Research Article

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Clinical and ultrasound concordance in the detection of synovitis in rheumatoid arthritis: a transversal study about 50 patients

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Objectives: Assessing the clinical ultrasound concordance in the detection of hands and wrists synovitis and determining the factors associated with such a concordance. Patients and methods: Single centre cross-sectional study related to 50 patients with Rheumatoid Arthritis (RA), included consecutively over a period of 21 months. The concordance between the clinical synovitis and the ultrasound one was assessed by calculating Cohen (k) coefficient. A correlation study between the concordance percentage at the patient scale with the clinical and biological parameters was conducted. Results: The concordance between the clinical examination and ultrasound in the detection of synovitis was too weak. The kappa coefficient varied from 0, 03 to 0, and 16. Likewise, the concordance between joint pain and ultrasound synovitis was overall at a low level (kappa between -0, 005 to 0, and 31) as well as the one between clinical signs (pain and/ or swelling) as well as ultrasound ones (synovial hypertrophy, effusion, Doppler signal) together, kappa coefficient was between 0, 03 and 0, 28. We objectified statistically significant positive correlations between the average concordance percentage and the low disease activity (DAS28<3, 2). Conclusion: Concordance between clinical examination and ultrasound in the synovitis detection was overall at a low level. These observations indicate the best ultrasound sensitivity. Disease activity was the major factor influencing such a concordance in the present study.

Keywords: rheumatoid arthritis • synovitis, clinical examination • hand ultrasound • concordance • associated factors

Introduction

Rheumatoid Arthritis (RA) displays rapid joint damage responsible for a major functional impairment. In order to avoid such a structural damage, the objectives of RA care evolved considerably aiming at the gain of a rapid as well as lasting clinical remission and the prevention of osteocartilaginous degradations [1]. Therefore, an early diagnosis together with a rigorous monitoring based on objective criteria is essential.

The clinical examination, of hands joints during RA, can prove to be tricky and often suffers from lack of sensitivity as well as objectivity. Some studies suggest that our examination is only able to detect less than half of the synovitis cases and often fail in the tenosynovitis detection [2-4]. Besides, patients within seeming clinic recovery can keep sub-clinical synovitis. Yet, the number of synovitis underestimation can be an obstacle to the treatment optimization. The control of the inflammation is then insufficient with a considerable risk of structural progression [5] and of recurrence in the short term [6-8]. A valid, accessible, reproducible and sensitive to changes examination is an undeniable need to help the practitioner in his therapeutic decisions.

The osteoarticuar ultrasound occupies for a long time a growing place in rheumatology [9-11]. Indeed, it allows the detection of synovitis and sub-clinical tenosynovitis, then displays, thanks to the power Doppler (DP), the synovial vascularization which is correlated to the histological synovial inflammation [12,13] and synonymous with the disease inflammatory activity.

We have established as an objective, during this study, to assess the concordance between the clinical examination and ultrasound in the detection of synovitis within a group of patients affected with RA and to look for the factors influencing such a concordance.

Patients and methods

Patients

This monocentric cross-sectional study, the first in Tunisian Centre, focused on patients affected with RA, meeting the criteria of 1987 Rheumatology American College [14].

The patients were included consecutively whatever the level of the illness activity. The non-inclusion criteria were manifested in the presence of severe or irreducible joint distortions compromising the completion of hands and wrists ultrasound, an osteoarthritis coexistence as well as hand surgery antecedent.

Methods

A rheumatologist was responsible, the same day for implementing the ultrasound and without having access to it, to collect the following data: age, sex, the duration of the illness evolution, the Patient's Global Assessment (PGA) by using a 0-100 Visual Analog Scale (VAS), the Number of Painful Joints (NPJ) and the Number of Swollen Joints (NSJ) of hands and wrists.

For each joint, pain and swelling were rated using a 0-1 scale. The disease activity was assessed by the Disease Activity Score 28 (DA S28) [15] and the functional consequences were estimated by the Health Assessment Questionnaire (HAQ) [16].

The erythrocyte sedimentation rate (ESR) first thing, the C-reactive protein (CRP), the presence or lack of the rheumatoid factor (RF) and of anti-cyclic citrullinated peptides (anti CCP) and the treatment were identified.

The whole hands and wrists ultrasounds were undertaken by a single radiologist with a Philips IU22 ultrasound scanner equipped with multi-frequency linear catheter (7.5 MHz).

The exploration was first carried out through dorsal stream then the palmar one. A total of 22 joints were explored for each patient: the wrists were studied through a cross-sectional and longitudinal section of the dorsal surface, wrist in a neutral position and probe centred on the third ray then through palmer scanning of the flexor tendons axial and longitudinal plane. As for the ultrasound data, were applied the Outcome Measures in Rheumatoid Arthritis Clinical Trials (OMERACT) group definitions [17,18].

Statistics

The data were analyzed using the Statistical Package for the Social Sciences (SPSS 18.0, Chicago, IL) software.

The concordance study between clinical and ultrasound data was assessed by calculating the percentage of concordance and the kappa coefficient for each of the 22 articulations (joints), whether it is the right or left side. κ interpretation was the following:

- $\kappa < 0$ means a discordance.
- $0 < \kappa \leq 0.20$ means a very low concordance.
- $0.20 < \kappa \leq 0.40$ means a low concordance.
- $0.40 < \kappa \leq 0.60$ means a moderate concordance.
- $0.60 < \kappa \leq 0.80$ means a good concordance.
- $0.811 < \kappa \leq 1.00$ means a very good concordance.

The links between two quantitative variables were studied by the Pearson correlation coefficient «r» which varies from -1 (perfect negative correlation: the higher a variable is, the lower the other and vice-versa to +1 (perfect positive correlation: the higher a variable is, the higher the other) by way of zero: No correlation. The meaning corresponds to «p», the meaning threshold being fixed at 0.05.

Results

Clinical and ultrasound data

One thousand one hundred joints were studied for 50 patients included in the study. Our population general characteristics are summarized in Table 1. Within the 1100 joints, the NPJ was of 224 (average NPJ about 4.4 ± 4.1). The NSJ was about 309 (average NSJ about 6.1 ± 4.5). An ultrasound synovial hypertrophy was detected in 738 articulations with an ultrasound synovitis number average number of 14.7 ± 6.1. The overall distribution of the painful and swollen articulations detail as well as the ultrasound data according to the articulation are illustrated in Table 2.

The clinical ultrasound concordance

Concerning the concordance between the clinical (joint swelling) and ultrasound synovitis detection (synovial hypertrophy), kappa coefficient equaled 0, 13 at the level of wrists,

Table 1. The population study general characteristics.

Sex	**Women n (%)**	**40 (80)**
	Men n (%)	**10 (20)**
Average age (years)		51.3 ± 15
Average disease duration (years)		5.5 ± 7.3
Average DAS28 DAS28 >3.2 n (%)		4.4 ± 1.5 40 (80)
Average HAQ		1.4 ± 0.8
Positive RF n (%)		37 (74)
Positive Anti CCP n (%)		35 (70)
Average ESR (accelerated SR%)		24.4 ± 17.9 (52)
CRP (High CRP %)		19.9 ± 30.5 (43.3)
Disease-modifying drug n (%)	cDMARDs	24 (48)
	bDMARDs	11 (22)
Corticosteroid therapy * n (%)		40 (80)

n: Number; %: Percentage; DAS28: Disease Activity Score; HAQ: Health Assessment Questionnaire; Anti CCP: Anti-Cyclic Citrullinated Peptide; RF: Rheumatoid Factor; ESR: Erythrocyte Sedimentation Rate; CRP: C Reactive Protein; cDMARDs: Conventional Disease Modifying Antirheumatic Drug; bDMARDs: Biologic Disease Modifying Antirheumatic Drug; *8 patients received le methylprednisolone in the form of boli the week before the ultrasound realization

Table 2. Global clinical and ultrasound data according to articulations.

	NPJ n(%)	**NSJ n(%)**	**Ult S n(%)**	**DP (+) n(%)**
Total	224 (20.3)	309 (28)	738 (67)	39 (3.5)
Wrists	54 (54)	52 (52)	61 (61)	14 (14)
MCP	110 (22)	180 (36)	325 (65)	25 (5)
IPP	50 (10)	71 (14.2)	352 (70.4)	-

MCP: Metacarpophangeal Joint; IPP: Proximal Interphalangeal Joint; NPJ: Number of Painful Joints; NSJ: Number of Swollen Joints; Ult S: Ultrasound Synovitis; DP (+): Positive Power Doppler signal

it varied from 0, 06 to 1, 6 at the level of MCP joint then from 0, 03 to 0,12 at the level of IPPs (Figure 1).

The percentage of concordance was of 57% at the level of wrists, it varied from 56 to 70% at the level of MCP and from 32 to 55% at the level of IPPs. Table 3 details concordance between clinical and ultrasound synovitis.

For the concordance between the joint pain and the ultrasound one, kappa coefficient and the concordance percentage were respectively 0, 12 and 57% at the level of wrists (Figure 2). Kappa coefficient varied from 0, 0A to 0.01 at the level of MCP and from -0.55 and 0.04 at the level of IPPs. The concordance percentage varied between 30 and 74% at the level of MCP and between 20 and 50% at the level of IPP. These concordance details are summed up in Table 4.

Finally, concerning global concordance between the combined clinical and ultrasound

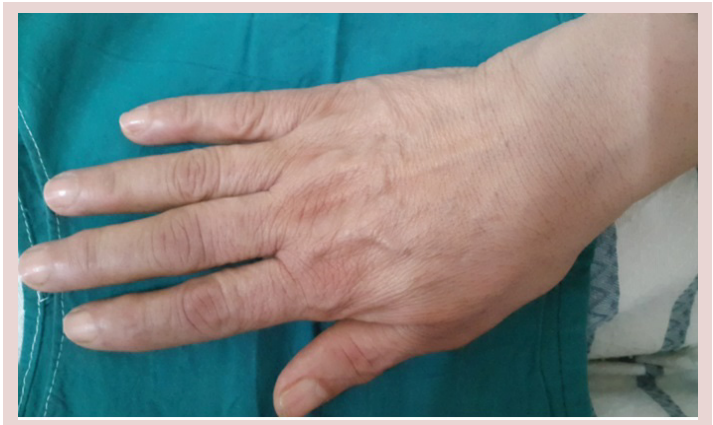

Figure 1. A female patient of 61 years, with RA ACCP+, RF-, whose complaining from polyarthralgia with morning stiffness of both hands. On clinical examination of wrist, MCP 2, 3, 4, 5 and PIP 2, 3 at the right hand were tender without swelling.

Table 3. Concordance between clinical and ultrasound synovitis.

Articulation	C S	Ult S		Kappa	IC à 95%	Concordance in%	95% IC
		Yes	No				
Wrists	Yes No	35 26	17 22	0.13	0-0.32	57	46.7-66.7
MCP1	Yes No	21 36	8 35	0.16	0-0.32	56	45.7-65.8
MCP2	Yes No	67 28	2 3	0.08	0-0.23	70	59.8-78.5
MCP3	Yes No	50 36	5 9	0.11	0-0.26	59	48.7-68.6
MCP4	Yes No	12 43	3 42	0.14	0.01-0.26	54	43.7-63.9
MCP5	Yes No	5 27	7 61	0.06	0-0.23	66	55.7-74.9
IPP1	Yes No	9 43	2 46	0.12	0.01-0.24	55	44.7-64.8
IPP2	Yes No	25 63	1 11	0.06	0-0.12	36	26.8-46.2
IPP3	Yes No	19 62	3 16	0.03	0-0.17	35	25.9-45.2
IPP4	Yes No	9 47	2 42	0.10	0-0.28	51	40.8-6.10
IPP5	Yes No	7 68	0 25	0.05	0-0.17	32	23.2-42.1

MCP: Metacarpianphalangeal Joint; IPP: Proximal Interphalangeal Joint; CI: Confidence Interval; CS: Clinical Synovitis; Ult S: Ultrasound Synovitis

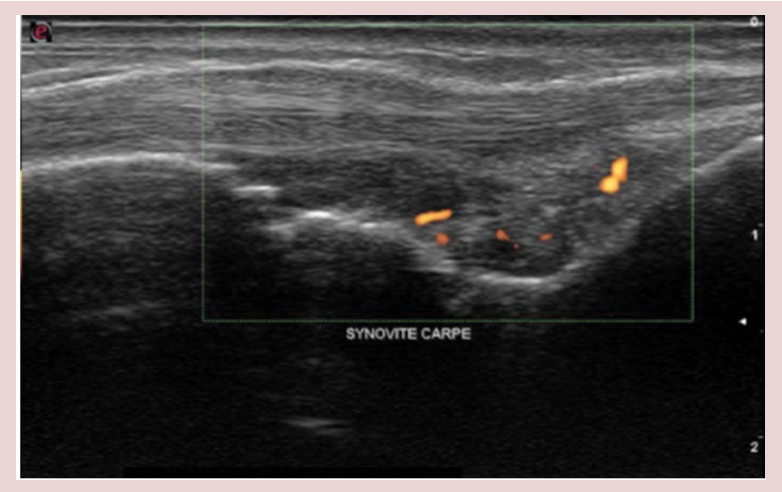

Figure 2. Ultrasound revealed a synovitis of the carp with positive powder doppler.

signs, kappa coefficient equaled 0.13 and the concordance percentage equaled 62% at the level of wrists. At the level of MCP, kappa coefficient varied from 0.02 to 0.28 and the concordance percentage varied from 56 to 68%. At the level of IPP, kappa coefficient and concordance percentage varied respectively between 0.02 and 0.13 and from 31 to 64%. These global concordance data are illustrated in Table 5.

Factors associated with the clinical-ultrasound concordance

At the patient's scale, the average concordance percentage between clinical and ultrasound in synovitis detection equaled 52.5% ± 19.2 (13, 6-81, 8%) (Figure 3). Correlations between this concordance percentage and the clinical parameters (age, evolution duration, DAS28, HAQ, EGP), as well as the biological parameters are illustrated in Table 6. Statistically significant correlations were objectified with the DAS28 and the EGP.

Discussion

Concordance between the clinical and the ultrasound synovitis

Table 4. Concordance between joint pain and ultrasound synovitis.

Joint	JP	Ult S		Kappa	95% CI	Concordance in %	95% CI
		Yes	No				
Wrists	Yes No	36 25	18 21	0.12	0-0.31	57	46.7-66.7
MCP1	Yes No	11 46	8 35	0.06	0-0.14	46	36-56.2
MCP2	Yes No	28 70	0 2	0.01	0-0.03	30	21.4-40.1
MCP3	Yes No	29 57	3 11	0.04	0-0.12	40	30.4-50.3
MCP4	Yes Non	13 42	2 43	0.17	0.05-0.3	56	45.7-65.8
MCP5	Yes No	11 21	5 63	0.31	0.11-0.5	74	64.1-82
IPP1	Yes No	5 47	3 45	0.03	0-0.13	50	39.9-60.1
IPP2	Yes No	9 79	1 11	0.005	0-0.04	20	12.9-29.4
IPP3	Yes No	11 70	5 14	-0.55	-	25	17.1-34.8
IPP4	Yes No	8 48	5 39	0.02	0-0.14	47	37-57.2
IPP5	Yes No	9 50	4 37	0.04	0-0.15	46	36-56.2

MCP: Metacarpianphalangeal joint; IPP: Proximal Interphalangeal Joint; CI: Confidence Interval; JP: Joint Pain; Ult S: Ultrasound Synovitis

Table 5. Global concordance between joint pain and ultrasound synovitis.

Joint	CE	UB+DP		Kappa	95% CI	Concordance in %	95% CI
		Yes	No				
Wrists	Yes No	44 18	22 16	0.13	0-0.33	62	49.7-69.5%
MCP1	Yes No	25 38	6 31	0.20	0.05-0.34	56	45.7-65.8
MCP2	Yes No	67 31	1 1	0.02	0-0.11	68	57.8 –76.7
MCP3	Yes No	53 36	4 7	0.10	0-0.24	60	49.7-695
MCP4	Yes No	18 40	4 38	0.19	0.05-0.33	56	45.7-65.8
MCP5	Yes No	17 29	5 42	0 .28	0.12-0.45	64	55.7-7.49
IPP1	Yes No	10 43	2 45	0.13	0.02-0.25	54	44.7-64.8
IPP2	Yes No	21 69	0 10	0.02	0.01-0.09	31	22.3-41.1
IPP3	Yes No	20 65	3 13	0.03	0-0.08	33	23.8-42.8
IPP4	Yes No	14 45	4 37	0.12	0-0.24	51	40.8-61
IPP5	Yes No	9 68	0 23	0.05	0.01-0.1	32	23.2-42.1

MCP: Metacarpianphalangeal joint; IPP: Proximal Interphalangeal Joint; CI: Confidence Interval; CE: Clinical Examination (Joint Pain and/or Swelling); UB+DP: B-Mode Ultrasound and Power Doppler Signal (synovial hypertrophy and /or effusion et/ou doppler sign)

Concordance between the clinical and the ultrasound synovitis was globally very low. These results are lower than those of Le Boedec et al. [19] and Garrigues et al. [20] and comparable to those of Ceponis et al. [21] who studied 612 joints (wrists and MCP) in 51 patients with former PR.

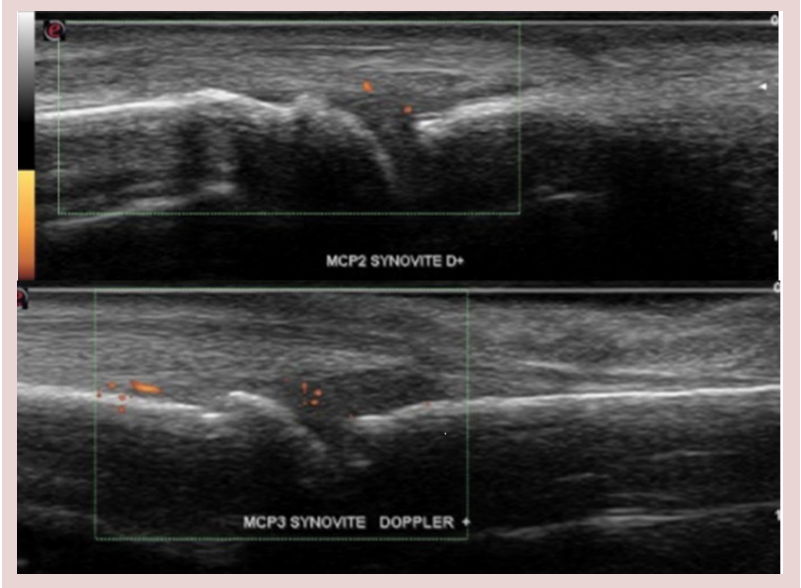

Figure 3. Inflammatory synovitis of the 2, 3 MCPs in the right hand.

Table 6. Correlations between the concordance percentage in the detection of synovitis and the clinical and biological data.

Biological and clinical parameters	Concordance %	r	p
Age (year)			
<40	55.6	0.03	0.90
≥40 et<60	48.7	0.06	0.79
≥60	51.5	0.06	0.82
Disease duration (year)			
< 2	52.1	0.23	0.34
≥ 2 et<10	47.2	0.51	0.83
≥10	60.3	-0.54	0.10
DAS28			
<3,2	59.3	0.68	0.03
≥3,2 et<5,2	77	-0.19	0.39
≥5,2	53.8	-0.094	0.71
HAQ			
<1	55	-0.087	0.72
≥1 et<2	47.4	0.2	0.39
≥2	56.3	-0.43	0.18
PGA			
<5	53	0. 33	0.09
≥5	50.1	-0.04	0.84
ESR (mm/h)			
<20	54.2	-0.20	0.36
≥20	49.8	0.17	0.38
CRP			
<6	53.5	0.32	0.14
≥6	48.9	0.31	0.12

DAS28: Disease Activity Score; HAQ: Health Assessment Questionnaire; ESR: Erythrocyte Sedimentation Rate; CRP:C reactive protein; PGA: Patient's global assessment.

Concordance between clinical and ultrasound synovitis was globally too low. These results were lower than those of Le Boedec et al. [19] and comparable to those of Ceponis et al. [21] who studied 612 joints (wrists and MCP) in 51 patients with former PR.

The concordance between joint swelling and synovial hypertrophy was very low with a kappa coefficient going from 0.06 to 0.17. Such a low concordance can be largely explained by the superiority of the ultrasound examination in the detection of synovitis and its complementary

potential interest to the clinical examination for an objective assessment of the disease progression. Moreover, the confusion between synovitis and tenosynovitis (false synovitis) during the clinical examination also contributes to such a low concordance [2,21].

Concordance between joint pain and ultrasound synovitis

The concordance between joint pain and ultrasound synovitis is very low at the level of wrists, MCP and IPPs. These results are similar to the study of Ceponis al. [21] where concordance equaled 0.11 at the level of wrists and varied between 0.01 and 0.17 at the level of MCPs. This concordance was lower than that of the clinical synovitis. This can be explained by several factors. We quote the high frequency of degenerative phenomena in particular at the level of IPPs (it may be recalled that the average age in our study was 53) and joint destructions secondary to old-established PR responsible for pains having no ultrasound translation especially without synovial hypertrophy [19].

Furthermore, the fibromyalgia associated with PR can be a plausible cause for joint pain. That's why some authors advise not to refer to DAS28 for the assessment of the disease activity in case of its association with fibromyalgia [22,23]. But rather to the Doppler ultrasound data [24,25] that reflect the PR real activity. Finally, some cold synovitis may ache.

Global concordance between clinical and ultrasound signs

The study of concordance between the reunited clinical parameters (pain and/or swelling) and the ultrasound ones (Doppler effusion, and/ hypertrophy and/or hyperemia) wasn't able to improve the concordance coefficient kappa except for MCP5. This coefficient remained globally low or even very low. These results are lower than those of Szkudlarek et al. [3] and al who found a concordance percentage equaling between 70 and 78% at the level of MCPs and of between 77% and 87% at the level of IPP by making this global comparison.

How to explain the difference between the clinical and ultrasound in the detection of synovitis?

Factors relative to assessment means

The main factor that could explain the gap between clinical and ultrasound is the non-objective character of our clinical examination attested by the important inter-practitioners variability as well as its non-discriminating character between articular and peri articular lesions [26-28]. It is commonly accepted that the clinical examination depends essentially on the examiner experience, so that a standardized formation in the clinical examination practice may reduce the variation in the detection of painful joints.

However, its impact on the swollen joints remains uncertain [29]. In Ogasawara et al. [30] study, 108 patients (1944 joints) were examined by the same practitioner. Afterwards, he achieved by him an osteoarticuar ultrasound in order to compare the clinical and ultrasound noticing. The concordance between the two was assessed at both the beginning and the end of the study. The final results were in favour of the improving of the concordance coefficient and the detection sensitivity of synovitis (40%) to the detriment of specificity decline by 18%. This auto-feedback rapidly improved the practitioner clinical competence. This study suggests that the ultrasound done by the rheumatologist himself improves his clinical examination which was not the case in the present work because of the ultrasound inaccessibility in rheumatologic department.

Ultrasound makes possible the sub-clinical synovitis detection. Its sensitivity is confirmed by taking the MRI as a reference method [3]. Although it is operator dependent, reproducibility between operators is good perhaps even excellent for an adequate apprenticeship of the ultrasound examination [31-34]. In this study, the ultrasound synovitis was assessed in a binary fashion. This binary response offers as benefit a good reproducibility in general, yet it is little sensitive to change [35,36]. The realization of an MRI as part of this study was not possible given the difficulty of its realization concurrently an ultrasound and especially its substantial cost.

Factors relative to patients and disease

Factors related to patients (age) and to disease (duration of the illness, biological and clinical activity signs), able to influence the concordance between the clinical and ultrasound in the detection of synovitis, have been studied. The influence of age is explained by the degenerative phenomena particularly at the level of IPP, able to compromise the synovial hypertrophy assessment which tends to be overestimated [31,37].

The influence of the disease progression duration is explained by the periarticular fibrosis and the structural damages without active inflammation during the old PR that can be confounded with a clinical synovitis [19]. A better concordance during recent PR than the established one was noticed in different studied [3,19]. In this way, the longer, the disease duration is, the worst the concordance is. This study found a non-significant negative correlation between an evolution duration superior to 10 years and the clinical-ultrasound concordance.

By contrast, this concordance was correlated in a positive way, with a significant difference, to the low disease activity attested by a lower than 3, 2 DAS 28. These results join those of Le Boedec et al. [19]. Finally, the HAQ, the EGP, the SR (Sedimentation Rate) and the CRP weren't significantly correlated to the clinical ultrasound concordance.

Methodology critics and the study limits

The number of patients was sufficient to allow the statistical analysis. Indeed, 50 patients were included and 1100 articulations were studied. Concordances between clinical and ultrasound data were practiced using Cohen Kappa coefficient which numbers the intensity or the capacity of the effective agreement between two variables by getting away from the random component.

However, the ultrasound results weren't compared to those of the MRI that remains the Gold standard in the detection of synovitis, of inflammation signs and of bone erosion.

Thus, the ultrasound results were not valid by a performing examination. This is due to the impossibility of access to the MRI within a short time in respect to the clinical examination as well as the ultrasound. In the absence of comparison with a gold standard, it is then impossible to provide a data comparison of the sensitivity and specificity of ultrasound in the detection of synovitis.

Conclusion

At the end of this pilot study, the first one in the Tunisian centre, we can conclude that there is a low concordance, between the clinical and the ultrasound examination in the detection of synovitis. This highlights the superiority of ultrasound in the assessment of PR activity. Some factors seem to influence this concordance in particular the disease activity. The osteoarticuar ultrasound integration in PR management, in current practice, is nowadays an undeniable need in order to improve the clinical examination unlikely to be enough to ensure the early diagnosis and the PR follow-up.

Declaration of interests

The authors declare not to have any interest conflicts in relation to this article.

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