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Comparison of cartilage thickness with radiologic grade of knee osteoarthritis

Filippo Agnesi^{1,2}, Kimberly K. Amrami³, Carlo A. Frigo², and Kenton R. Kaufman^{1,4}

¹ Motion Analysis Laboratory, Division of Orthopedic Research, Mayo Clinic, Rochester, MN, USA

² Department of Bioengineering, Polytechnic of Milan, Milan, Italy

³ Department of Radiology, Mayo Clinic, Rochester, MN, USA

⁴ Motion Analysis Laboratory, Department of Orthopedic Surgery, Mayo Clinic/Foundation, Charlton North L-110L, Rochester, MN 55905, USA e-mail: kaufman.kenton@mayo.edu

Abstract

Objective—To compare joint space width (JSW) measurements obtained from magnetic resonance imaging (MRI) with a semi-automated computer algorithm to the Kellgren and Lawrence grading of osteoarthritis (OA).

Materials and methods—Three hundred and six patients (234 female, 72 male) with a mean age of 56.7 years (range 31–81 years) underwent MRI of their knees with a fast oblique spiral spoiled gradient (SPGR) sequence. A board-certified musculoskeletal radiologist graded the OA of all the patients in accordance with the Kellgren and Lawrence OA scale. A previously validated computer algorithm was used to determine the minimum JSW for both the tibiofemoral joint and the patellofemoral joint. An analysis of variance (ANOVA) with the Student–Newman–Kuels post-hoc test was used to determine if there were differences in JSW as a function of OA grade.

Results—The radiologic grade of OA was inversely associated with the JSW. In the medial compartment the JSW did not change significantly between grade 1 and grade 2, but there was a significant decrease in JSW between grade 0 (normal) and grade 1 and for each OA grade above grade 2. In the lateral compartment no statistical differences were found till grade 2, while grade 3 was found to be statistically different from the previous one. The number of patients with a grade 4 patellofemoral OA was too low for the statistical significance to be assessed. In the patellofemoral joint the JSW did not change significantly until grade 2, while a statistically significant reduction was found for both grade 3 and grade 4.

Conclusion—This study showed that an inverse non-linear relationship exists between radiologic grade and JSW. The relationship differs for the tibiofemoral and the patellofemoral joint.

Keywords

Osteoarthritis; MRI; Knee; Musculoskeletal disease; Cartilage; Computer program

Introduction

Osteoarthritis (OA) severity is commonly graded from radiographic images in accordance with the Kellgren and Lawrence scale [1] or from magnetic resonance imaging (MRI) according to the modified Outerbridge classification [2]. Although the use of radiography is less expensive

and more easily accessible than MRI, its potential for quantitative analysis is limited. MRI is more sensitive and allows a much finer discrimination between different anatomic structures based on differences in tissue contrast that cannot be distinguished on radiography.

A widely used method to track the progression of OA is the manual measurement of the joint space width (JSW) on radiographs. This technique has a large intra-user and inter-user variability [3] and relies on a single image to represent the whole joint. The use of a semi-automated computer algorithm can overcome the variability related to manual measurements [4], while the use of MRI can lead to a more precise tracking of the disease. Therefore, the purpose of this study was to compare the radiologic grading of OA patients with the JSW measurements obtained from MRI images, using a previously validated computer algorithm [4].

Methods

Data collection

Recruitment and consent of the research participants, and the testing procedures, were approved by the local institutional review board prior to the subjects' enrollment. There were 306 patients (234 female, 72 male, mean age 56.7 years, range 31–81 years) enrolled in this study. They all suffered chronic stable pain and/or stiffness in one or both knees during weight-bearing activities, radiographic signs of mild or moderate arthritis, and mild joint space narrowing. Inclusion criteria required also that the involved joint be the primary factor limiting physical or functional activity. Exclusion criteria included major reconstructive surgery of the lower extremities or involvement of multiple major joints.

Bilateral anteroposterior (AP) and lateral radiographs of the knees were acquired with a Fuji 5000 instrument plus reader with a 36 cm×43 cm Fuji ST-VI CR imaging plate (Fuji Medical Systems, Tokyo, Japan). Computed radiography of each knee was obtained with the subject standing in a semi-flexed position as previously described by Buckland-Wright et al. [5] in both the AP and lateral positions. The full, uncompressed, DICOM images were viewed on a standard clinical workstation and graded by a board-certified musculoskeletal radiologist in accordance with the Kellgren and Lawrence scale.

All subjects underwent bilateral acquisition of magnetic resonance (MR) images in the sagittal plane with a 1.5 T GE Signa MRI Scanner, EXCITE 11.0 (General Electric Medical Systems, Waukesha, WI, USA). The subjects were imaged in a supine position with padding under their knees to ensure an approximate flexion angle of 20°. An oblique sagittal spiral fast spoiled gradient (SPGR) sequence was used, with a field of view of 15 cm×15 cm, an effective resolution of 0.58 mm, a flip angle of 90° and a matrix of 4096×24/2.00 was used. The images obtained were composed of 512 pixels×512 pixels with a pixel size of 0.292969 mm and 16 bits of gray scale encoding. Each sagittal slice had a thickness of 3 mm, and 1 mm spacing between slices.

Computer algorithm

The images were analyzed using a custom-written Matlab (The Mathworks, Inc., Natick, MA, USA) program [4]. On each MRI acquisition the user analyzed only the regions that were normally weight bearing during gait (in the tibiofemoral joint) or regions characterized by a consistent engagement between patellar and femoral cartilage (in the patellofemoral joint). On slices belonging to these regions the user defined the actual regions of interest where the border between bone and cartilage had to be identified for the distal femur, proximal tibia and patella. The computer algorithm then recognized and tracked the bone–cartilage interfaces and measured the minimum cartilage thickness (distance between detected edges) encountered for

each slice (JSW). For each patient, only the slice showing the minimum distance was considered for the analysis.

In a previous study [4] performed on healthy subjects, this program had shown a consistently better reproducibility than manual measurements had shown, and, thus, it is a reliable tool for JSW evaluation. In the tibiofemoral joint an intra-user variability of 0.004 ± 0.07 mm was found for the automated measurements, compared to 0.12 ± 0.21 mm for the manual measurements. The inter-user variability was 0.001 ± 0.11 mm for the automated measurements and 0.37 ± 0.59 mm for the manual measurements. In the patellofemoral joint an intra-user variability of 0.009 ± 0.11 mm was found for the automated measurements compared to 0.13 ± 0.29 mm for the manual measurements. The inter-user variability was 0.0006 ± 0.1 mm for the automated measurements and 0.31 ± 0.66 mm for the manual measurements.

Analysis

For the tibiofemoral joint only the regions that are normally loaded during gait were selected for the analysis. Therefore, only slices belonging to the midpoint of the medial and lateral compartment not adjacent to the intercondylar notch were included in the analysis. On average, between three and four slices were selected for each compartment. For the patellofemoral joint, only slices where the femoral and patellar cartilages were opposing each other were chosen for the analysis. On average, between six and seven slices were selected for analysis of each patellofemoral joint.

An analysis of variance (ANOVA) with a Student–Newman–Keuls post-hoc test was used to determine if there were differences in JSW as a function of OA grade. Statistical significance was set at $P=0.05$.

Results

A total of 1,177 tibiofemoral compartments from 589 knees in 301 patients were analyzed (13 knees were not included in the analysis due to artifacts). Of these compartments, 191 were rated as normal (grade 0), 387 as grade 1, 378 as grade 2, 176 as grade 3, and 47 as grade 4. The average JSWs were 4.23 ± 0.96 mm, 3.97 ± 1 mm, 3.74 ± 1.04 mm, 2.8 ± 1.14 mm and 1.8 ± 1.05 mm, respectively (Fig. 1). There was a significant difference in JSW versus OA grade. The Student–Newman–Keuls post-hoc test grouped grades 1 and 2 together, while grades 0, 3 and 4 differed significantly from each other (Table 1).

Medial and lateral compartments were also analyzed separately. In the medial compartment 34 knees were rated as normal (grade 0), 184 as grade 1, 191 as grade 2, 135 as grade 3, and 45 as grade 4. The average JSWs were 3.73 ± 1.05 mm, 3.38 ± 0.7 mm, 3.12 ± 0.69 mm, 2.54 ± 0.95 mm and 1.74 ± 0.9 mm, respectively (Fig. 2). In the medial compartment, the Student–Newman–Keuls test reported a significant difference in JSW versus OA grade, which was the same as the combined compartments. (Table 1)

In the lateral compartment 157 knees were rated as normal (grade 0), 203 as grade 1, 185 as grade 2, 41 as grade 3 and only two as grade 4. The average JSWs were 4.34 ± 0.91 mm, 4.51 ± 0.93 mm, 4.37 ± 0.97 mm, 3.66 ± 1.28 mm and 3.22 ± 3.31 mm (only two grade 4), respectively (Fig. 2b). Again, there was a significant difference between different OA grades, although this was not as discrete as the differences in the medial compartment or combined tibiofemoral joint. The Student–Newman–Keuls post-hoc test grouped grades 0, 1, and 2 together, while grade 3 was significantly different (Table 1). The sample size for grade 4 tibiofemoral OA in the lateral compartment was too small for the statistical significance to be assessed.

In general, the medial compartment had a greater JSW than the lateral compartment. However, there were 20 patients that had a medial compartment which was thicker than the lateral compartment (average medial/lateral thickness rate was 0.75) and was not entirely explainable by the OA grading. In these patients, the medial compartment was graded as having more severe OA than the lateral compartment.

A total of 591 patellofemoral joints were analyzed, with 100 graded normal, 241 as grade 1, 175 as grade 2, 64 as grade 3 and 11 as grade 4. The mean JSWs were 3.53 ± 0.89 mm, 3.31 ± 0.91 mm, 3.33 ± 0.96 mm, 2.73 ± 1.39 mm and 2.07 ± 1.11 mm, respectively (Fig. 3). There was a significant change in JSW with OA grade. The Student–Newman–Keuls post-hoc test grouped grades 0, 1 and 2 together, while grade 3 and grade 4 were each grouped individually (Table 1).

Discussion

This study focused on the minimum distance between bone–cartilage interfaces in specific regions of the knee joint. The main issue for patients with OA is limitation of functional movements, particularly ambulatory function. Accordingly, we concentrated our measurements on cartilage weight-bearing regions involved in gait. These regions are subjected to cyclic peak loads. They are also more likely to degenerate and be responsible for movement impairments.

This study showed a significant non-linear decrease in JSW measured by MRI compared to the radiologic grade of knee OA. As was expected, this was more significant in the medial compartment than in either the patellofemoral or lateral compartments. The fact that the JSW in early stages of OA did not change significantly might be related to structural changes in the cartilage, including increases in free-water content that might occur before loss of height or thickness is seen on imaging studies. With the progression of OA, the cartilage loses its ability to maintain its internal structure, and the JSW decreases [6]. Previous work, although focused on cartilage volume, has reported similar results, showing an increase of volume between grade 0 and grade 1 (modified Outerbridge scale), followed by a reduction of volume in grades 2 and 3 [7]. No grade 4 cartilage was included in that study. In our study we found an increase in the cartilage thickness only in the lateral compartment of the tibiofemoral joint. These findings were consistent, since initial loss of integrity in one region of the cartilage might cause increased permeability and increased hydration leading to increased JSW in another region of the knee. Other studies have found a reduction in the cartilage volume, starting from grade 1, particularly in the lateral compartment [8,9]. These differences can be explained, since the authors analyzed only the tibial cartilage and their data were adjusted for age, gender, body mass index and bone size. In this study the tibial and femoral cartilage were analyzed together to calculate the JSW. Further, the data were not adjusted.

An alternative explanation for the difference in the medial and lateral compartment data may relate to the fact that involvement of the lateral compartment is significantly less common than OA of the medial compartment, which carries more load [10]. In the absence of the significant narrowing of the joint space commonly seen medially, other factors included in the Kellgren and Lawrence grading system, such as the presence of osteophytes and subchondral sclerosis, contribute increased grade of OA. Additionally, the progression of medial compartment OA is often associated with a progressive valgus deformity of the knee, which, by itself, may lead to an apparent increase in the lateral joint space width. Our study measured total joint space in each compartment and not cartilage thickness per se. This may represent a less ideal method for evaluating the lateral compartment in the early stages of OA, but, as stated above, this is less common than disease of the medial compartment, where our method showed good sensitivity to differences in grades of OA.

Interestingly, a few anomalies were found in the data. In 20 patients the medial compartment was found to be thicker than the lateral, despite a more severe OA grading. This may have been due to osteophytes, cysts, or subchondral sclerosis. It may also have been caused by OA variants which show relative sparing of the medial compartment, such as calcium pyrophosphate deposition disease [11]. Our further studies will try to address these anomalies by comparing these findings with gait analysis data.

There were two limitations to this study. First, the MR images were acquired while the knees were not weight bearing. This study was performed on a large cohort of patients who were participants in a research study and were imaged by standard clinical MRI. A goal of this study was to evaluate the feasibility of using MRI imaging for longitudinal studies of OA. Another limitation was the small number of patients with severe (grade 4) OA of the patellofemoral and lateral compartments. Of a total of 612 knees which were graded radiographically, only two lateral compartments and 11 patellofemoral compartments were graded as severe OA (Kellgren and Lawrence grade 4). This was partly due to the study inclusion criteria, which specified inclusion of subjects with mild-to-moderate radiographic changes of OA, but also is explainable by the much more common medial compartment changes at the knee. Lateral or patellofemoral compartment arthritis is much less common than either medial or combined medial and patellofemoral OA [12].

The use of MRI for evaluation of degenerative changes of the knee joint is still in the early stages of development but is rapidly becoming the imaging method of choice for mild-to-moderate OA in clinical as well as investigational settings. Because of this fact, there is an increasing need for reproducible and accurate quantitative methods of measurement that could be used to document cartilage changes over time and which will correlate with other validated measures of OA progression, such as the well-established grading systems currently used in all longitudinal studies of OA involving imaging. This capability would also be useful for assessing disease progression and treatment efficacy, particularly treatments for early OA, where degeneration of articular cartilage might be interrupted or even reversed [13]. Several semi-quantitative, multi-feature scoring methods for whole-organ evaluation of knee osteoarthritis have been proposed [14,15]. These whole-joint measurement systems are more comprehensive than the MRI of JSWs performed in our study. However, these scoring systems are also much more time consuming. The JSW measurements are likely to correlate with the whole-organ evaluation of knee OA. Joint space narrowing provides an assessment of only one aspect of the disease process. This is evident by the fact that the JSW did not change between the more moderate grades of OA. The main advantage of JSW measurement is the limited time required to perform the evaluation. Future studies will assess the relative importance of both techniques.

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Fig. 1.
Combined tibiofemoral compartments

Fig. 2.
a Medial compartment. **b** Lateral compartment

Fig. 3.
Patellofemoral compartment

Table 1
JSW average ± standard deviation and results of statistical analysis for each joint/compartment. *Different letters represent statistically significant differences between averages*

OA grade	Combined tibiofemoral		Medial		Lateral		Patellar	
	Thickness (mm)	Group	Thickness (mm)	Group	Thickness (mm)	Group	Thickness (mm)	Group
0	4.23±0.96	A	3.73±1.05	A	4.34±0.91	A	3.53±0.89	A
1	3.97±1.00	B	3.38±0.7	B	4.51±0.93	A	3.31±0.91	A
2	3.74±1.04	B	3.12±0.69	B	4.37±0.97	A	3.33±0.96	A
3	2.8±1.14	C	2.54±0.95	C	3.66±1.28	B	2.73±1.39	B
4	1.8±1.05	D	1.74±0.9	D	3.22±3.31	N/A	2.07±1.11	C