently been examined at the tibiofemoral joint, where it was found that the mean tibial cartilage volume loss in healthy postmenopausal women was between 1.5 and 3.2% per year[5]. We have shown that in OA, patella cartilage volume is lost at a rate between 3.7 and 5.3% per year, with no association between change in patellar cartilage volume and change in either medial or lateral tibial cartilage volume[6]. However no information is available on patella cartilage change in healthy subjects or the factors that affect it. We examined a cohort of healthy middle aged people with no symptoms of knee OA to examine change in patella cartilage over 2 years, and to examine factors which may affect this change.

MATERIALS AND METHODS

Study participants. All healthy subjects who had magnetic resonance imaging

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(MRI) scans 2 years apart within our department were studied. These 85 subjects (28 men and 57 women) were recruited through advertising in newspapers, sporting clubs, hospital staff, and through women's health clinics[7,8]. This study was approved by the Alfred Hospital Human Research Ethics Committee, and all participants gave written informed consent.

Exclusion criteria included previous significant knee injury requiring non-weight bearing treatment for > 24 h or surgery (including arthroscopy), evidence of radiographic OA, osteoporosis, and contraindication to MRI including pacemaker, metal sutures, or presence of shrapnel or iron filings in the eye.

Subjects completed a questionnaire that included demographic data, past medical and surgical history, and current physical activity[9]. Weight was measured to the nearest 0.1 kg using a single pair of electronic scales with shoes, socks, and bulky clothing removed. Height was measured to the nearest 0.1 cm using a stadiometer with shoes and socks removed. Body mass index (BMI) (weight/height^2 kg/m^2) was calculated. Pain was assessed using the pain dimension of the knee specific Western Ontario and McMaster Universities OA Index (WOMAC)[10].

Measurements. At baseline, each subject had an MRI scan performed on their dominant knee and approximately 2 years later. The dominant knee was defined as the lower limb, from which they stepped off when walking. Knees were imaged in the sagittal plane on the same 1.5-T whole body magnetic resonance unit (Signa Advantage HiSpeed GE MedicalSystems Milwaukee, WS, USA) using a commercial receive-only extremities coil. The following sequence and variables were used: T1-weighted fat suppressed 3D gradient recall acquisition in the steady state; flip angle 55 degrees; repetition time 58 ms; echo time 12 ms; field of view 16 cm; 60 partitions; 512 × 192 matrix; one acquisition time 11 min 56 s. Sagittal images were obtained at a partition thickness of 1.5 mm and an in-plane resolution of 0.31 mm × 0.83 mm (512 × 192 pixels). Patella and tibial cartilage volumes and patellar bone volume were determined by means of image processing on an independent work station using the software program Osiris as described[11,12]. Two readers measured all the MRI, blinded regarding their time sequences. The coefficients of variation (CV) were 2.1% for patella cartilage volume and 3.4% and 2.0% for the medial and lateral tibial cartilages respectively[11,13]. The principal outcome variables assessed were annual change in patella cartilage volume defined as (initial volume - second volume) ÷ time between scans; and annual percentage change in patella cartilage volume defined as [(initial volume - second volume) ÷ (initial volume)(time between scans)] × 100. The results were compared for all cartilage and bone measurements. If the duplicate results were within ± 20%, an average of the duplicate results was used. If agreement between the duplicates was outside this range, the measurements were repeated until the independent measures were within ± 20%, and the average used. Repeat measurements were made blind to the results of the comparison of the previous results, similar to the described method[7].

Statistical analysis. With a sample size of 85 we had 80% power to show a correlation of 0.3 between the change in cartilage volume and the risk factors we examined (alpha error 0.05, 2-sided significance). Descriptive statistics for characteristics of the subjects were tabulated. Independent t tests were used for comparison of means. Chi square tests or Fisher's exact test (where appropriate) were used to compare characteristics between the groups. The null hypothesis was no change in patella cartilage volume. A single sample t test was used to determine whether the rate of change observed was significantly different from zero. Multiple linear regression techniques were used to explore the factors affecting the rate of change in cartilage volume. All analyses were performed using the SPSS statistical package (version 10.0.5, SPSS, Cary, NC, USA).

RESULTS

Demographic features of the 85 study participants are presented in Table 1. Men tended to be younger ($p = 0.04$), taller ($p < 0.001$), heavier ($p < 0.001$), have lower initial patellar cartilage volume ($p = 0.01$), larger patellar bone volume ($p = 0.04$), and larger medial and lateral tibial cartilage volumes ($p < 0.001$).

Mean volume of total patella cartilage lost per year was 0.57 ml (Table 2). Annual mean percentage of patellar cartilage loss was 2.1% of total patella cartilage [95% confidence interval (CI): 1.1-3.2] (Table 2). The rate of patella cartilage loss seemed to be greater in men versus in women, 3.8% (95% CI: 1.44-6.13) versus 1.3%, (95% CI: 0.23-2.32); however this was not statistically significant.

Other possible associations between potential risk factors and change in cartilage in healthy subjects were explored. Univariate and multivariate analysis showed no statistically significant associations between age, BMI, initial patella cartilage volume, or initial patellar bone volume with patellar cartilage loss (Table 3). There was no effect of baseline pain or physical activity on patella cartilage loss (data not shown).

Our study showed a weak association between change in patellar cartilage volume and change in lateral tibial cartilage volume ($R = 0.23$, $p = 0.03$) but not medial tibial cartilage volume ($R = 0.09$, $p = 0.43$).

DISCUSSION

In this cohort study of 85 healthy subjects, followed over 2 years, we found that the average rate of patella cartilage loss was 2.1% (95% CI: 1.1-3.2) per year. No factors were identified to account for differences in change in patellar cartilage volume. There was a significant but weak correlation between patella cartilage loss and loss of lateral tibial cartilage, but not medial tibial cartilage.

No data are available on longitudinal change in patella cartilage volume in healthy subjects. There is also little information available on the rate of progression of patellofemoral OA, even as measured radiologically. However, we have previously shown that in subjects with OA, the average annual percentage of patella cartilage loss is between 3.5 and 5.3%, which is higher than our findings in this study[6]. In contrast, we found that in healthy subjects, both men and women, the rate of loss of cartilage volume was similar in patella versus tibial cartilage[5].

We have shown the average change in cartilage volume of the cohort. Measurement error means that there is error in the measurements at baseline and at followup, which are used to calculate the change in patella cartilage volume. This measurement error is likely to make it more difficult to detect a true change in patella cartilage volume. All efforts were made to minimize measurement error and the resultant measure of reproducibility, the coefficient of variation, is low, being only 2.1%. The null hypothesis was that there would be no change in patella cartilage volume. In testing whether the rate of change we observed was significantly different from zero (i.e., no change in patella cartilage volume), we found that the average change patella cartilage volume in this population was 2.1% (95% CI: 1.1-3.2%, $p < 0.001$). Thus the change in patella cartilage volume we observed is significantly different

Table 1. Characteristics of study population. Statistical analysis included men and women compared using unpaired t tests (p value for difference). Data are reported as mean (SD). Comparisons were made using students t test, or Fishers exact test.

	Total (n = 85)	Men (n = 28)	Women (n = 57)	p
Age, yrs	55.5 (9.3)	52.5 (13.2)	57.1 (5.8)	0.04
Height, cm	1.7 (0.1)	175.3 (5.8)	163.4 (0.07)	< 0.001
Weight, kg	73.6 (14.1)	79.9 (12.4)	70.2 (13.8)	< 0.001
BMI, weight (kg)/height^2 (m^2)	26.1 (4.6)	25.6 (3.5)	26.3 (5.1)	0.4
Physical activity	7.4 (1.7)	8.8.4 (2.7)	7.4 (1.7)	0.30
Pain	2.0 (3.1)	1.9 (1.8)	2.1 (3.1)	0.23
Time between scans, yrs	2.3 (0.27)	2.0 (0.0)	2.5 (0.16)	< 0.001
Patella cartilage volume at baseline, ml	2.8 (0.67)	2.5 (0.7)	2.9 (0.6)	0.01
Patella bone volume, ml	19.1 (3.0)	19.8 (2.8)	18.4 (3.1)	0.04
Medial tibial cartilage volume, ml	1.9 (0.6)	2.5 (0.5)	1.5 (0.3)	< 0.001
Lateral tibial cartilage volume, ml	2.4 (0.7)	3.2 (0.6)	2.0 (0.4)	< 0.001

BMI: body mass index.

Table 2. Annual change in patella cartilage in healthy subjects. Results are reported as mean (95% confidence interval).

	Total	Men	Women	Difference between men and women (95% CI)
Annual patella cartilage volume loss, μm^3*	57.4 (31.4, 83.4)	90.7 (39.7, 141.7)	41.1 (11.2, 70.9)	49.6 (-8.7, 107.9)
Annual percentage change, %	2.1 (1.1, 3.2)	3.8 (1.44, 6.13)	1.3 (0.23, 2.32)	2.5 (-0.04, 5.1)

* (initial cartilage volume — second cartilage volume)/ time between scans (2 years).

Table 3. Factors affecting annual patella cartilage loss in healthy subjects.

	Univariate Analysis Regression Coefficient (95% CI)	p	*Multivariate Analysis Regression Coefficient (95% CI)	p
Age[a]	–1.9 (–4.9, 1.1)	0.21	-46×10^{-2} (–3.6, 2.7)	0.77
Gender[b]	49.6 (–5.1, 104.2)	0.08	175.09 (–34.5, 384.1)	0.10
BMI[c]	1.2 (–4.7, 7.2)	0.68	2.0 (–3.9, 8.0)	0.51
Patellar bone volume[d]	4×10^{-3} (–0.01, 0.009)	0.08	-1.3×10^{-2} (–0.037, 0.01)	0.25
Initial patellar cartilage volume[e]	15×10^{-2} (–0.02, 0.05)	0.46	12.3×10^{-2} (–0.5, 0.3)	0.16

* Multivariate analysis with age, gender, BMI, initial patella bone and initial cartilage volume in regression equation. [a] Change per 1 year increase in age. [b] Females compared to males. [c] Change per unit increase in BMI. [d] Change per ml increase in bone volume. [e] Change per ml increase in baseline patella cartilage volume.

from zero. However, these results do not allow us to comment on whether or not an individual lost cartilage. For an individual, the minimum detectable difference in percentage change (at a 5% level of significance) can be estimated by multiplying the coefficient of variation for a single volume measurement by 2.8[14]. As the coefficient of variation in our study was 2.1% for measurement of patella cartilage volume, this would be ± 5.9% per year. Thus at the individual level, we can be sure, with 95% confidence, that 2 subjects gained cartilage (i.e., change in cartilage of > 5.9%) and 14 subjects lost cartilage (i.e., lost > 5.9%).

Our results suggest that, in healthy subjects, the factors influencing changes in cartilage volume differ in tibial versus patellar cartilage. In healthy subjects, initial cartilage volume has been shown to be a significant determinant of change in tibial cartilage volume[5,8]. We found no effect of initial cartilage volume on change in patellar cartilage in healthy adults. In addition, we showed no correlation with joint cartilage loss at the patella and either the medial or tibiofemoral joints. In contrast, there was a significant correlation between cartilage loss in an individual subject in the medial and lateral tibiofemoral joints. Thus, our data lend some support to the notion that OA at the tibiofemoral and patellofemoral joints may have different pathogenetic mechanisms.

It may be that factors affecting change in patellar cartilage differ in health and disease. In subjects with knee OA, women with higher BMI and higher baseline pain lost cartilage most rapidly[6]. In our cohort, these factors did not have a significant

effect, although our power to detect an effect was more limited than in the previous OA study. Based on our sample size of 85, we had 80% power to detect correlations between the risk factors we examined and change in patella cartilage volume down to 0.3, thus explaining up to 9% of the variance in change in patella.

Measurement of cartilage volume is limited by the contrast between articular cartilage and the adjacent tissues. Our method has been validated against cadavers and has excellent reproducibility, with coefficients of variation of 2 to 3%[11,12]. To improve in-plane resolution, we use a matrix of 512×192 pixels, resulting in an in-plane resolution of 0.31×0.83 mm. To the best of our knowledge, this is the only published longitudinal study of MRI measured patella knee cartilage volume in healthy subjects. Nevertheless, it is likely that, given the number of subjects we have, longer duration of followup will be needed to determine the role of other potential risk factors such as current activity level, grade of patellofemoral OA, and change in body weight.

In healthy subjects, patella cartilage volume is lost at about 2.1% per annum. The poor correlation between patella cartilage loss and cartilage loss in the tibial compartment suggests that the pathogenetic mechanisms for OA in the patellofemoral and tibiofemoral joint may differ. These data may be useful to calculate sample size estimates for those doing studies investigating either preventive strategies or chondroprotective agents in patellofemoral joint OA. Further work will be required to determine whether the rate of patella cartilage loss in OA is steady or phasic, and to determine which factors can be modified to reduce cartilage loss.

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