CLINICAL STUDY

Ultrasonographic evaluation of the femoral cartilage thickness in patients with chronic renal failure

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ABSTRACT

Objective To investigate the effects of chronic renal failure (CRF) on the distal femoral cartilage thickness by using ultrasonography and to determine the relationship between cartilage thickness and certain disease-related parameters.

Design Fifty-seven CRF patients (41 male and 16 female) (mean [SD] age, 44.7 [12.1] years) and 60 healthy controls (41 male and 19 female) (mean [SD] age, 43.5 [13.3] years) were enrolled in this study. Demographic and clinical characteristics were recorded. Cartilage thickness measurements were taken from the medial and lateral condyles, and intercondylar areas of both knees.

Results Groups were similar in terms of age, weight, height, body mass index and gender (all p > 0.05). The mean cartilage thickness was found to be less in CRF patients than in controls (statistically significant for medial condyles and intercondylar areas both in right and the left knees [all p < 0.05]). Cartilage thickness showed no correlation with eGFR, and with the levels of serum urea, creatinine, calcium, magnesium, phosphor, hemoglobin, uric acid and as well as steroid use (all p > 0.05) in CRF patients.

Conclusion In the light of our findings, we imply that patients with CRF have thinner femoral cartilage than healthy controls. This result may support the view that patients with CRF are at increased risk for developing early knee osteoarthritis. Last but not least, clinicians should be aware of the importance of rehabilitation strategies aimed at decreasing onset and progression of knee osteoarthritis in patients with CRF.

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Introduction

Osteoarthritis (OA) is the most common form of arthritis characterized pathologically by focal loss of both articular cartilage and changes of the subchondral bone, mainly in weight-bearing joints. There are several local (previous injury, malalignment, muscle weakness) and systemic (age, female gender, race, genetic susceptibility, obesity) risk factors for OA. Chronic renal failure (CRF) has been reported to alter joint cartilage as well.

Previous studies of patients with CRF have noted degenerative changes but have not established whether this is in some way related to clinical parameters of CRF or is simply related to age. Moreover, plain radiographs have been used for the assessment joint space width. However, problems resulting from positioning of the joint, misalignment of the X-ray beams, and radiographic magnification have been postulated to impact the reproducibility of joint space width measurement.

Not to mention, previous studies have evaluated the small joints of the hands.

Joint pain which is a main consequence of cartilage loss, is an important problem in individuals with CRF. Moreover, main problem in this group of patient is the limited choices of medications because of the impaired renal functions. Thus, management strategies focusing on the pathophysiology of this issue may help the clinicians dealing with CRF. To the best knowledge of the authors, the effect of CRF on distal femoral cartilage has not been evaluated with ultrasonography (US) in the hitherto literature.

Accordingly, the present study aimed to investigate the effects of CRF on the distal femoral cartilage thickness by using US and to determine the relationship between cartilage thickness and certain disease-related parameters. In this regard, we used US—a valid and reliable method for such measurements.
Methods
Fifty-seven CRF patients (41 men and 16 women) who were admitted to our Nephrology outpatient clinic between October 2014 and August 2015 and 60 age- and sex-matched as well as body mass index (BMI)-matched healthy controls were enrolled in this study. Demographic and clinical characteristics of the patients including age, weight, height and BMI, estimated Glomerular Filtration Rate (eGFR), levels of serum urea, creatinine, calcium, magnesium, phosphor, hemoglobin, uric acid, as well as steroid use were recorded. Subjects who had a history of any other systemic disease (e.g., diabetes mellitus, thyroid abnormalities), knee trauma, any inflammatory/infectious arthritis, knee surgery, or intra-articular injection within the last 6 months were excluded. Also patients receiving dialysis and patients with disease duration less than 3 months were excluded from the study. Laboratory tests were not performed in healthy subjects. All patients and the controls were informed about the study procedure and they consented to participate. The Local Ethics Committee approved the study protocol.

The thickness of femoral articular cartilage was measured by a 7–12-MHz linear probe while the subjects were lying in supine position with their knees in maximum flexion. The transducer was positioned axially above the patellar outer edge. Cartilage thickness measurements were taken from the central points of the right medial condyle (RMC), the right lateral condyle (RLC), the right intercondylar area (RIA), the left medial condyle (LMC), the left lateral condyle (LLC), and the left intercondylar area (LIA). The distance between the thin hyperechoic line at the synovial space–cartilage interface and the sharp hyperechoic line at the cartilage–bone interface was measured as the cartilage thickness (Figure 1).

Statistical analysis
Data are expressed as mean (standard deviation) or percentage. Kolmogorov–Smirnov test was used to determine whether data followed a normal distribution or not. T-test was used to compare mean cartilage thickness values between the groups. Categorical variables were compared with the $\chi^2$ test. Among the patients, correlations between cartilage and disease-related parameters were analyzed by Pearson correlation coefficients. Statistical analysis was performed using the SPSS 16.0. Our study has a power of 90%. The level of significance was set at $p<0.05$.

Results
The demographic and clinical characteristics of the patients and the controls are presented in Table 1.
Groups were similar in terms of age, weight, height, BMI and gender (all $p>0.05$). The mean cartilage thickness was found to be less in CRF patients than in controls (statistically significant for medial condyles and intercondylar areas both in right and the left knees [all $p<0.05$], but not significant for lateral condyles) (Table 2).

Age has negative correlation with cartilage thickness for all regions both in CRF patients and controls (all $p<0.05$). Cartilage thickness has no correlation with eGFR, and the levels of serum urea, creatinine, calcium, magnesium, phosphor, hemoglobin, uric acid and as well as steroid use (all $p>0.05$) in CRF patients. Weight, height and BMI also have no correlation with cartilage thickness for all regions (all $p>0.05$).

**Discussion**

In this study, the authors aimed to explore the effects of CRF on the distal femoral cartilage thickness by using US and the relationship between cartilage thickness and certain disease-related parameters for the first time in the literature and the results of this study showed that femoral cartilage is thinner in CRF patients than in healthy controls, and that certain disease-related parameters of the patients did not have correlation with the femoral cartilage thickness.

Recent advances in musculoskeletal US have enabled quantitative assessment of articular cartilage thickness in different joints. In addition, due to its several advantages (i.e., being a quick, dynamic and cost-effective method), US was used as the imaging method in this study.

Arthralgia is commonly seen in CRF patients. Kart-Köseoglu et al. reported 37.8% and Kessler et al. reported 45% of CRF patients have joint pain. The pathogenesis of articular damage in CRF remains speculative. Several factors related to CRF have been identified as contributors to impaired joint cartilage proliferation and they include protein and calorie malnutrition, metabolic acidosis, growth hormone resistance, anemia, and renal osteodystrophy (secondary hyperparathyroidism, osteomalacia, osteoporosis, aluminum overload, adynamic bone disease, $\beta$-microglobulin deposition, osteitis fibrosa). Moreover, the interference of uremia and reduced mRNA levels for collagen X, parathyroid hormone/parathyroid hormone-related peptide receptor, and matrix metalloproteinase, as well as normal mRNA and protein expression for vascular endothelial growth factor and chondromodulin I, peptides related to the control of angiogenesis in CRF are suggested for impaired process of chondrocyte differentiation. In addition, a decreased immunohistochemical signal for growth hormone receptor and low insulin-like growth factor I mRNA in the proliferative zone of uremic cartilage are reported to be supportive of reduced chondrocyte proliferation.

In the current study, femoral cartilage in medial condyles and intercondylar areas both in right and the left knees was significantly thinner in CRF patients. This data supports the literature suggesting impaired chondrocyte proliferation and cartilage damage in CRF patients. However, cartilage thickness has no correlation with eGFR, and the levels of serum urea, creatinine, calcium, magnesium, phosphor, hemoglobin, uric acid and as well as steroid use. This would stem from the chronic process of the disease which is multifactorial and ubiquitous.

In this study, femoral cartilage was thinner in CRF patients; however it was significant for medial condyles and intercondylar areas both in right and the left knees, but not significant for lateral condyles. The reason may be dynamic biomechanical loading. In normal knee joints, the maximum femoral cartilage thickness is reported to be located in the middle of the femoral trochlea and in the intercondylar areas, where high contact pressures are known to act. The thicker cartilage in medial condyles and intercondylar areas represents the increased cartilage proliferation which would be interfered by the abovementioned processes in CRF patients.

The present study does have some limitations; primarily the small patient group with male predominance, and the lack of long term follow-up, as well as the
lack of duration of the disease. However, exact onset of the disease cannot be identified in considerable amount of patients who were diagnosed accidentally. A potential bias would have ensued due to the fact that the physician who performed the US was not blinded. Nevertheless, the results appear to be significant.

Overall, in the light of our findings, we imply that patients with CRF have thinner femoral cartilage than healthy controls. Although, whether this thinning predisposes to early degeneration of the knee joint remains to be elucidated in future studies, this result may support the view that patients with CRF are at increased risk for developing early knee OA. Last but not least, clinicians should be aware of the importance of rehabilitation strategies aimed at decreasing onset and progression of knee OA in patients with CRF.

Disclosure statement

Financial disclosure statements have been obtained, and the authors claim, there are no conflicts of interest associated with content of this article.

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