The USSe (UltraSound Score for Erosions) in the evaluation of bone erosions in RA compared to the SHSe (Van der Heijde-modified Sharp score for erosions)

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ABSTRACT

Objective: To evaluate the relationship between the UltraSound Score for Erosions (USSe) and the Van der Heijde-modified Sharp score for erosions (SHSe).

Methods: 108 rheumatoid arthritis (RA) patients were included. On radiography: SHSe was evaluated by two or three blinded readers (in case of discordance). On ultrasonography: erosions were scored on six bilateral joints (MCP2,3,5; MTP2,3,5) with a four-point scale to calculate the USSe.

Results: The Pearson's correlation was good (r=0.68, p<0.001) and the agreement illustrated by a Bland-Altman plot was excellent (91%) between the two scores, which were complementary to detect erosions.

Conclusion: The USSe seems to be a valuable tool for assessing erosive damage in RA.

INTRODUCTION

The detection of bone erosions in rheumatoid arthritis (RA) is crucial since structural damages play a key role in diagnostic procedures, are indicative of a poor outcome and, thus, condition the therapeutic decision (1). Currently, radiography (RX) is considered as the gold standard for visualizing and quantifying bone lesions in patients with RA in clinical practice (2). The Van der Heijde-modified Sharp score (SHS) (3) with its good intra- and inter-reader reliabilities and good sensitivity to change (4), is considered as the standard scoring method to assess structural damage in RA in clinical trials. Many studies have shown that Ultrasonography (US) can detect more erosions than RX can at the joint level, with higher sensitivity and specificity than RX (5). Several qualitative (0/1) and semiquantitative (0-3) US scoring systems have been proposed (5–13), but to date, an international standardized erosion score does not exist. A recent literature review (14) showed that US appears as a valid and reliable tool for evaluating erosions in RA .

We have previously shown the interest of the USSe (UltraSound Score for Erosion), calculated from the examination of 12 selected Joints (30 joint facets analysed), was able to detect 2.0 times more eroded RA patients than radiography based on SHS for erosions (SHSe) (15).

The aim of this study was to evaluate the correlation and agreement between the USSe and the SHSe, and to identify the parameters that make the two scores diverge.

METHODS

Population

In this monocentric retrospective study performed at the department of Rheumatology between 2005 and 2016, RA patients fulfilling the ACR 1987 and/or ACR/EULAR 2010 were screened. US and RX examinations of the hands and feet were performed within 6 months. A complete assessment of the disease was performed (clinical, biological, RX, and US evaluations).

Radiography assessment

Postero-anterior views of hands and antero-posterior views of feet were performed and scored blindly of clinical and US information. Two independent readers (AP, MC) determined the modified Sharp/van der Heijde score for erosions (SHSe) with sub-scores for the hands and feet (16). In the case of discordance between them for a number of eroded joints less than or equal to three (corresponding to the threshold of EULAR 2013 definition of erosive RA), a third reader (ICV) served as blinded adjudicator. The SHSe corresponded to the mean of the scores from the two or three readers.

Ultrasound assessment

Standardized US examinations were performed by two operators (12 years of musculoskeletal practice) (ICV, DL) after several sessions conducted to calibrate the erosion scores. The equipment used throughout the study was the same: a Philips HD11 machine with a multi-frequency linear array transducer (5-12 MHz) with the focal length adjusted to the joint depth. US information was acquired under optimal technical conditions at 12 MHz (spatial resolution 0.1 mm) by operators blinded to the clinical and radiological data. Twelve pre-selected targeted joints have been systematically examined on B mode: metacarpophalangeal joints (MCPs) 2, 3, and 5 and metatarsophalangeal joints (MTPs) 2, 3, and 5. MCP4 and MTP4 joints, less commonly eroded in RA (5,17); MCP1 and MTP1 joints, affected by degenerative changes or metabolic diseases, were not included. Wrists were also excluded because of the lack of precise anatomic localization of the erosions in axial and longitudinal planes.

Localization and grading of erosions

Erosions were searched for on the dorsal (D) and palmar or plantar (P) facets of each joint and on the lateral (L) facet when accessible (MCP2, MCP5 and MTP5). On each facet, erosion was defined as a cortical defect with an irregular bone surface, observed in axial and longitudinal planes. Erosions were scored semi-quantitatively according to 4 grades: grade 0 = no erosion; grade 1 = single erosion <2 mm in its largest dimension; grade 2 = single erosion ≥2 mm and <3 mm in its largest dimension or no more than two erosions <2 mm; and grade 3 = single erosion ≥3 mm in its largest dimension or multiple erosions (n>2) (Supplementary Figure 1). The total US score for erosions (USSe) was the sum of the erosion grades for all eroded joints and ranged from 0 to 90.

Intra- and inter-examiner US reproducibility

Intra-examiner reproducibility was assessed on 11 RA patients according to two complete examinations per patient within 24 hours. Inter-examiner reproducibility was assessed on 14 RA patients examined independently on the same day by each operator. The intra-class correlation coefficient (ICC) values of the erosion US score for intra- and inter-examiner studies were 0.96 (CI95: 0.93–0.98) and 0.97 (CI95: 0.92–0.99), respectively. The inter reader reliability for the diagnosis of erosion (binary analysis) was excellent (Gwet's AC1: 0.80) (15). The inter reader reliability for the erosion grades at the facet level was moderate (Cohen's kappa: 0.59 (CI95: 0.51-0.65)).

Statistical analysis

The characteristics of the patients are presented as numbers and percentages for categorical variables and as means and standard deviations for continuous variables. Correlations between USSe and SHSe were analysed by Pearson's correlation coefficient. A Bland-Altman plot was applied on standardized value (= [X–mean]/standard deviations) in order to assess the agreement between the two scores. The significance level was set at 0.05 for the entire study. These statistical analyses were performed with SPSS version 23.0 (IBM Corp.). The ethical committee of Nancy approved the study in June 2017 (number: R2017-17). The consents of the patients were given orally.

RESULTS

Characteristics of the population

During the study period, 108 RA patients were included (Mean age: 55 ± 14 years old; Gender: 72.2% women; Disease duration: 71.3% ≥ 2 years; Mean DAS28:

3.6 ± 1.4; Mean CRP (mg/L): 9.4 ± 20.3; ACPA-positive: 72.2%; RF-positive: 58.3%). Means SHSe and USSe were 12.2 ± 19.9 and 9.6 ± 11 respectively.

Correlation between USSe and SHSe

Overall there was a good correlation between the two scores (Hands: r = 0.58, p<0.001; Feet: r = 0.67, p<0.001; Total: r = 0.68, p<0.001).

Agreement between USSe and SHSe

Bland-Altman plot showed an excellent agreement between the US and RX scores (Figure 2), since 98/108 patients (91%) had a mean difference between the two scores within -1.96 SD and +1.96 SD. Six patients (shown in red on Figure 2) were above the + 1.96 SD line and thus had considerably much more erosions found by the SHSe than by the USSe; their characteristics are detailed in Table 1. Four patients (shown in blue on Figure 2) were below the -1.96 SD line and thus had considerably much more erosions found by the USSe than by the SHSe; their characteristics are detailed in Table 2.

DISCUSSION

USSe is a reliable method to assess erosions in RA patients. At the facet level, the diagnosis of erosion is moderate while USSe was highly correlated between operators. Explanation may be advanced: erosion localized at 5 o'clock on the lateral facet of the MTP5 joint for example may be scored by one operator on the lateral facet and on plantar facet by the second one.

We demonstrated a good correlation between the USSe performed on 12 targeted joints and the SHSe, with an excellent agreement between both imaging techniques (91%).

Concerning the six patients having SHSe considerably higher than USSe, it can be firstly explained by the presence of massive erosions on wrist not examined on US. Except for the distal ulna, the wrist is too complex to be examined with precision by US in two different planes (18). Secondly, it can be explained by the presence of multiple erosions on other joints not examined or less accessible on US, such as MTPs1 and 4, MCP1 and 4 and PIPs joints.

Concerning the four patients having USSe considerably higher than SHSe, it can be explained by the presence of erosions on sites where US is known to be better than RX such as MTP5, MCP2 and MCP5 joints (14,18–20). The access to three facets allowing a near 180° assessment, potentiates the sensitivity of detection of erosions especially on the lateral facet more frequently affected (15) (7,9,19). Moreover, a facet with several erosions (n>2) yields a USSe of 3 while the radiography may be doubtful or graded 2 in this case.

Recently, Szkudlarek et al. showed in a review that researchers most frequently use US to assess finger and toe joints, where second and fifth MCP and fifth MTP were recommended as target joints, followed by the wrists and shoulders (14).

This scoring system could be useful as a clinical instrument to detect bone erosions with an acceptable time of acquisition. Future researches would be warranted to use it for clinical trials: contribution of additional localizations (ulna apophysis, shoulder, elbow, PIPs joints….), comparison to MRI which is considered as a more sensitive method to detect erosion, and finally an external validation process such as the OMERACT filter.

The USSe seems to be a useful tool for assessing erosive damage in RA, since it showed a good correlation and an excellent agreement with the SHSe, combined with an excellent reproducibility. US and RX remain complementary and must be combined to optimize the evaluation of structural damage in RA.

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Supplementary Figure 1. USSe grading of erosions (A: grade 0 = no erosion; B: grade 1 = single erosion <2 mm in its largest dimension; C: grade 2 = single erosion ≥2 mm and <3 mm in its largest dimension or no more than two erosions <2 mm; D: grade 3 = single erosion ≥3 mm in its largest dimension or multiple erosions (n>2)).

Figure 2. Bland and Altman plot showing the agreement between the SHSe and the USSe (SD: Standard Deviation).

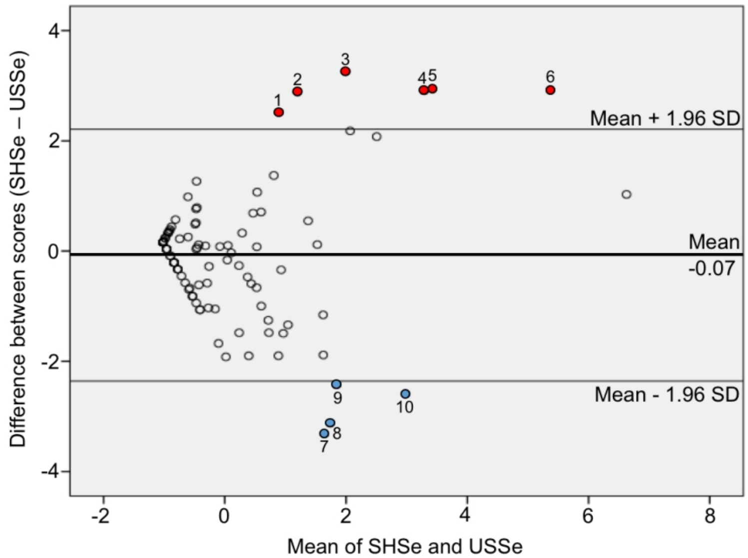


Figure 2. Bland and Altman plot showing the agreement between the SHSe and the USSe (SD: Standard Deviation).

338x190mm (108 x 108 DPI)

Table 1. Characteristics of the 6 patients (shown in red on Figure 1) who exceed the upper agreement limit and thus have SHSe considerably much higher than USSe.

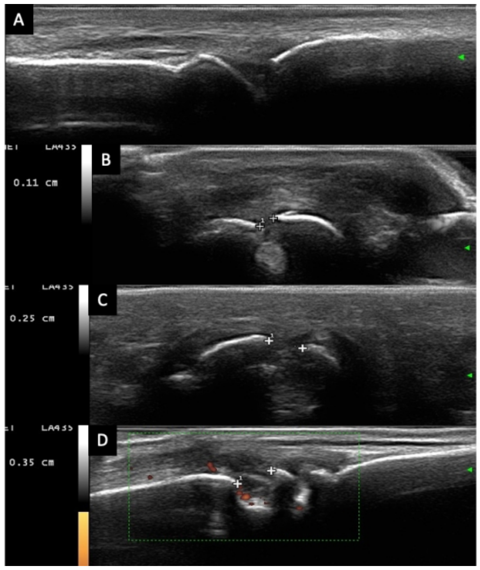
Patient	Disease duration (years)	SHSe (Total and at joint level ranked in descending order)	USSe (Total and at joint level ranked in descending order)
1	7	**Total = 40** Wrist = 32.5; MTP5 = 4.5; MTP4 = 2; MCP4 = 1	**Total = 6** MTP5 = 6 (L = 3, P = 3)
2	9	**Total = 46.3** Wrist = 31; MTP4 = 4; MTP1 = 3; PIPs = 2.7; MTP5 = 2.7; MTP3 = 1.3; MTP2 = 0.7; MCP1 = 0.7; MCP3 = 0.3	**Total = 7** MTP5 = 6 (L = 4; P = 2), MCP5L = 1
3	15	**Total = 59** Wrist = 29.5; MTP3 = 11; MTP2 = 5.5; MTP1 = 4.5; MCP2 = 3.5; MTP4 = 3.5; MCP3 = 1.5	**Total = 12** MCP2 = 6 (L = 4, D = 2); MTP3 = 4 (P = 2, D = 2); MTP5L = 1; MCP3D = 1
4	22	**Total = 73.5** Wrist = 40.5; MTP3 = 11.5; MTP2 = 9; MTP5 = 8.5; MCP2 = 2; PIPs = 1; MTP4 = 1	**Total = 24** MTP5 = 12 (L = 6, P = 6); MCP5L = 5; MCP2L = 4; MTP2P = 3
5	15	**Total = 75.5** Wrist = 37.5; MTP2 = 7.5; MTP5 = 7.5; MTP4 = 5.5; MTP3 = 5; MCP1 = 4; PIPs = 3.5; MCP2 = 1.5; MCP5 = 1.5; MCP3 = 1; MCP4 = 1	**Total = 25** MTP5 = 14 (P = 6, L = 5, D = 3); MCP2L = 6; MCP5L = 3; MTP2P = 2
6	34	**Total = 100.5** Wrist = 41; MTP3 = 12; MTP5 = 11; MCP2 = 10; MTP4 = 9.5; PIPs = 4.5; MTP1 = 2.5; MTP2 = 2.5; MCP1 = 2; MCP4 = 2; MCP5 = 2; MCP3 = 1.5	**Total = 41** MCP2 = 17 (L = 6, D = 6, P = 5); MTP5 = 13 (L = 6, P = 5, D = 2), MTP3 = 5 (P = 3, D = 2), MCP3 = 4 (P = 2, D = 2), MTP2P = 2

L: Lateral facet; P: Palmar/Plantar facet; D: Dorsal facet

Table 2. Characteristics of the 4 patients (shown in blue on Figure 1) who exceed the lower agreement limit and thus have USSe considerably much higher than SHSe.

Patient	Disease duration (years)	SHSe (Total and at joint level ranked in descending order)	USSe (Total and at joint level ranked in descending order)
7	1	**Total = 12** MTP4 = 3.3; MTP5 = 2.7; PIPs = 2; MCP2 = 1.3; MTP3 = 1; Wrist = 0.7; MTP2 = 0.7; MTP1 = 0.3	**Total = 36** MTP5 = 13 (L = 6, P = 6, D = 1); MCP2 = 9 (L = 6, P = 2, D = 1); MTP3 = 6 (P = 3, D = 3); MTP2 = 5 (D = 3, P = 2); MCP5 = 3 (L = 2, P = 1)
8	8	**Total = 14.5** Wrist = 8; MTP5 = 3; MCP2 = 1.5; MCP3 = 1; PIPs = 1	**Total = 36** MCP2 = 17 (L = 6, P = 6, D = 5); MCP5 = 9 (L = 6, D = 3); MTP5L = 6; MCP3D = 4
9	12	**Total = 20.3** MTP5 = 4.7; Wrist = 3.3; PIPs = 2; MCP2 = 2; MCP3 = 2; MTP1 = 1.7; MTP2 = 1.3; MTP3 = 1.3; MCP1 = 1; MCP5 = 0.7; MTP4 = 0.3	**Total = 34** MCP5 = 10 (L = 6, D = 4); MCP2 = 9 (L = 6; D = 3); MTP5 = 6 (L = 3, D = 3); MCP3D = 5; MTP2D = 3; MTP3D = 1
10	10	**Total = 34** MTP3 = 10.2; MTP2 = 7.8; MTP5 = 3.3; MCP2 = 3.3; MTP4 = 2.3; PIPs = 2; MCP3 = 1.7; MTP1 = 1.3; MCP1 = 1; Wrist = 0.7; MCP4 = 0.3	**Total = 44** MTP5 = 16 (L = 6, P = 6, D = 4); MCP2 = 14 (L = 6, P = 4, D = 4); MCP3D = 6; MCP5L = 5; MTP3P = 3

L: Lateral facet; P: Palmar/Plantar facet; D: Dorsal facet



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