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Evaluation of Bone Erosions in Rheumatoid Arthritis: The Ultrasound Score for Erosions Versus the Modified Sharp/van der Heijde Score for Erosions

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ABSTRACT. ***Objective.*** To evaluate the relationship between the UltraSound Score for Erosions (USSe) and the modified Sharp/van der Heijde score for erosions (SHSe).

Methods. One hundred eight patients with rheumatoid arthritis (RA) were included. On radiography, SHSe was evaluated by 2 or 3 blinded readers (in case of discordance). On ultrasonography, erosions were scored on 6 bilateral joints (metacarpophalangeal joints 2,3,5; metatarsophalangeal joints 2,3,5) with a 4-point scale to calculate the USSe.

Results. The Pearson correlation was good (r = 0.68, $P < 0.001$) and the agreement illustrated by a Bland-Altman plot was excellent (91%) between the 2 scores, which were complementary in detecting erosions.

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

Key Indexing Terms: joint erosions, radiography, rheumatoid arthritis, ultrasonography

The detection of bone erosions in rheumatoid arthritis (RA) is crucial because structural damages play a key role in diagnostic procedures, and as bone erosions are indicative of a poor outcome, they influence the therapeutic decision[1]. Currently, radiography is considered as the gold standard for visualizing and quantifying bone lesions in patients with RA in clinical practice[2]. The modified Sharp/van der Heijde score (SvdH)[3], with its good intra- and interreader 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 radiography can at the joint level, with higher sensitivity and specificity than radiography[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 previous literature review[14] showed that US appears to be a valid and reliable tool for evaluating erosions in RA.

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We have previously shown that the USSe (UltraSound Score for Erosion), calculated from the examination of 12 selected joints (30 joint facets analyzed), was able to detect 2.0-times more eroded RA patients than radiography based on SvdH 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 variables that make the 2 scores diverge.

MATERIALS AND METHODS

Population. In this monocentric retrospective study performed at the Department of Rheumatology between 2005 and 2016, patients with RA fulfilling the American College of Rheumatology (ACR) 1987 and/or ACR/European League Against Rheumatism (EULAR) 2010 were screened. US and radiographic examinations of the hands and feet were performed within 6 months. A complete assessment of the disease was performed (clinical, biological, radiographic, and US evaluations).

Radiographic assessment. Postero-anterior views of hands and antero-posterior views of feet were taken and scored blinded to clinical and US information. Two independent readers (AP, MC) determined the SHSe with subscores for the hands and feet[16]. In the case of discordance between them for the number of eroded joints ≤ 3 (corresponding to the threshold of the EULAR 2013 definition of erosive RA), a third reader (ICV) served as blinded adjudicator. The SHSe corresponded to the mean scores from the 2 or 3 readers.

US assessment. Standardized US examinations were performed by 2 operators (12 yrs of musculoskeletal practice; ICV, DL) after several sessions were conducted to calibrate the erosion scores. The equipment used throughout the study was the same: a Philips HD11 machine with a multifrequency 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 preselected targeted joints have been systematically examined on B mode: metacarpophalangeal (MCP) joints 2, 3, and 5 and metatarsophalangeal (MTP) joints 2, 3, and 5. MCP4 and

MTP4 joints, less commonly eroded in RA[5,17], and MCP1 and MTP1 joints, which are 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 and palmar or plantar facets of each joint, and on the lateral 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 semiquantitatively 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 2 erosions < 2 mm; and grade 3 = single erosion ≥ 3 mm in its largest dimension or multiple erosions (n > 2; Supplementary Figure 1, available with the online version of this article). 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 interexaminer US reproducibility. Intraexaminer reproducibility was assessed on 11 RA patients according to 2 complete examinations per patient within 24 h. Interexaminer reproducibility was assessed on 14 RA patients examined independently on the same day by each operator. The intraclass correlation coefficient (ICC) values of the erosion US score for intra- and interexaminer studies were 0.96 (95% CI 0.93–0.98) and 0.97 (95% CI 0.92–0.99), respectively. The interreader reliability for the diagnosis of erosion (binary analysis) was excellent (Gwet AC1 0.80)[15]. The interreader reliability for the erosion grades at the facet level was moderate (Cohen κ 0.59, 95% CI 0.51–0.65).

Statistical analysis. The characteristics of the patients are presented as numbers and percentages for categorical variables and as means and SD for continuous variables. Correlations between USSe and SHSe were analyzed by Pearson correlation coefficient. A Bland-Altman plot was applied on standardized value [= (X−mean)/SD] to assess the agreement between the 2 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 consent of the patients was given orally.

RESULTS

Characteristics of the population. During the study period, 108 patients with RA were included (mean age: 55 ± 14 yrs; sex: 72.2% women; disease duration: 71.3% ≥ 2 yrs; mean Disease Activity Score in 28 joints: 3.6 ± 1.4; mean C-reactive protein: 9.4 ± 20.3 mg/L; anticitrullinated protein antibody–positive: 72.2%; rheumatoid factor–positive: 58.3%). Mean SHSe was 12.2 ± 19.9 and mean USSe was 9.6 ± 11.

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

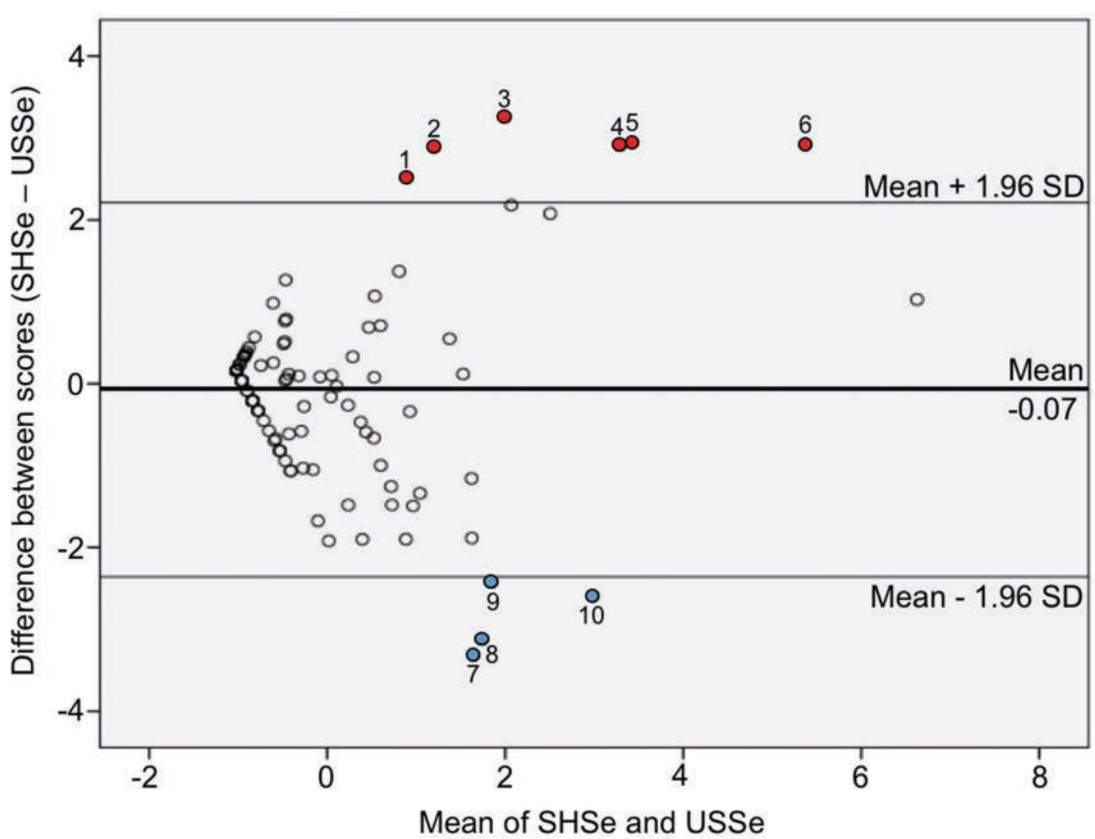

Figure 1. Bland-Altman plot showing the agreement between the SHSe and the USSe. SHSe: modified Sharp/van der Heijde score for erosions; USSe: UltraSound Score for Erosions.

DISCUSSION

USSe is a reliable method to assess erosions in patients with RA. At the facet level, the diagnosis of erosion is moderate while USSe was highly correlated between operators. The 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 the plantar facet by the second operator.

We demonstrated a good correlation between the USSe performed on 12 targeted joints and the SHSe, with an excellent agreement between the 2 imaging techniques (91%).

Concerning the 6 patients having SHSe considerably higher than USSe, it can first be explained by the presence of massive erosions on the wrist not examined on US. Except for the distal ulna, the wrist is too complex to be examined with precision by US in 2 different planes[18]. Second, it can be explained by the presence of multiple erosions on other joints not examined or less accessible on US, such as MTP1 and 4, MCP1 and 4, and proximal interphalangeal (PIP) joints.

Concerning the 4 patients having USSe considerably higher than SHSe, it can be explained by the presence of erosions on sites where

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

Patient	Disease Duration, yrs	SHSe*	USSe*
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; PIP = 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; PIP = 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; PIP = 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; PIP = 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

* Total and at joint level ranked in descending order. D: dorsal facet; L: lateral facet; MCP: metacarpophalangeal joints; MTP: metatarsophalangeal joints; P: palmar/plantar facet; PIP: proximal interphalangeal joint; SHSe: modified Sharp/van der Heijde score for erosions; USSe: UltraSound Score for Erosions.

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

Patient	Disease Duration, yrs	SHSe*	USSe*
7	1	Total = 12 MTP4 = 3.3; MTP5 = 2.7; PIP = 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; PIP = 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; PIP = 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; PIP = 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

* Total and at joint level ranked in descending order. D: dorsal facet; L: lateral facet; MCP: metacarpophalangeal joints; MTP: metatarsophalangeal joints; P: palmar/plantar facet; PIP: proximal interphalangeal joint; SHSe: modified Sharp/van der Heijde score for erosions; USSe: UltraSound Score for Erosions.

US is known to be better than radiography, such as MTP5, MCP2, and MCP5 joints[5,14,18,19]. The access to 3 facets allowing a near 180° assessment potentiates the sensitivity of detection of erosions, especially on the lateral facet more frequently affected[5,7,9,15]. 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.

In 2016, Szkudlarek, *et al* showed in a review that researchers most frequently use US to assess finger and toe joints, where the 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 research would be warranted to use it for clinical trials in terms of contributing additional localizations (ulna apophysis, shoulder, elbow, PIP joints, etc.) and making comparisons to magnetic resonance imaging, which is considered as a more sensitive method to detect erosion. This scoring system could also be useful as an external validation process such as the Outcome Measures in Rheumatology (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 radiographs remain complementary and must be combined to optimize the evaluation of structural damage in RA.

ONLINE SUPPLEMENT

Supplementary material accompanies the online version of this article.

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