Diagnostic accuracy of musculoskeletal ultrasound and conventional radiography in the assessment of the wrist triangular fibrocartilage complex in patients with definite diagnosis of calcium pyrophosphate dihydrate deposition disease

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Abstract

Objective

To compare the diagnostic accuracy of musculoskeletal ultrasound (MSUS) and x-ray in evaluating wrist triangular fibrocartilage complex (TFCC) in patients with calcium pyrophosphate dihydrate deposition disease (CPPD) and to investigate the agreement between the extent of the calcium pyrophosphate dihydrate (CPP) crystal deposits assessed by MSUS and the radiographic findings.

Methods

We enrolled 84 patients: 36 patients with "definite" CPPD and 48 controls. The Ryan and McCarty diagnostic criteria were used. A rheumatologist performed bilateral MSUS examinations of the TFCC in all patients, assessing both the presence and absence of CCP crystals deposits and their extent (0–3; 0: absent; 1: 1–2 spots; 2: more than two spots covering <50% of the volume of the structure; 3: deposits covering >50% of the volume of the structure). A radiologist evaluated the presence/absence of x-ray calcifications at TFCC level in both groups.

Results

MSUS and x-ray sensitivity was 77.8% and 76.4%, respectively, whereas MSUS and x-ray specificity was 90.6% and 96.9%, respectively. Total agreement between MSUS and radiographic findings indicative of calcifications at TFCC level was 88.7%.

Conclusion

This study supports the diagnostic accuracy of MSUS and x-ray in evaluating TFCC crystal deposits in patients with CPPD. Sensitivity and specificity of MSUS and x-ray resulted comparable. The highest MSUS score of the extent of the deposits correlated better with x-ray findings.

Key words

musculoskeletal ultrasound, conventional radiography, wrist triangular fibrocartilage complex, calcium pyrophosphate dihydrate deposition disease, diagnostic imaging

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Received on October 10, 2016; accepted in revised form on January 16, 2017.

Competing interests: none declared.

Introduction

Calcium pyrophosphate dihydrate deposition disease (CPPD) is a crystal related arthropathy characterised by deposition of calcium pyrophosphate dihydrate (CPP) crystals at articular and periarticular structures.

According to the criteria proposed by Ryan and McCarty, the diagnosis of CPPD is based on microscopic identification of CPP crystals in the synovial fluid and on imaging evidence of the typical calcifications on plain x-ray (1). Since the first descriptions of musculoskeletal ultrasound (MSUS) features of CPPD (2), MSUS has progressively gained a key diagnostic role (3) and its application is encouraged in the last European League Against Rheumatism (EULAR) recommendations for CPPD diagnosis (4). Two recent systematic reviews and meta-analysis carefully analysed the diagnostic performances of MSUS in CPPD (5, 6). Sensitivity and specificity of MSUS appeared excellent, at least as equal as those of conventional x-ray. Most of the MSUS studies were focused at knee level. Only two articles examined CPP crystals deposition with MSUS at triangular fibrocartilage complex (TFCC) of the wrist (7, 8). In the study conducted by Ellaban *et al*. (7), the authors compared MSUS and x-ray performances at wrist level: specificity was 100% for both the imaging techniques, whereas the sensitivity of MSUS resulted much higher than x-ray.

The objectives of the present study were: to compare the sensitivity and specificity of MSUS and x-ray findings indicative of CPP crystals deposition at the TFCC using the Ryan and McCarty criteria for the diagnosis of CPPD as gold standard and to investigate the agreement between the extent of the CPP deposits assessed by MSUS and the presence/absence of x-ray calcifications.

Patients and methods

Patients

A total of 84 patients attending the outpatient's clinic of the Clinica Reumatologica of the Università Politecnica delle Marche, Ancona, Italy, were consecutively enrolled in this study: 36 patients diagnosed with "definite" CPPD according to Ryan and McCarty criteria (both x-ray and synovial fluid analysis positive for the presence of CPP crystals) and 48 disease controls diagnosed with other rheumatic diseases according to the international diagnostic/classification criteria (17 rheumatoid arthritis, 9 psoriatic arthritis, 7 primary osteoarthritis, 7 ankylosing spondylitis, 5 systemic lupus erythematosus, 2 reactive arthritis, 1 gout). All controls were found negative for detection of CPP crystals using the synovial fluid analysis. In 6 out of 48 controls (3 patients with rheumatoid arthritis, 2 with psoriatic arthritis and 1 with osteoarthritis) conventional radiography of wrists and knees detected calcifications in only one anatomic site: in 3 patients at TFCC level and in the other 3 patients at knee level (*i.e*. medial meniscus). These patients, according to the Ryan and McCarty criteria, were also diagnosed with "possible" CPPD.

Knees, hands and wrists x-ray performed within the previous 12 months and synovial fluid analysis were required for patient eligibility. Exclusion criteria were: prior remarkable TFCC injuries or surgery procedures, severe wrists osteoarthritis not allowing MSUS or x-ray adequate visualisation of TFCC, age less than 55 years or more than 80 years in order to obtain better demographic homogeneity. The present investigation was carried out according to local regulations and the declaration of Helsinki. All the patients gave their informed consent.

Clinical examination

A clinically experienced rheumatologist (F.S.) collected demographic (age and gender) and clinical data of all patients (disease duration, synovial fluid analysis results and radiographs).

MSUS examination

A rheumatologist (A.D.M.) with 5 years of experience with MSUS, trained in the Clinica Reumatologica of the Università Politecnica delle Marche, Ancona, Italy, blinded to clinical and radiographic data, performed bilateral MSUS examinations of the TFCC in all patients. MSUS examinations were carried out using a Logiq 9 ultrasound

system (General Electrics Medical Systems, Milwaukee, WI, USA) working with a linear probe operating at 15 MHz. The scanning protocol included the movement of the probe from the dorsal aspect to the lateral one using a longitudinal scan passing through the extensor carpi ulnaris tendon sheath. The patients were asked to place the wrist lying in a prone position and slight radial deviation on the examination table. Parameters of grey-scale gain were adapted in order to enhance CPP crystals recognition (crystal deposits maintain high reflectivity, similar to the bony cortex, even at low level of gain value). MSUS-CPP crystal deposits at fibrocartilage level were defined as several thin hyperechoic spots rounded or amorphous-shaped, according to previously published criteria (9, 10).

First, a dichotomous score for presence/absence of MSUS-CPP crystals was assigned. Then, the sonographer evaluated the extent of the deposits according to the semiquantitative scoring system proposed by Filippou *et al*. (0–3; 0: absent; 1: 1–2 spots; 2: more than two spots covering <50% of the volume of the structure; 3: deposits covering >50% of the volume of the structure) (8) (Fig. 1). As suggested by Filippou *et al*., the scores were assigned based on the examination of the whole structure and not on the assessment of a single sonographic image.

X-ray examination

A radiologist experienced in the imaging assessment of musculoskeletal diseases (M.C.), blindly to both clinical and MSUS data, carefully evaluated wrists x-ray of both groups in order to evaluate the presence/absence of calcifications at TFCC level, according to the specific radiographic features suggested by Resnick *et al*. and Martel *et al*. (11, 12).

Statistical analysis

Data evaluation and statistical analysis were performed using MedCalc (Belgium, release 10.5) for Windows XP. Data were summarised with mean and S.D. Categorical data were analysed using chi-squared tests. Any value of $p<0.05$ was considered significant.

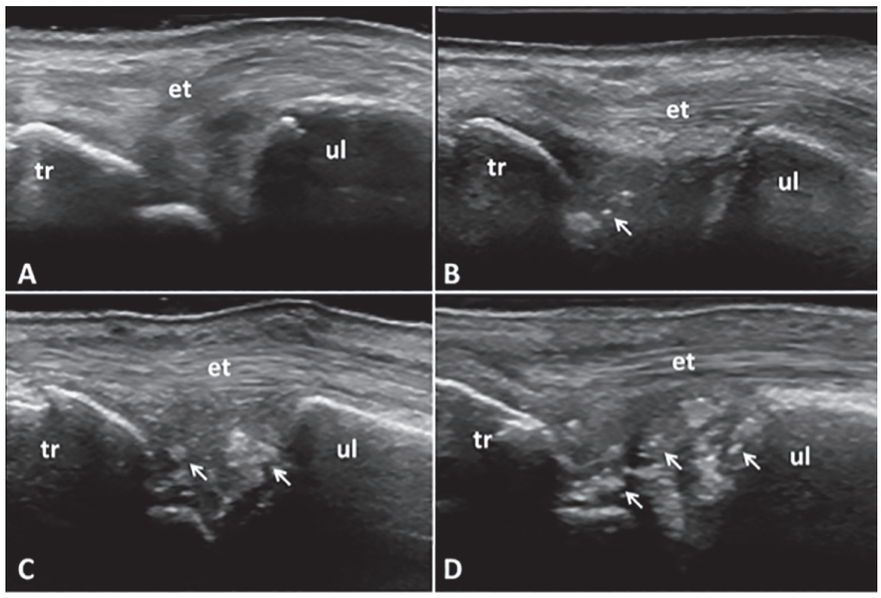

Fig. 1. MSUS images acquired using a longitudinal scan of the TFCC showing representative examples of the different extent of the CPP crystal deposits (representative hyperechoic spots are pointed out by arrows). A: no hyperechoic spots; B: 1–2 hyperechoic spots; C: more than two hyperechoic spots covering <50% of the volume of the TFCC; D: deposits covering >50% of the volume of the TFCC. et: extensors carpi ulnaris tendon; ul: ulna, tr: triquetrum.

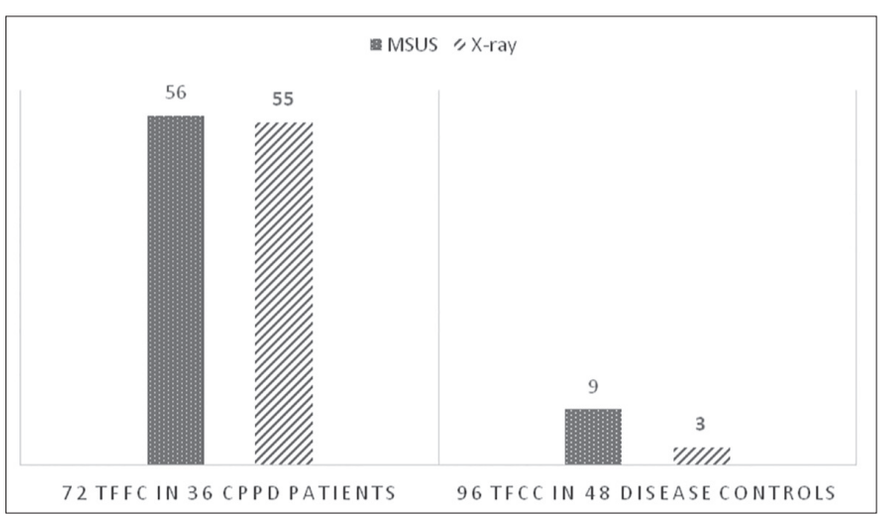

Fig. 2. Number of TFCC found positive for CPP crystal deposits using MSUS and conventional radiography in patients with CPPD and in controls. TFCC: triangular fibrocartilage complex.

Agreement between the MSUS findings (presence/absence and extent of the deposits) and the presence/absence of x-ray calcifications was calculated by overall agreement (percentage of observed exact agreement).

Results

We assessed 84 patients and a total of 168 TFCC (72 TFCC in CPPD patients and 96 TFCC in the controls).

The mean age in CPPD patients and controls were 74.8 years (range 56–80) and 68.1 years (range 58–78) respectively. Mean disease duration in CPPD patients and controls were 8.8 years and 13.4 years respectively. Female prevalence was 80.5% in CPPD patients and 60.6% in controls.

MSUS findings indicative of CPP crystal deposits were found in at least one wrist in 33 out of 36 CPPD patients (91.7%) and in 9 out of 48 controls (18.8%).

Radiographic calcifications were found in at least one wrist in 31 out of 36 CPPD patients (86.1%) and in 3 out of 48 controls (6.5%). In the 5 CPPD

patients without x-ray calcifications at wrist level, radiographic findings indicative of CPPD were detected at knee level bilaterally.

MSUS signs of CPP crystal deposits were detected in 65 out of 168 TFCC (38.7%): 56 in 72 wrists of CPPD patients (77.8%) and 9 in 96 wrists of controls (9.4%). Radiographic calcifications were detected in 58 out of 168 TFCC (34.5%): 55 in 72 wrists of CPPD patients (76.4%) and 3 in 96 wrists of controls (3.1%) (Fig. 2). The value of sensitivity and specificity of MSUS and x-ray is reported in Table I.

MSUS findings indicative of CPP crystal deposits were found in 33 CPPD patients: in 23 patients bilaterally (69.7%), in 10 patients unilaterally (30.3%). MSUS findings evocative of CPP crystal deposits were detected in only one wrist of 9 P controls. X-ray findings indicative of CPP crystal deposits were found in 31 CPPD patients: in 27 patients bilaterally (87.1%), in 4 patients unilaterally (12.9%). Intra-articular calcifications were detected by x-ray in only one wrist of 3 controls. The distribution of the different grades of the extent of deposits at TFCC level (based on the MSUS semiquantitative score previously illustrated) in CPPD patients and in controls is reported in Figure 3.

Agreement between the MSUS findings (presence/absence and extent of the deposits) and the presence/absence of x-ray calcifications is reported in Table II. Presence of CPP crystals using MSUS was defined with a grade higher than 1 because, according to Frediani *et al*., positivity requires the detection of "several" hyperechoic spots (*i.e*. more than 2 spots).

Table I. Sensitivity and specificity of MSUS and x-ray findings indicative of CPP crystal deposits at the TFCC using the Ryan and McCarty criteria for the CPP diagnosis as gold standard.

Imaging technique	Sensitivity	Specificity
MSUS	77.8%	90.6%
X-ray	76.4%	96.9%

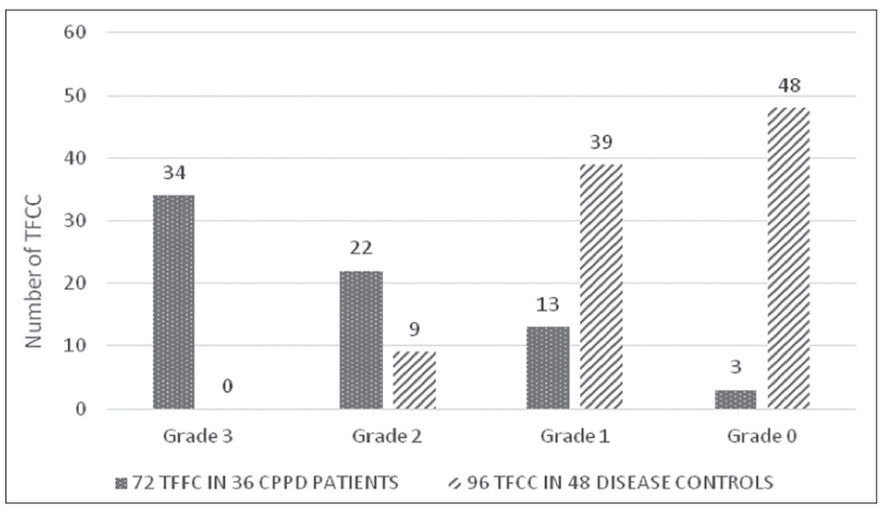

Fig. 3. Distribution of the different sonographic scores defining the extent of the deposits among the patients with CPPD and controls. In patients with CPPD, 34 out of 72 TFCC showed a grade 3 (47.2%), while in controls no grade 3 was found. A grade 0 was found in 3 out of 72 wrists of CPPD patients (4.2%) and in 48 out of 96 TFCC of controls (50%).

Discussion

Most of the available data regarding MSUS diagnostic accuracy for the detection of crystal deposits in CPPD patients rely on studies focused on the knee involvement (13-16). Our work supports the validity of MSUS in the detection of CPP crystal deposits at the wrist level using the definite diagnosis according to Ryan and McCarty criteria as gold standard. This is also the first study testing the accuracy of MSUS findings indicative of calcifications at wrist level by means of the scoring system recently introduced by Filippou *et al*.

Sensitivity of MSUS and x-ray resulted comparable (77.8% for MSUS, 76.4% for x-ray) whereas x-ray showed a slightly higher specificity than MSUS (96.9% *vs*. 90.6%). The grade of agreement of the two imaging techniques was noteworthy, although in some cases results of MSUS and x-ray differed. In 6 cases (3 patients with CPPD, 3 controls) calcifications were detected by plain x-ray but not by MSUS. This could be related to the fact that in some patients TFCC has a deep location, very close to the bone, which may impair the comprehensive evaluation of the structure by MSUS. In these 6 cases, in fact, calcifications on x-ray were located adjacent to the ulnar bone, an area difficult to explore with MSUS due to the presence of the overlying ulnar styloid process. Conversely, in 13 cases (4 patients with CPPD, 9 controls) crystal deposits were detected by MSUS but not by x-ray. Different density of calcifications and higher resolution of MSUS, which allows the detection of even submillimeter microcrystal aggregates, could explain why these deposits were not visible on x-ray (17). However, we cannot exclude that these hyperechoic spots were interpreted erroneously as CCP crystal deposits by the sonographer. The anatomical position of the TFCC and the presence of conditions which may be associated with hyperechoic spots (*e.g*. degenerative or traumatic injuries), as well as potential pitfalls, may lead to misinterpretation of the MSUS findings (18).

In the present study we also tested at TFCC level a recently proposed semiquantitative scoring system for assessing the extent of the CPP crystal deposits. The evidence we obtained is that higher MSUS scores better correlate with conventional x-ray findings and may decrease the risk of false positive. Conversely, when lower grades were found agreement with conventional x-ray and "specificity" progressively decreased. The detection of MSUS findings indicative of CPP crystal deposits in the controls (false positives) may be

Table II. Agreement between MSUS and x-ray findings.

	Radiographic findings		
MSUS findings showing a grade > 1	Presence	Absence	Total
Presence	52	13	65 (38.7%)
Absence	6	97	103 (61.3%)
$p<0.0001$	58 (34.5%)	110 (65.5%)	168
Total agreement: 88.7%			
	Radiographic findings		
MSUS findings indicative of grade 3	Presence	Absence	Total
Presence	33	1	34 (20.2%)
Absence	25	109	134 (79.85)
$p<0.0001$	58 (34.5%)	110 (65.5%)	168
Total agreement: 84.5%			
	Radiographic findings		
MSUS findings indicative of grade 2	Presence	Absence	Total
Presence	19	12	31 (18.5%)
Absence	39	98	137 (81.5%)
$p<0.0011$	58 (34.5%)	110 (65.5%)	168
Total agreement: 69.6%			
	Radiographic findings		
MSUS findings indicative of grade 1	Presence	Absence	Total
Presence	3	49	52 (31.0%)
Absence	55	61	116 (69.0%)
$p<0.061$	58 (34.5.0%)	110 (65.5%)	168
Total agreement: 38.1%			

mainly related to an increased reflectivity of collagen fibres that is the predominant component of fibrocartilage structures.

To note, when MSUS findings indicative of CPP crystal deposits were found in both wrists the diagnostic accuracy increased.

These findings prompt the following observations: in subjects with a clinical history suggestive of CPPD, the presence of MSUS grade 3 strongly supports the diagnosis; the detection of MSUS grade 1 or grade 2 provides a circumstantial but important evidence and should lead to seek for further sonographic findings of CCP crystal deposits in other anatomical areas characteristically involved in CPPD; last but not least, in the clinical setting evocative of crystal-related arthropathy, hands and wrists x-ray should be performed in case of negative or uncertain MSUS findings.

The present study has some limitations. First, the three examinations (MSUS, x-ray and synovial fluid analysis) were not performed simultaneously but within an interval time of 12 months. This may be relevant since we ignore the time required by the crystals to become detectable by these three different methods.

Another limitation is the lack of the synovial fluid analysis of the wrist joints in the 3 controls in which radiographic calcifications were detected at TFCC level. In these patients, the synovial fluid was aspirated from the knee, and its analysis was found negative for the detection of CPP crystals. Thus, these three patients did not satisfied the Ryan and McCarty diagnostic criteria of definite CPPD.

Conclusions

Our study demonstrates very good sensitivity and excellent specificity of both MSUS and conventional x-ray at assessing crystal depositions in CPPD patients at wrist level. The fibrocartilage echotexture and the anatomical position of TFCC may make this area difficult to assess with MSUS. This study provides additional evidence in support of the accuracy of MSUS in detecting and scoring TFCC calcifications. The extent of the deposits is an important factor to consider when assessing the TFCC in CPPD patients, as well as the unilateral or bilateral detection of the TFCC findings. MSUS grade 3 has a diagnostic value comparable to that of conventional radiography, whereas MSUS grade 1 and 2 provide circumstantial evidence for supporting the diagnosis of CPPD. Further studies are needed to integrate the semiquantitative scoring system with a pattern analysis based approach. In fact, CPP crystal aggregates may exhibit morphologic expressions highly disease specific not necessarily related to their extent and distribution.

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