Sensitivity and Reproducibility of Ultrasonography in Calcium Pyrophosphate Crystal Deposition in Knee Cartilage: A Cross-sectional Study

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ABSTRACT. ***Objective.*** To compare the ability to detect calcium pyrophosphate (CPP) crystals deposition (CPPD) in knee cartilage by ultrasonography (US) and radiography.

Methods. Patients with knee effusion were consecutively included and underwent radiography and US evaluation of knees. Diagnosis of CPPD was made by the identification of CPP crystals. Two blinded rheumatologists performed US assessment.

Results. We included 51 patients (25 with CPPD). US revealed hyperechoic spots in all 25 patients with CPPD (sensitivity 100%, specificity 92.3%), whereas radiography revealed CPPD in 16 (sensitivity 64%, specificity 100%; $p < 0.0001$).

Conclusion. US of knees is more sensitive than radiography for CPPD diagnosis. (First Release June 15, 2015; J Rheumatol 2015;42:1511–13; doi:10.3899/jrheum.141067)

Key Indexing Terms:
ULTRASOUND PYROPHOSPHATE PSEUDOGOUT

In the last decade, ultrasonography (US) has been found useful in diagnosing gout[1] and calcium pyrophosphate disease (CPPD)[2]. When synovial fluid (SF) analysis is not available, deposition of calcium pyrophosphate (CPP) crystals can be identified by imaging[3]. To date, radiography is the main imaging modality used to detect CPPD[4,5]. The sensitivity of radiography is low[6] and US might represent an alternative imaging modality[7]. US appears to be highly specific and sensitive in detecting CPPD[8,9,10,11,12,13,14], and European League Against Rheumatism (EULAR) recommendations for CPPD highlighted its utility for the diagnosis of CPPD[3]. However, calcifications of hyaline cartilage and fibrocartilage seen on radiography can contain CPP crystals as well as basic calcium phosphate crystals[15,16]. Thus, in the absence of CPP in SF, the term *chondrocalcinosis* is recommended for calcification of hyaline cartilage and fibrocartilage[3]. In addition, comparison between US and radiography for detecting CPPD, and the reproducibility of US in this disease, have not been widely investigated.

We aimed to compare the diagnostic performance of US and radiography in detecting CPP deposition in knee cartilage.

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MATERIALS AND METHODS

Patients and study design. We consecutively included patients with knee effusion who underwent joint fluid analysis in this single-center cross-sectional study. All patients were recruited in a 6-month period in the rheumatology department of Bichat Hospital (Paris, France). Exclusion criteria were age < 18 years, previous knee surgery or trauma, and corticosteroid injection within the previous 3 months.

All patients underwent a clinical evaluation, including disease history and clinical examination. SF was analyzed by use of a compensated polarizing microscope to validate the presence of CPP crystals. Polarized light microscopy was performed by 1 senior rheumatologist (PD) who was blinded to clinical and imaging data. All patients underwent radiography of knees in both anteroposterior and lateral views and US evaluation. CPPD was diagnosed by the identification of CPP crystals in SF in accordance with recommendations[3]. Patients without CPP crystals in SF were considered controls.

Ethics statement. The Institutional Review Board (No. 12-011) of Paris North Hospitals approved this study. All patients gave their written informed consent.

US assessment. Two rheumatologists (SO and PAJ) used an Esaote Technos echograph (linear probe, 7.5–18 MHz) for bilateral US evaluations. The 2 sonographers had different experience in US (> 5 yrs for SO and < 1 yr for PAJ); they were blinded to clinical, laboratory, and radiographic findings. Each sonographer performed the US examinations blinded to US findings obtained by the other sonographer.

Before starting the study, the sonographer with less experience (PAJ) was trained for 1 month to detect CPP deposition (10 CPPD-proven patients). A consensus for US detection was defined before US evaluation.

Knee cartilage was explored on the transversal and longitudinal suprapatellar plane in maximal flexion. Lateral and medial knee menisci were assessed in flexion (30°) and complete extension.

Both knees were assessed for US features of CPPD (Figure 1). Hyperechoic spots within the cartilage were considered CPP crystal deposits. Meniscal calcifications were identified as hyperechoic spots within the meniscal fibrocartilage with similar echogenicity of bone despite low level of gain.

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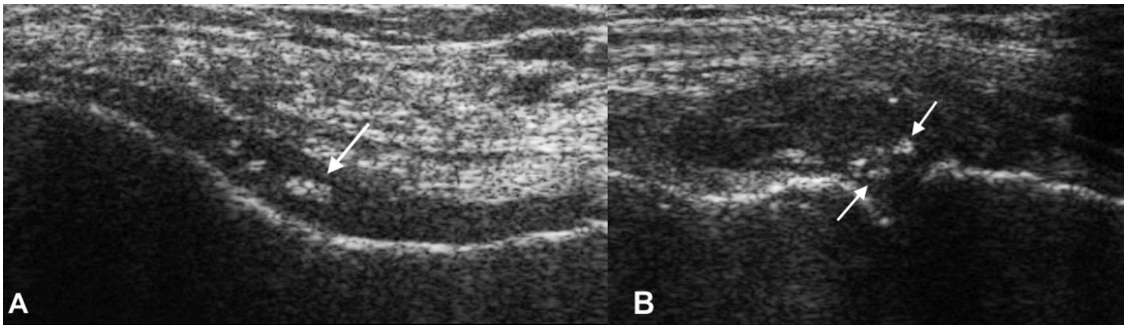

Figure 1. Ultrasound features of calcium pyrophosphate disease of the knee. Hyperechoic spots (white arrows) in the meniscus (A; lateral view with complete extension of knee) and trochlear cartilage (B; transversal view in maximal flexion).

In case of disagreement between the sonographers, the results obtained by the more experienced sonographer (SO) were used for calculating sensitivity and specificity. Interobserver agreement was assessed by the κ coefficient for each US feature. The intraobserver reliability of 1 sonographer (SO) was calculated with images obtained for 17 patients. These images were reanalyzed under blinded conditions at least 1 month after the initial assessment.

Radiography. Radiography of knees in both anteroposterior and lateral views was analyzed by a senior rheumatologist (AA) who was blinded to clinical data, laboratory findings, and US assessment. The presence of cartilage and/or menisci calcification was assessed to diagnose radiographic CPPD[3].

Statistical analysis. Data are presented as mean ± SD or number (%). We estimated the sensitivity (Se), specificity (Sp), and accuracy for US and radiography. Wilcoxon's test was used for quantitative variables and chi-squared test for categorical data. A 2-sided $p < 0.05$ was considered statistically significant. Interobserver and intraobserver agreement were estimated by the κ coefficient.

RESULTS

We included 51 patients (32 males, 63%) with knee effusion. The mean age was 66.1 ± 14.3 years. In all, 25 patients (49%) showed CPP crystals in SF. The remaining 26 patients without CPPD (controls) had gout (n = 9), spondyloarthritis (SpA; n = 8), osteoarthritis (n = 6), and rheumatoid arthritis (n = 3).

US and radiographic assessment (Tables 1 and 2). US revealed hyperechoic spots in menisci and/or cartilage in all 25 patients with CPP crystals (Table 2; Se 100%, Sp 92.3%), whereas radiography revealed CPPD in 16 (Se 64%, Sp 100%; $p < 0.0001$). The accuracy of US and radiography for the diagnosis of CPPD was 96.1% and 82.4%, respectively (Table 2).

US revealed menisci calcifications in 24 of the 25 patients with CPPD (96%) and in 2 of the 26 controls (7.7%). Left and right knees did not differ in prevalence of meniscal calcifications (76.7% vs 73.1%, respectively), and the lateral menisci tended to be more involved (92.3% vs 76.9%, $p = 0.12$). Hyperechoic spots in cartilage were noted in 19 patients with CPPD (76%) and 1 control patient (3.8%; $p < 0.0001$). No controls had radiographic features of CPPD.

Among the 2 control patients with US-observed calcifications, one 60-year-old male patient with gout had only 2 small spots in the medial right meniscus. The other control patient was a 78-year-old male with SpA who had small hyperechoic spots on the 2 right menisci and hyaline cartilage.

Interobserver and intraobserver agreement. Exact agreement between the 2 sonographers was obtained for 96% of US scans. Interobserver agreement was almost perfect ($\kappa = 0.87$) for overall US findings of CPPD (menisci and/or cartilage calcifications) and almost perfect for both menisci and hyaline cartilage calcification (both $\kappa = 0.81$). The interobserver agreement was better for lateral than medial menisci (0.96 vs 0.86). The intraobserver agreement was almost perfect ($\kappa = 0.918$).

Table 1. Ultrasonography (US) and radiography findings of calcium pyrophosphate disease (menisci and/or cartilage) in the whole sample. Data are number, or number (%) of patients.

	Radiography Features		
	Presence	Absence	Total
US features			
Presence	16	11	27 (52.9)
Absence	0	24	24 (47.1)
Total ($p < 0.0001$)	16 (21.4)	35 (68.6)	51

Table 2. Ultrasonography (US) and radiographic diagnostic performance by microscopy identification of calcium pyrophosphate crystals in synovial fluid.

	Sensitivity	Specificity	Accuracy
US overall calcifications*	100	92.3	96.1
US menisci calcifications	96	92.3	94.1
US cartilage calcifications	76	96.2	86.3
Radiography findings*	64	100	82.4

* Menisci and/or cartilage.

DISCUSSION

Our results confirm the ability of US for the diagnosis of CPPD. The accuracy of US used to detect CPPD in knee cartilage was high. These results reinforce the EULAR recommendations, which include US as a diagnostic tool for CPPD[3]. The specificity and sensitivity of US for the diagnosis of CPPD was also high. These results agree with

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previous studies of US, finding a high specificity (> 85%) and a sensitivity ranging from 68.7% to 96% for the assessment of menisci and/or cartilage[10,11,12,14,17].

In our study, US was able to detect CPPD in knees of all patients, whereas only 56% of patients had radiography findings of CPPD. This higher sensitivity of US as compared with radiography was emphasized by EULAR recommendations and previous studies[12,14,18]. The discrepancy between the 2 imaging techniques could be explained by the better spatial resolution of US and the possibility of analyzing a larger proportion of cartilage. Indeed, as suggested by Gutierrez, *et al*, the femoral cartilage is easily seen with US in parapatellar views[14]. Finally, the superimposition of bone and potential joint space narrowing (concomitant osteoarthritis) with radiography limits the detection of CPP deposits.

Additionally, US more frequently detected menisci than cartilage calcification (93% vs 75%). This better ability to detect CPPD in menisci than cartilage was also noted by Gutierrez, *et al*[14]. The authors observed meniscal calcifications in more than 90% of patients with CPPD but cartilage calcifications in only 60%. We found higher sensitivity of US for hyaline cartilage calcifications (76% vs 60%). This difference could be explained by the presence of effusion that could increase the visualization of calcifications in hyaline cartilage. Thus, in patients suspected to have CPPD despite normal radiographs, US may be useful for detecting chondrocalcinosis.

Although US is an operator-dependent imaging technique, the reproducibility of US in CPPD was good in our study. The second sonographer was a trainee, but interobserver agreement was almost perfect for each US feature of CPPD. This good reliability between sonographers, also mentioned in previous studies[10,14], suggests that US of CPPD is easy to learn. Additionally, US appears feasible for clinical practice in that all US examinations were performed in < 5 min (data not shown).

Our study was limited to the analysis of knees. Hence, further studies are required to examine US sensitivity for CPP detection in the wrist and other CPP deposition sites. In addition, the proportion of patients with CPPD seemed to be high in our study. One confounding factor would be that all patients were recruited in the Department of Rheumatology of a university hospital, which suggests a more severe clinical presentation, including pseudogout. In addition, our conclusions should be tempered by the possibility of detecting crystals other than CPP. Calcifications of hyaline cartilage and fibrocartilage seen on radiography can contain CPP crystals and also basic calcium phosphate crystals[15,16,19]. Thus, the US visualization of calcification in the absence of SF analysis could represent crystal deposition other than CPPD.

Finally, US seems to have better ability than radiography to diagnose CPPD, with good interobserver reliability.

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