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Atlas-based knee osteophyte assessment with ultrasonography and radiography: relationship to arthroscopic degeneration of articular cartilage

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Objectives: To investigate intra- and inter-reader agreement of ultrasonography (US) and conventional radiography (CR) for the evaluation of osteophyte presence and size within the tibiofemoral joint. In addition, to correlate these findings with arthroscopic degeneration of the articular cartilage.
Method: Forty adult patients with knee pain were enrolled in this study. Knee CR and US scanning of the medial and lateral bone margins were performed on all patients. A novel atlas for the US grading of knee osteophytes was used in the evaluation. The number and size of the osteophytes were evaluated semi-quantitatively in two rounds from both the CR images (four readers) and the US images (14 readers). The Noyes grading system was used for the evaluation of arthroscopic degeneration of the articular cartilage in 26 patients.
Results: On average, intra- and inter-reader US and CR agreement was substantial and comparable to each other ($\kappa = 0.60$–0.72). US detected more osteophytes than CR at both the medial (65% vs. 48%) and lateral (70% vs. 60%) compartments. A statistically significant correlation between CR- or US-based osteophyte and arthroscopy grades was observed only for US at the medial compartment ($r_s = 0.747$, $p < 0.001$).
Conclusions: The detection of knee osteophytes using the novel US atlas is as reproducible as reading conventional radiographs. US is more sensitive to detect knee osteophytes than CR. Furthermore, osteophytes detected with US correlate significantly with arthroscopic cartilage changes at the medial knee compartment whereas those detected by CR do not.

Knee osteoarthritis (OA) is a very common musculoskeletal disease that is becoming increasingly prevalent with the ageing of the population. Conventional radiography (CR) is generally the first and most widely used imaging method routinely applied to patients with suspected knee OA. Joint space narrowing, sclerosis of subchondral bone, subchondral cysts, and the formation of osteophytes are the key features revealed by CR in knee OA (1, 2). The formation of osteophytes can be regarded as a particularly important radiographic sign of OA as it has been reported that knee osteophytes detected with CR are accurate indicators of arthroscopic degeneration of the articular cartilage within the tibiofemoral joint (2). Kijowski et al (1) also reported that knee osteophytes were the most common radiographic finding in early OA (1).

Ultrasonography (US) is a promising, non-invasive imaging technique for the evaluation of knee OA that, in contrast to CR, involves no ionizing radiation and also makes the detailed imaging of soft tissue structures

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possible. US enables us to detect the presence of femoral and tibial osteophytes, joint effusion, synovitis, and also degenerative changes in parts of the femoral condylar cartilage (3). With regard to the detection of osteophytes, it has been shown that US can detect more osteophytes than CR in the small joints of the hand (4, 5). In the case of the tibiofemoral joint, the inter-reader agreement for detecting the presence of osteophytes by US is reported to range from substantial to excellent according to two experienced sonographers (6). However, there are no studies systematically comparing the performance of US and CR in the detection of osteophytes in the tibiofemoral joint using arthroscopy as a reference for the OA stage. Furthermore, in earlier US and CR studies of tibiofemoral OA, only osteophyte presence was typically evaluated and the size of the osteophyte was not taken into account.

The primary aim of this study was to systematically investigate intra- and inter-reader agreement of US- and CR-based evaluations of osteophytes and their size within a tibiofemoral joint. A novel image atlas was developed for the evaluation of osteophyte size by US. A secondary aim was to relate US- and CR-based osteophyte findings to the arthroscopic degeneration of the articular cartilage.

Method

Study group

Forty patients with knee pain [20 women and 20 men, mean age 56 (range 39–87) years] were randomly selected for the study. The patients fulfilled the American College of Rheumatology (ACR) criteria for classification of idiopathic OA (7). Twenty-six of the patients were from an orthopaedic clinic and underwent a diagnostic arthroscopy because of suspicion of a meniscal tear. The remaining 14 patients were consecutive in the daily patient list in a rheumatological outpatient clinic. All patients underwent weight-bearing knee radiography (CR) and knee US. The severity of the patients' OA was determined from radiographs with the traditional Kellgren–Lawrence (K-L) scoring system ranging from 0 (intact) to IV (severe OA) (8). K-L grades were distributed as follows: grade 0 = 22 knees, grade I = 8 knees, grade II = 7 knees, grade III = 2 knees, and grade IV = 1 knee. All patients gave their informed written consent and the study was approved by the ethics committee of Mikkeli Central Hospital.

CR

Conventional weight-bearing knee radiography (CR) was conducted on all of the patients using the anteroposterior technique, that is the knee in extension with the weight distributed evenly on both legs. The CR images for each patient were saved on a DVD and sent for evaluation to four radiologists with experience in musculoskeletal radiology.

The number and size of osteophytes on the medial and lateral femur and tibia were evaluated semi-quantitatively on CR images by four radiologists who used the Altman and Gold image atlas (9). This atlas uses the following semi-quantitative grading scale: 0 = no osteophyte, 1 = small osteophyte, 2 = medium osteophyte, and 3 = large osteophyte. After the first evaluation round, the radiographs were randomized and evaluated again by the same radiologists after 2 months. All the radiologists were blinded to the clinical, US, and arthroscopic findings on both rounds.

US

The US equipment used was Esaote Technos with a 13-MHz linear probe (LA424; Esaote Biomedica, Genova, Italy). The greyscale settings of the machine were kept constant for every patient and were as follows: depth = 35 mm, gain = 145 dB, enhancement = 11, mechanical index = 0.9, soft tissue thermal index = 0.5, processing parameter = 8, and scan correlation parameter = 6. US examination of the knee was performed on all patients by an experienced rheumatologist (JMK) within 4 months of the radiography. The rheumatologist was blinded to the knee radiographs and arthroscopic findings. In the US examination, the probe position was orientated longitudinally on the medial or lateral side of the joint space. The patient was in a supine position with the knee extended and the medial and lateral bone margins were scanned by moving the transducer over the joint space on both the femoral and tibial sides.

An osteophyte is defined as an abnormal step-up prominence of the bone usually located on the margins of the bone (2). A new US atlas for scoring osteophytes of the knee joint was developed before the study. It includes a semi-quantitative grading scale similar to that used in radiography, and was used for the first time in this study (Figure 1). After the US examinations, representative US images of each patient were saved on a DVD and sent for evaluation to 14 rheumatologists with experience in musculoskeletal sonography. After the first evaluation round, the US images were re-randomized and sent to the same rheumatologist for a second evaluation after 2 months. All the rheumatologists were blinded to the clinical, radiographic, and arthroscopic findings on both rounds.

Arthroscopy

An orthopaedic surgeon performed a knee arthroscopy on 26 patients after the imaging procedures. The surgeon was blinded to the US findings and grades but not to the clinical history or CR imaging findings. A semi-quantitative Noyes scoring system including a seven-step scale was used during the arthroscopy to grade

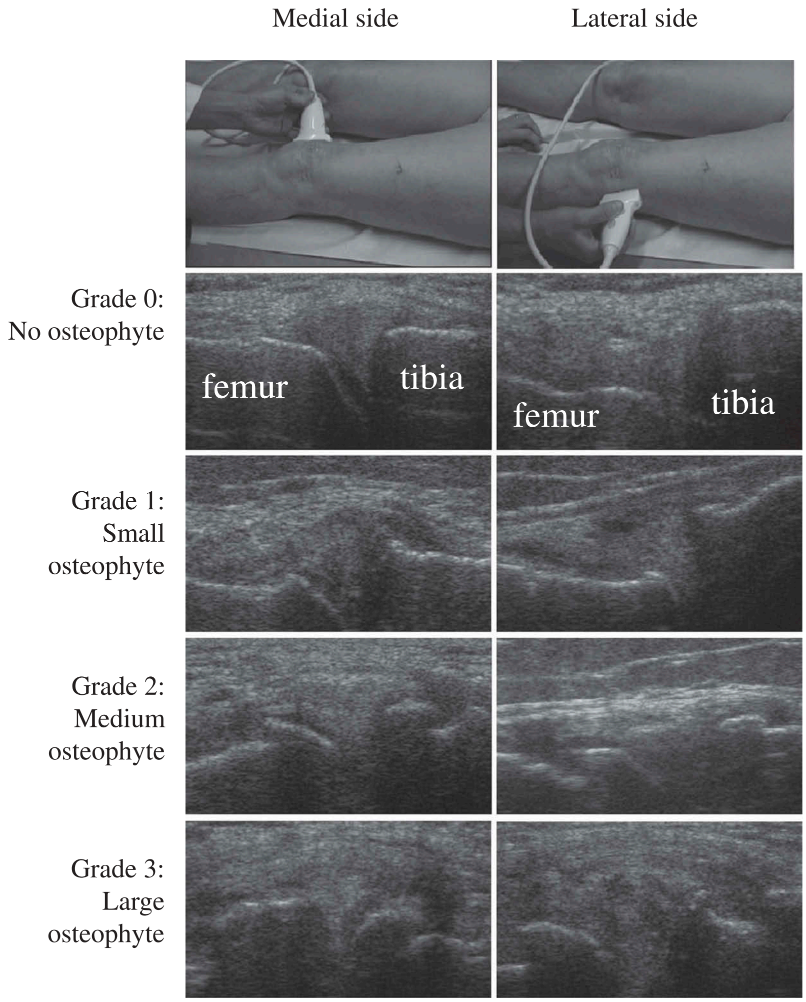

Figure 1. The ultrasonography (US) atlas created for knee osteophyte detection. All the readers had the atlas at their disposal during the grading process on both rounds.

the articular cartilage surface of the femoral medial condyle, the femoral intercondylar notch area, the femoral lateral condyle, and also the medial and lateral tibial plateaus (10).

Statistical analysis

Intra- and inter-reader US and CR agreement at each site was assessed by calculating a kappa coefficient between the readers. The kappa coefficients were calculated with an online calculator (11). A Randolph's free-marginal multi-rater kappa was calculated because the observers were not forced to assign a certain number of cases to each category (12). The kappa coefficient agreement was classified as: $\kappa = 0$, poor; $\kappa = 0.01–0.20$, slight; $\kappa = 0.21–0.40$, fair; $\kappa = 0.41–0.60$, moderate; $\kappa = 0.61–0.80$, substantial; $\kappa = 0.81–1.00$, excellent (13).

The grades of all the evaluators from both rounds were subsequently averaged and rounded to the nearest integer and the summed US, CR, and Noyes grades were calculated for the medial and lateral compartments of the tibiofemoral joint (medial femur, tibia, and lateral femur and tibia, respectively). As the grading scale for one site was 0–3 and both compartments included two sites, the summed US and CR grades varied between 0 and 6. Cross-tabulation and a χ^2 test were conducted to evaluate the differences in the distribution of summed osteophyte grades between US and CR in the medial and lateral compartments. Spearman's correlation analysis was used when relating grades between US, CR, and arthroscopy. Patients were finally divided into groups according only to the presence of osteophytes (size not taken into account) for both compartments separately and a one-way analysis of variance (ANOVA) was used to test the differences between the groups. All statistical analyses were conducted with SPSS version 19 (SPSS Inc, Chicago, IL, USA).

Results

Inter-reader US agreement was substantial on both rounds at the medial compartment ($\kappa = 0.601–0.649$) as well as the lateral femur ($\kappa = 0.698–0.704$) whereas it remained moderate at the lateral tibia ($\kappa = 0.456–0.478$) (Table 1). An average intra-reader US agreement was substantial at every site ($\kappa = 0.636–0.750$). The intra-reader agreement between the first and second rounds of evaluation was always at least fair ($\kappa > 0.50$)

Table 1. Intra- and inter-reader agreement for detection of osteophytes and their sizes using ultrasound (US) and conventional knee radiography (CR).

Location	Intra-reader κ values, mean (range)	Inter-reader κ values Round 1	Round 2
US			
Medial femur	0.750 (0.367–0.933)	0.649	0.639
Medial tibia	0.745 (0.567–0.967)	0.602	0.601
Lateral femur	0.752 (0.167–0.933)	0.704	0.698
Lateral tibia	0.636 (0.500–0.967)	0.478	0.456
CR			
Medial femur	0.742 (0.667–0.833)	0.744	0.728
Medial tibia	0.550 (0.300–0.733)	0.622	0.472
Lateral femur	0.558 (0.467–0.833)	0.688	0.411
Lateral tibia	0.658 (0.567–0.767)	0.606	0.506

to generally moderate (κ > 0.60) for all the observers separately, except for one observer who had only slight agreement at the lateral femur (κ = 0.167) and fair agreement at the medial femur (κ = 0.367). By contrast, there was only one observer who had excellent agreement at every site (κ > 0.90).

Inter-reader CR agreement was substantial at most of the sites in round one (κ = 0.606–0.744) but remained moderate at the lateral compartment (κ = 0.411–0.506) and the medial tibia (κ = 0.472) (Table 1). The average intra-reader CR agreement varied from moderate (κ = 0.550–0.558) to substantial (κ = 0.658–0.742). The intra-reader agreement between the first and second rounds of evaluation was always at least moderate (κ > 0.47) for all the observers separately, except for one observer who had fair agreement at the medial tibia (κ = 0.300). In contrast to US, none of the observers had excellent agreement at every site.

In general, US detected more osteophytes than CR at both the medial and lateral compartments (65% vs. 48% for US and CR at the medial compartment and 70% vs. 60% at the lateral compartment, respectively). The distributions of the summed grades between US and CR were significantly different at both compartments ($p < 0.001$, χ^2 test), being generally higher in the case of US.

The summed US and CR grades correlated significantly with each other at the medial compartment [$r_s = 0.574$, $p < 0.001$, 95% confidence interval (CI) 0.270–0.781; Figure 2A] whereas the correlation was lower at the lateral compartment ($r_s = 0.398$, $p = 0.011$, 95% CI 0.077–0.660; Figure 2B). A strong correlation between the summed US grade and the arthroscopic Noyes grade was observed at the medial compartment ($r_s = 0.747$, $p < 0.001$, 95% CI 0.505–0.888; Figure 3A) whereas the correlation between the summed CR grade and the Noyes grade was not statistically significant ($r_s = 0.289$, $p = 0.153$, 95% CI –0.191 to –0.615; Figure 3B). Neither the US grade nor the CR grade correlated with the Noyes grade at the lateral compartment (Figures 3C and 3D). When only osteophytes in the medial or lateral compartments were counted and the sum compared with the summed Noyes grades from the medial and lateral compartments, a statistically significant difference in the Noyes grade was observed only in the case of US at the medial compartment ($p < 0.001$ for US at the medial compartment, otherwise $p > 0.114$; Figure 4).

Discussion

This is the first study to report a systematic comparison of intra- and inter-reader agreement for US- and CR-based evaluations of the presence and size of osteophytes within the tibiofemoral joint. This study also cross-relates US- and CR-based osteophyte grades with arthroscopic grading, which has also not been reported previously. The current results suggest that using US for the detection of osteophytes and estimation of their sizes within the tibiofemoral joint is as reliable and reproducible as using CR, the current gold standard. The results also clearly demonstrate that US detects osteophytes with more sensitivity than CR and the osteophyte sizes

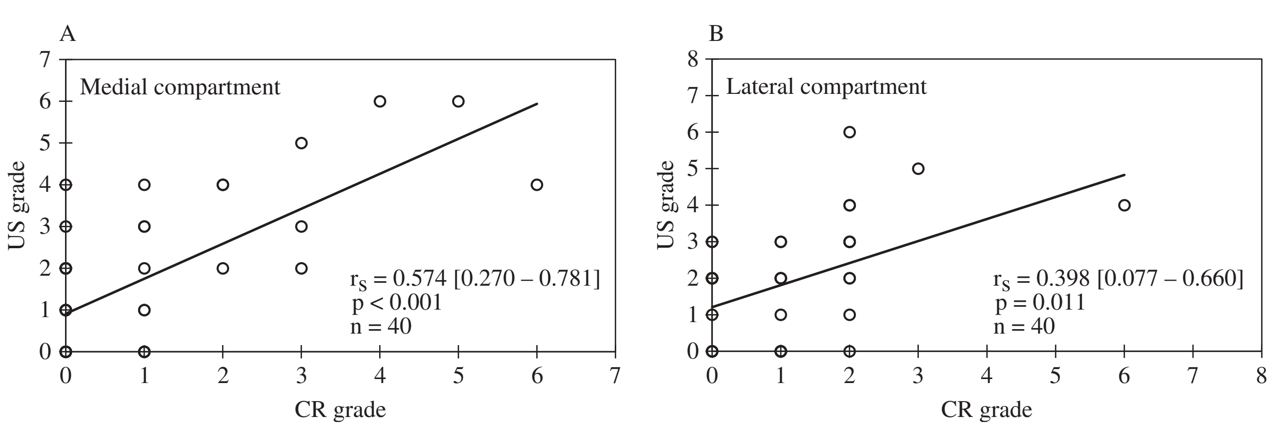

Figure 2. Spearman's correlation between the summed ultrasonography (US) and conventional radiography (CR) grades at (A) the medial compartment and (B) the lateral compartment. The linear fit is used solely for the purpose of illustrating the general trend of the relationship.

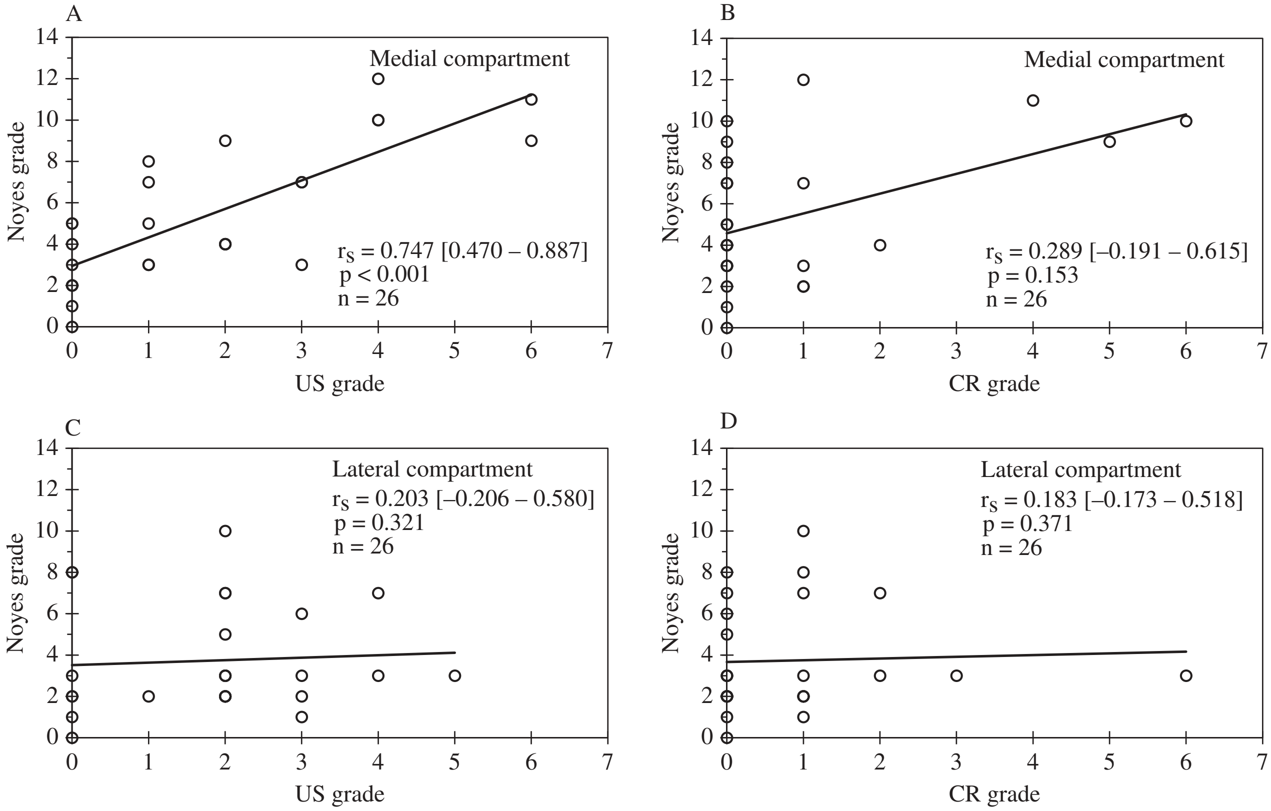

Figure 3. Spearman's correlation between: (A) the summed ultrasonography (US) grade and the arthroscopic Noyes grade at the medial compartment, (B) the summed conventional radiography (CR) grade and the arthroscopic Noyes grade at the medial compartment, (C) the summed US grade and the arthroscopic Noyes grade at the lateral compartment, and (D) the summed CR grade and the arthroscopic Noyes grade at the lateral compartment. The linear fit is used solely for the purpose of illustrating the general trend of the relationship.

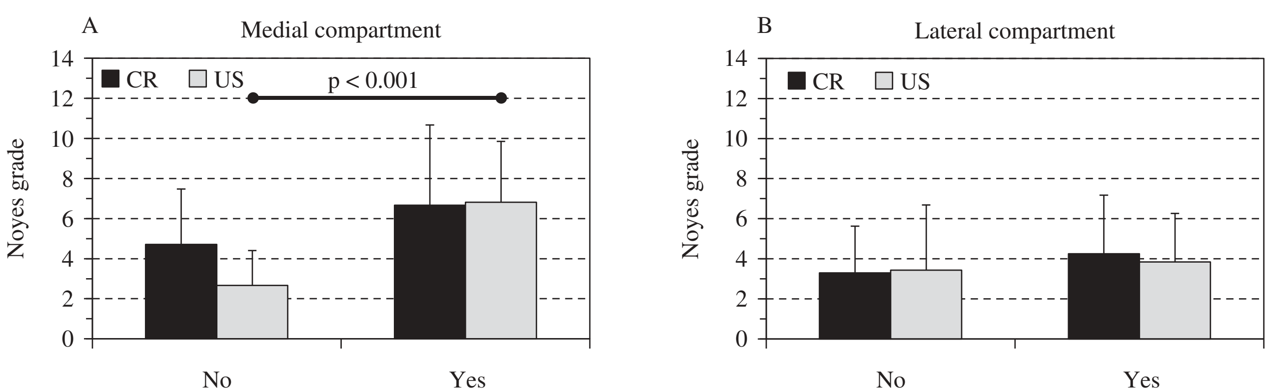

Figure 4. Average (± sd) Noyes grades as a function of the presence of osteophytes in (A) the medial compartment and (B) the lateral compartment. The statistically significant difference in Noyes grade was observed only for ultrasonography (US) at the medial compartment.

were generally larger in the US evaluation. Finally, we found a significant correlation between osteophyte size (summed US grade) and the arthroscopic grade of degenerative changes of the articular cartilage at the medial compartment whereas only a slight and statistically insignificant correlation between the summed CR grade and arthroscopy was observed.

A new semi-quantitative knee osteophyte grading atlas from US images was developed and used in this study. The atlas developed was essentially similar to a recently developed atlas for osteophyte scoring in finger joints (5). Both atlases include a semi-quantitative grading between 0 and 3. Mathiessen et al (5) also reported very high intra- and inter-reader agreement for their hand osteophyte atlas from two experienced readers (mean κ values > 0.91) (5). In a recent Outcome Measures in Rheumatology (OMERACT) study, 10 patients with hand OA were examined by 10 experienced sonographers using the hand OA atlas (14). In that report, the intra- and interobserver reliabilities of osteophyte scores were substantial to excellent (κ = 0.68–0.89). With our tibiofemoral osteophyte atlas, agreement was lower than that of Mathiessen et al (5), with an average of 0.72 and 0.60 for intra- and inter-reader agreement, respectively. There is an obvious explanation for this because Mathiessen et al (5) had only two experienced readers whereas 14 readers were used in this study and 10 readers in the OMERACT study (14). More readers naturally induce more variation in average agreement results but they also increase the strength of the current study as the average agreement was still substantial. The present US agreement results were also comparable to the current gold standard for osteophyte detection (the average κ values for CR were 0.63 and 0.60 for intra- and inter-reader agreement, respectively). Our results indicate that the inter-reader agreement of US for detecting osteophytes in the lateral tibia was worse than that of the other sites. However, the number of osteophytes detected with either US or CR did not differ significantly between the lateral and medial sites. Thus, it seems to be more difficult to detect osteophytes in the lateral tibia from US images using the current atlas. This issue warrants further investigations. However, we still suggest that this type of atlas for semi-quantitative grading of knee osteophytes will prove useful to the clinical and research community in the future.

The finding that US detected more and larger osteophytes in the tibiofemoral joint than CR has not been reported before. However, there are many studies in which the same findings have been reported for the small joints of the hand (4, 5, 15, 16). In their case it has been speculated that the main reason for this is the multiplanar nature of US whereas postero-anterior (PA) projection-based CR is mainly limited to lateral and medial osteophytes (5). The same explanation may apply to our findings as well. In contrast to hand joints, where also dorsal and palmar osteophytes can be seen with US (5), OA typically shows only medial and lateral osteophytes in the tibiofemoral joint. However, it is still possible to evaluate both sides in more detail with US than with PA-based CR. In a US examination, the beam is projected directly onto the osteophytes, with only soft tissues separating the transducer from the osteophytes. By contrast, PA-based CR projection includes a summation of all bony and soft tissue structures in front of and behind the osteophyte. Therefore, if the osteophyte is small and its density has not yet significantly increased, it may be missed in CR projection but can still be detected from the side with US. Overall, our results suggest that US is more sensitive than CR in detecting osteophytes in the knee, but the current study set-up cannot provide definitive proof. To confirm the specificity of the positive US findings, other three-dimensional (3D) imaging modalities (computed tomography or magnetic resonance imaging) or even direct visualization at autopsy should be used as a reference.

Another important finding of the present study is that osteophyte size, as detected with US, correlates significantly with articular cartilage degeneration at the medial compartment as verified by arthroscopy. Our earlier report, based on the same patient material, shows that the semi-quantitative US-based grading of degenerative changes in the femoral condylar cartilage has a high positive predictive value for actual arthroscopic degenerative changes (17). However, on the basis of the good correlation between the US-detected osteophyte grade and the Noyes grade (Figure 3A), and the significant difference in Noyes grade depending on the presence of medial osteophytes (Figure 4A), it seems that the presence and size of osteophytes evaluated with US is a significant predictor for arthroscopic degenerative changes in the articular cartilage. This is important because, with US, the evaluation of osteophytes is a very rapid (up to 5 min) and straightforward clinical procedure. It is also easy for new sonographers to learn.

This study has a few limitations that need to be addressed. First, US is well known to be an operator-dependent imaging modality. In this study only one sonographer (JMK) conducted the US examinations and selected representative images were saved on a DVD and sent for evaluation. Although this sonographer has had more than 25 years of experience in musculoskeletal US, the performance and agreement of knee US for osteophyte evaluation should also be investigated by different sonographers, including those with different levels of experience (from beginners to experts). In this regard, this aspect has been investigated in a study where the authors demonstrated that knee US in OA can be reliably performed even by operators with limited experience (18). However, in that study, agreement between sonographers on the presence of medial osteophytes could not be calculated because all the patients had one or several medial osteophytes. In addition, the authors did not evaluate the sizes of the osteophytes. In conclusion, agreement studies of US-based osteophyte evaluation in the tibiofemoral joint performed by different sonographers should be conducted in the future. The second limitation was that we only had four evaluators for knee CR. Because of time restrictions, we were unfortunately unable to recruit more radiologists willing to evaluate knee radiographs. However, many agreement and reproducibility studies have used only two evaluators. We therefore believe that the possible source of error from this particular circumstance should be acceptable. The final limitation is the low number of knee joints with K-L grade II or more (n = 10) and the relatively low number of patients included (n = 40). Thus, these findings should be replicated in the future using a larger sample with equally distributed K-L grades.

In conclusion, CR has traditionally been regarded as the gold standard for osteophyte evaluation. This study highlights the potential role of US in this diagnostic field due to its higher sensitivity. Furthermore, based on the strong association between osteophyte size and arthroscopic cartilage changes at the medial knee compartment, and the fact that US is an inexpensive and widely available imaging modality, it may be that US turns out to be a valuable first-line screening and diagnostic tool for patients with knee symptoms and OA.

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