

# A simplified radiographic score effectively predicts radiographic progression of early arthritis in a large nationwide French cohort

Guillermo Carvajal Alegria <sup>1,2,\*</sup>, Morgane Milin<sup>3,\*</sup>, Frédérique Gandjbakhch<sup>4,5</sup>, Alain Saraux <sup>1,2</sup>, Florian Bailly<sup>6,7</sup>, Sandrine Jousse-Joulin<sup>1,2</sup>, Thierry Schaevebeke<sup>8</sup>, Cédric Lukas<sup>9</sup>, Violaine Foltz<sup>4,5</sup>, Bruno Fautrel<sup>4,5</sup> and Valérie Devauchelle-Pensec<sup>1,2</sup>

## Abstract

**Objective.** Evaluating radiographic progression is a key component of the follow-up of patients with RA. Existing scores are ill-suited to everyday clinical practice. The objective here was to validate a new simplified radiographic score (SRS) for evaluating radiographic progression in patients with early arthritis.

**Methods.** Patients with arthritis of <6 months' duration were included in the large, prospective, nationwide, French ESPOIR cohort. Radiographs of the hands and feet were obtained at inclusion then 1 and 5 years later. The modified Sharp scores and SRS were determined by blinded readers. Interobserver reliability and intraobserver repeatability of each score, as well as agreement between the two scores, were assessed by computing the intraclass correlation coefficients. The rates of progression over the first year and the next 4 years were determined.

**Results.** The 506 patients with complete data for the first 5 years were included. At inclusion, the intraclass correlation coefficient between the two scores was good for erosions (0.715,  $P < 0.001$ ), joint space narrowing (0.892,  $P < 0.001$ ) and the total score (0.896,  $P < 0.001$ ). Agreement between the two scores was also good for radiographic progression after 1 year (0.781,  $P < 0.001$ ). The SRS had good positive and negative predictive values for slow and for rapid progression. SRS determination was less time consuming.

**Conclusion.** The SRS is effective for monitoring radiographic progression in early arthritis and is easier to use and less time-consuming than the Sharp score. The usefulness of the SRS in clinical practice deserves further evaluation.

**Key words:** radiographic score, erosion, joint space narrowing, RA

### Rheumatology key messages

- The simplified radiographic score and the modified Sharp score do correlate.
- The simplified radiographic score has good predictive values for structural progression in RA.
- The simplified radiographic score only takes 1' 40" to assess one set of radiographs.

## Introduction

RA is a chronic autoimmune disease characterized by synovial inflammation and joint destruction [1]. Its prevalence in France is 0.3% [2]. Persistent inflammation leads to destructive joint lesions including erosions and joint space narrowing (JSN). Standard radiographs are

recommended for the diagnosis and follow-up of RA. In patients with early arthritis, radiographs are crucial to the diagnosis, as the presence of a typical erosion is pathognomonic for RA [3]. Furthermore, radiographic findings contribute to assessment of disease severity and help to adjust the treatment. Several scores have been developed for measuring radiographic progression in RA [4, 5]. The

<sup>1</sup>UMR1227, Lymphocytes B et Autoimmunité, Université de Brest, Inserm, LabEx IGO, Brest, <sup>2</sup>Rheumatology Department, Cavale Blanche Hospital, Brest, <sup>3</sup>Rheumatology Department, Hôpital Yves Le Foll, Saint-Brieuc, <sup>4</sup>Sorbonne Université, UMR S 1136, Institut Pierre Louis d'Epidémiologie et Santé publique, Paris, <sup>5</sup>APHP, Pitié Salpêtrière Hospital, Rheumatology Department Unit, Paris, <sup>6</sup>Sorbonne University, Paris, <sup>7</sup>Pitié Salpêtrière Hospital, APHP, Pain Unit, Paris, <sup>8</sup>Rheumatology Department, Pellegrin Hospital, Bordeaux and <sup>9</sup>Rheumatology Department,

Montpellier University, Montpellier Hospital and EA2415, Montpellier, France

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\*Guillermo Carvajal Alegria and Morgane Milin contributed equally to this paper.

Correspondence to: Valérie Devauchelle-Pensec, Unit of Rheumatology, Hôpital de la Cavale Blanche, BP 824, F 29609 Brest cedex, France. E-mail: valerie.devauchelle-pensec@chu-brest.fr

most commonly used in clinical research on biologic agents is the Sharp score modified by van der Heijde (SvHS) [6]. Special training and considerable time are needed to determine the SvHS [7], which is consequently not used in clinical practice. In 1999, van der Heijde proposed the simpler Simple Erosion Narrowing Score (SENS) based on the same parameters and joints as the SvHS [8]. The SENS requires less training and less time than the SvHS but is less sensitive to change and may be limited by a major ceiling effect.

The rate of radiographic progression is highest during the first 2 years after RA onset, and most of the damage occurs in the first 5 years. The presence of one or more erosions and/or of JSN at onset strongly predicts radiographic progression [9]. Other predictors of radiographic progression are the presence of ACPA, high RF titres and marked CRP elevation. Furthermore, a faster rate of progression over the first year predicts further rapid progression as assessed using the SvHS [10]. Many controlled trials support early intensive treatment according to a treat-to-target strategy as a means of improving patient outcomes [11]. The most appropriate treatment target was found to be a complete remission defined not only as the absence of signs and symptoms of RA but also as the absence of continuing radiographic progression [12, 13]. Therefore, a simplified radiographic score (SRS) suitable for use by rheumatologists in their everyday practice would be valuable.

In a prospective 2-year investigation into whether synovitis predicted radiographic progression in patients with RA, erosions and JSN were assessed using a simplified semi-quantitative 4-point score (from 0, none, to 3, major) [14]. In addition, at each joint, global progression, erosions and JSN were assessed in a binary fashion (0, no change; 1, worsening).

Our objective here was to validate a SRS vs the SvHS (the current reference standard) for assessing radiographic structural damage in a cohort of patients with early arthritis, at baseline then 1 and 5 years later. To this end, we used radiographs obtained in the prospective ESPOIR cohort of patients with arthritis onset within the past 6 months.

## Methods

### Study population

The Société Française de Rhumatologie (French Society for Rheumatology, SFR) established the nationwide, multi-centre, prospective ESPOIR (Etude et Suivi des Polyarthrites Indifférenciées Récentes) cohort [15, 16] (NCT03666091) to enable investigations of the diagnosis, outcome markers, epidemiology, pathogenesis, and medico-economics of early arthritis and RA. General practitioners and rheumatologists referred patients with early arthritis to hospitals participating in the ESPOIR project. The main inclusion criterion was a definitive or probable clinical diagnosis of RA or of polyarthritis not better explained by another aetiology. Other inclusion criteria were age older than 18 years and younger than 70 years,

swelling in at least two joints for at least 6 weeks but no longer than 6 months, availability of radiographs of the hands and feet taken at inclusion then 1 and 5 years later, and no prior treatment with DMARDs or glucocorticoids except, for the latter, in a mean dosage  $\leq 20$  mg/day for  $\leq 2$  weeks with discontinuation at least 2 weeks earlier. Follow-up was 15 years, with an evaluation every 6 months for 2 years then once a year for 13 years by an ESPOIR study rheumatologist, for a total of 18 evaluations. During follow-up, the treatments were not randomized but were given in compliance with international recommendation and standard clinical practice. Therapeutic decisions were taken by each patient's rheumatologist based on findings including radiographic progression, but without using the SvHS to assess radiographic damage.

The study was approved by the institutional review board of the coordinating centre for this nationwide study (Montpellier University Hospital, Montpellier, France) and conducted in compliance with the Declaration of Helsinki. Before inclusion, all patients gave informed consent to participation in the study.

### Study design

The baseline assessment included a standardized interview; a general physical examination; blood tests with blood counts, CRP, viral serologies (parvovirus B19, HBV, HCV, HIV), and immunological tests [ELISA for IgM, IgG and IgA RF; tests for ACPA and antinuclear antibodies (ANA)]; HLA-DR phenotype determination; urine tests; and radiographs of the chest, pelvis, hands and feet. The inclusion and subsequent follow-up evaluations included determination of the DAS on 28 joints (DAS 28). Follow-up was stopped if a diagnosis other than RA was established. All evaluations were free of charge.

### Radiographic evaluation

For each patient, standard radiographs including postero-anterior views of both hands and wrists and of both feet and oblique views of both feet were obtained at inclusion then 1, 2, 3 and 5 years later in each centre. Joint positioning, exposure and other technical parameters were standardized. The radiographs taken at inclusion then after 1 and 5 years were sent to the coordinating centre for scoring by readers who had been specifically trained in SvHS determination and had passed a test validating their competence in using the SvHS.

### Reproducibility assessments

All sets of radiographs (baseline, year 1 and year 5) were read by the same observer (M.M.) using the SvHS and the SRS. This reader (M.M.) also read 30 of the same radiograph sets at least 2 months later to allow an assessment of intraobserver repeatability. Radiographs from 85 patients were read by another observer (F.B.) for assessments of the interobserver reliability of the SvHS and SRS. The readers were blinded to the therapeutic strategy and patient identity but scored the radiographs in chronological order.

### Radiographic scores

The SvHS score [17] assesses joint erosions and JSN. Joint erosions are scored in 32 joints at the hands and wrists and 12 joints at the feet. The erosion score per joint can range from 0 to 5 at the hands and wrists and from 0 to 10 at the feet. JSN is scored in 30 joints at the hands and wrists and 12 joints at the feet. JSN scores per joint can range from 0 to 4 at the hands, wrists and feet. The maximum total erosion score is 280 and the maximum total JSN score is 168. The total score is the sum of the total erosion and total JSN scores and has a maximum of 448.

The SRS score assesses the same joints as the SvHS for erosions and JSN. Erosions and JSN are each scored on a 3-point scale where 0 indicates absent, 1 doubtful and 2 present (Fig. 1). The maximum total erosion score is 88, the maximum total JSN score is 84, and the maximum total score computed as the sum of the erosion and JSN scores is therefore 172. For our study, the SRS score was determined at baseline and radiographic progression in the same joints after 1 and 5 years was evaluated in a binary fashion, by separately scoring erosions and JSN as unchanged (score of 0) or worsened (score of 1).

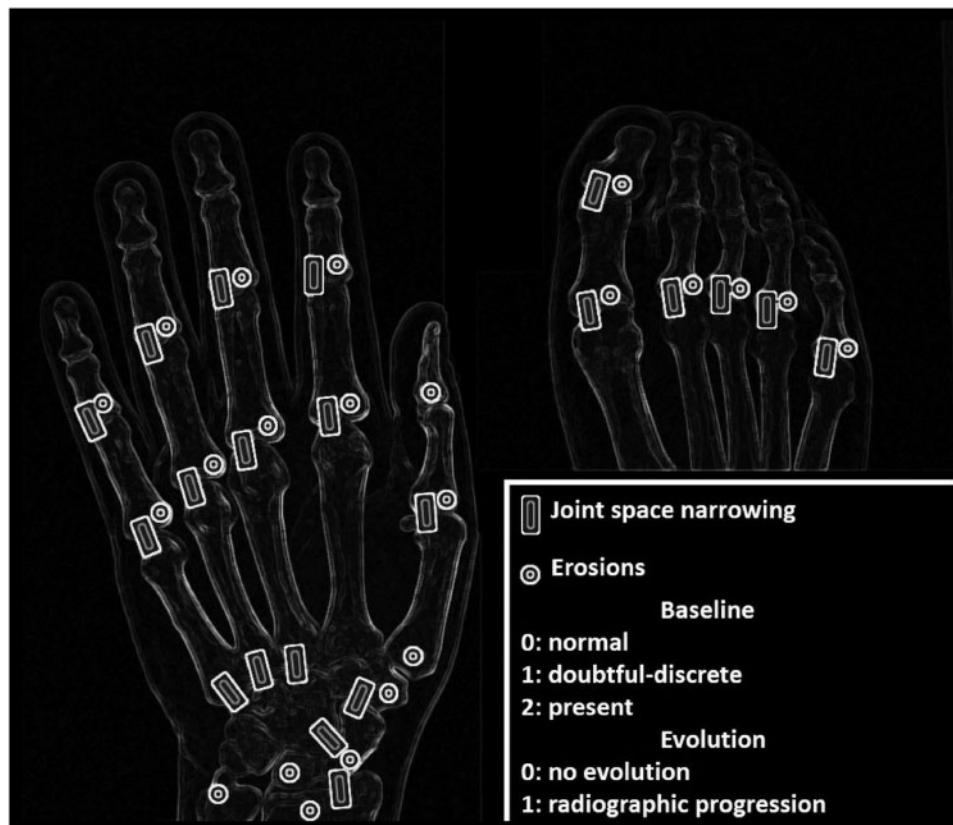
### Statistical analysis

The statistical analysis was performed with SPSS Statistics v. 22 (IBM Corp., Armonk, NY, USA). Quantitative variables were described as mean (s.d.) and qualitative variables as number (%). Patient groups were compared using the  $\chi^2$  test for qualitative variables and the Mann-Whitney *U*-test for quantitative variables. Values of *P* less than 0.05 were considered statistically significant.

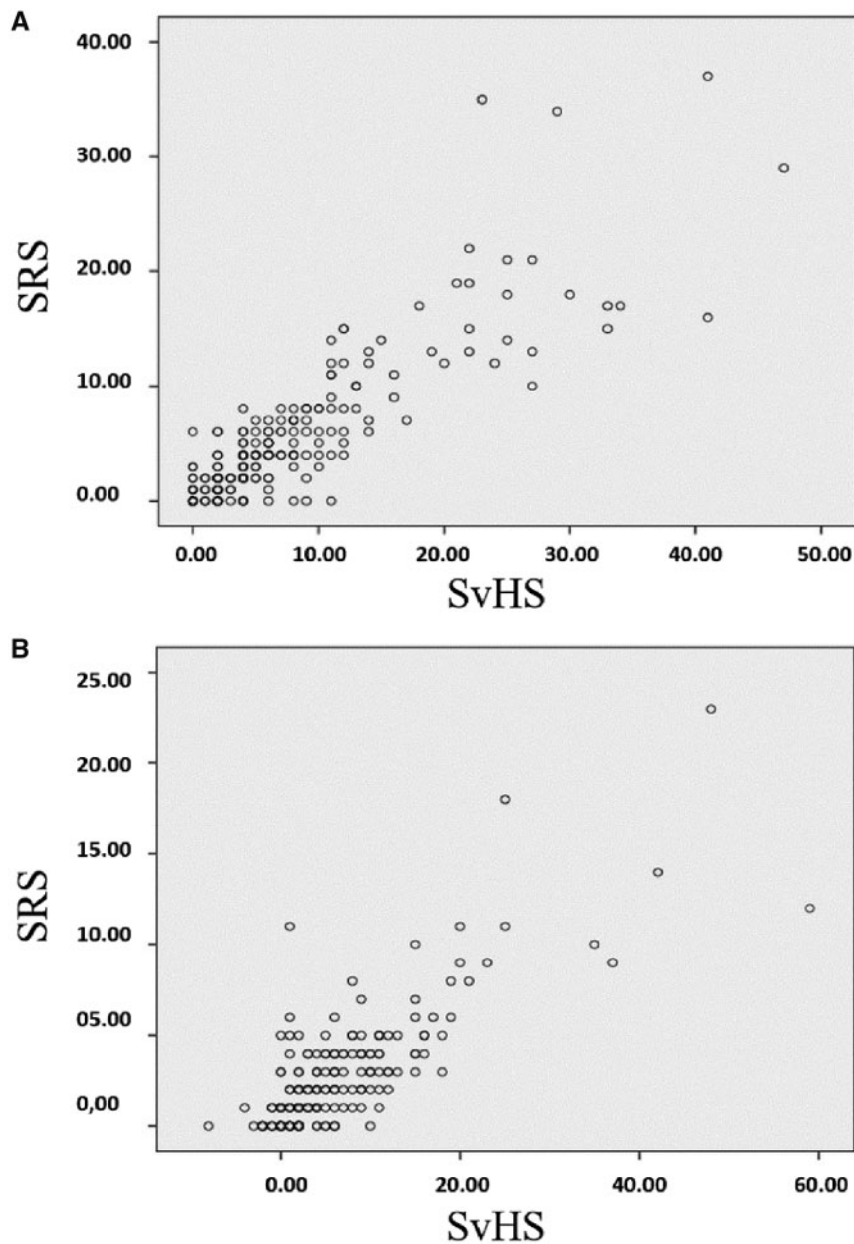
Time needed to read one set of radiographs was measured by one reader (M.M.). Mean time was calculated for set radiograph at inclusion, year 1 and year 5 and the sum of the mean time was calculated. The intraclass correlation coefficients (ICCs) with their 95% CIs were computed to assess intraobserver repeatability and interobserver reliability, as well as agreement between the SvHS and SRS values at baseline and at year 1 [18]. ICC values were interpreted as follows: 0.81–1.00, almost perfect agreement; 0.61–0.80, substantial agreement; 0.41–0.60 moderate agreement; 0.21–0.40, fair agreement; 0–0.20, slight agreement; and –1 to 0, no agreement.

The ability of change in SRS in the first year to predict disease progression at year 5, compared with SvHS (the

**Fig. 1** The simplified radiographic score



Each hand and foot are evaluated. The total maximal score at baseline is 172 (88 for erosion and 84 for joint space narrowing).

**Fig. 2** Correlation between the total SvHS and the total SRS**(A)** At baseline; **(B)** after 1 year. SRS: simplified radiographic score; SvHS: Sharp/van der Heijde score.

current reference standard) was tested by receiver operating characteristic (ROC) curve analysis [19]. Six different cut-offs for defining radiographic progression according to SvHS at 5 years were used (SvHS increase at year 5 vs year 1 of 1, 4, 8, 12, 16 and 20 points, respectively). We then compared the sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) of the change in the SvHS and SRS from baseline to year 1 for predicting radiographic progression (SvHS) between year 1 and year 5 (to reach the cutoff previously defined for radiographic progression). Sensitivity and specificity

were calculated for the optimal cut-off, defined as the value nearest the north-west corner of the ROC plot and associated with >70% specificity.

## Results

### Population

Of the 813 patients included in the ESPOIR cohort, 506 had complete radiographic data at the 1-year and 5-year time points. The main reason for excluding patients from the analysis was the unavailability of radiographs.

**TABLE 1** Ability of early score changes to predict subsequent SvHS change

Score change over the first year	Subsequent score increase per year	Sensitivity	Specificity	Positive predictive value	Negative predictive value
SvHS > 1 point	> 0.25 point	157/268 (58.6)	192/239 (80.3)	157/204 (76.9)	192/303 (63.4)
SRS > 1 point	> 0.25 point	129/268 (48.1)	202/239 (84.5)	129/166 (77.7)	202/341 (59.2)
SvHS > 1 point	> 1 point	115/160 (71.9)	258/347 (74.4)	115/204 (56.4)	258/303 (85.1)
SRS > 1 point	> 1 point	89/160 (55.6)	270/347 (77.8)	89/166 (53.6)	270/341 (79.2)
SvHS > 2 points	> 2 points	66/96 (68.8)	296/411 (72)	66/181 (36.5)	296/326 (90.8)
SRS > 1 point	> 2 points	61/96 (63.5)	305/411 (74.5)	61/166 (36.7)	306/341 (89.7)
SvHS > 2 points	> 3 points	48/70 (68.6)	304/437 (69.6)	48/181 (26.6)	304/326 (93.3)
SRS > 1 point	> 3 points	45/70 (64.3)	316/437 (72.3)	45/166 (27.1)	316/341 (92.7)
SvHS > 3 points	> 4 points	27/51 (52.9)	358/456 (78.5)	27/125 (21.6)	358/382 (93.7)
SRS > 1 point	> 4 points	34/51 (66.7)	324/456 (71.1)	34/166 (20.5)	324/341 (95)
SvHS > 3 points	> 5 points	20/36 (55.6)	366/471 (77.7)	20/125 (16)	366/385 (95.8)
SRS > 1 point	> 5 points	24/36 (66.7)	329/471 (69.9)	24/166 (14.5)	329/341 (96.5)

Data are presented as number/total (percentage) [confidence interval at 95%]. Bold number are the value of sensitivity, specificity, positive predictive value and negative predictive value. SRS: simplified radiographic score; SvHS: Sharp/van der Heijde score.

Mean patient age was 49.1 (11.1) years and mean disease duration 232.6 (272.9) days at baseline. Of the 506 patients, 389 (76.9%) were women, 248 (49%) tested positive for RF, and 230 (45.5%) tested positive for ACPA. Mean baseline values were 29 (24.9) mm for the erythrocyte sedimentation rate, 22.9 (32.5) mg/l for the CRP level, and 5.12 (1.3) for the DAS 28.

### Assessment of radiographs

For the total SvHS, the ICCs were 0.97 for interobserver reliability and 0.99 for intraobserver repeatability. For the total SRS score, the ICC interobserver repeatability was 0.84 for progression after 1 year and 1.0 for progression after 5 years. Mean time needed to determine the SRS based on the three sets of radiographs of the hands and feet taken at baseline and after 1 and 5 years was 5 min per patient (1 min 40 s for each set of radiographs).

### Agreement between the two scores

The ICC between the total SvHS and the total SRS at baseline was 0.896 ( $P < 0.001$ ) (Fig. 2A). The ICC between the erosion SvHS and the erosion SRS was 0.715 ( $P < 0.001$ ) and the corresponding value for JSN was 0.892 ( $P < 0.001$ ). The ICCs between the two scores determined after 1 year were 0.781 ( $P < 0.001$ ) for the total scores (Fig. 2B), 0.704 ( $P < 0.001$ ) for the erosion scores and 0.714 ( $P < 0.001$ ) for the JSN score.

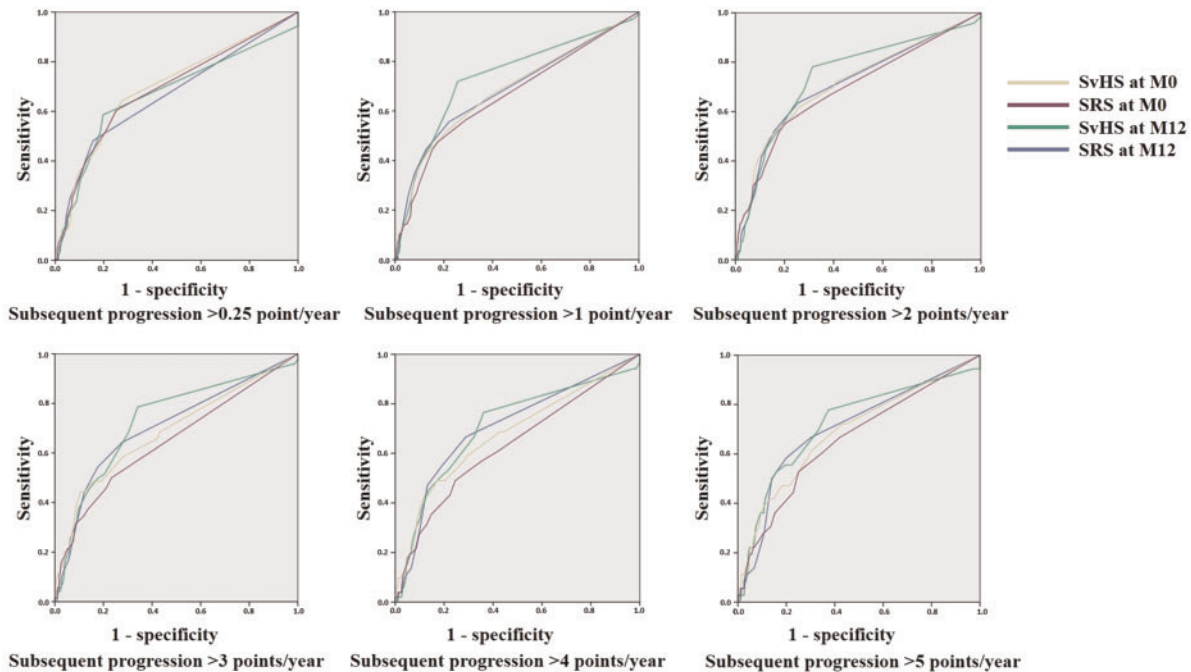
### Ability of the progression during the first year to predict progression between years 1 and 5

We compared the sensitivity, specificity, NPV and PPV of the change in the SvHS and SRS from baseline to year 1 for predicting radiographic progression between year 1 and year 5, defined as an SvHS increase at year 5 vs year 1 of 1, 4, 8, 12, 16 or 20 points (0.25, 1, 2, 3, 4 or 5 points/year) (Table 1, Fig. 3). Sensitivity, specificity, NPV and PPV were similar between the SvHS and the SRS. Thus, a >8-point SvHS increase at year 5 vs year 1 (i.e. >2 points/year) was predicted with 68.8% sensitivity, 72% specificity, 36.5% PPV and 90.8% NPV by the SvHS change between baseline and year 1; and the corresponding values for the SRS were 63.5%, 74.5%, 36.7% and 89.7%, respectively.

For an SvHS change of >1 point between baseline and year 1, sensitivity was best (71.9%) for predicting a >4-point SvHS increase between years 1 and 5 (i.e. >1 point/year) and specificity was best (80.3%) for predicting a >1-point SvHS increase between years 1 and 5 (i.e. >0.25 point/year). For an SRS change of >1 point over the first year, sensitivity was best (66.7%) for predicting a >20-point increase between years 1 and 5 (i.e. >5 points/year) and specificity was best (84.5%) for predicting a >1-point increase between years 1 and 5 (i.e. 0.25 point/year).

## Discussion

Our results demonstrate that the SRS correlated well with the SvHS for assessing radiographic joint damage at

**Fig. 3** Change in SvHS and SRS over the first year predict the change in the SvHS between years 1 and 5

SvHS: Sharp/van der Heijde score; SRS: simplified radiographic score.

baseline then 1 and 5 years later. The correlation was good for the total score and for the erosion and JSN sub-scores. Furthermore, the SRS change over the first year predicted the SvHS change between 1 and 5 years.

The treatment of RA aims to decrease both disease activity and radiographic progression. Conventional radiography is still the reference standard for assessing joint damage in RA. In the randomized controlled trials conducted to evaluate all the drugs available for RA, including biologics, radiographic progression was consistently assessed. However, this assessment was usually based on the SvHS, which is not suitable for daily clinical practice. Simple and rapid methods for assessing radiographic structural damage over time in patients receiving follow-up for RA are needed. Among the available radiograph assessment tools, some provide information on the total burden of structural damage in the patient (Steinbrocker index) [20] or on the overall structural damage in each joint (Larsen score) [21]. Others give separate measurements of the amount of erosions and severity of JSN (SvHS and SENS) [6, 17]. Reproducibility and sensitivity to change are important features of scoring methods. Although easy to determine in daily practice, the Steinbrocker index is not used, due to its limited sensitivity to change. In individual patients, the SvHS has demonstrated better reliability and less measurement error in assessing change compared with the Larsen score [22]. The SENS separately characterizes erosions and JSN as present or absent and, therefore, can only detect the first erosion or first evidence of JSN in each joint; once an erosion or JSN has appeared, the development of further

erosions or worsening of the JSN does not change the score.

According to the latest recommendations of the French Society for Rheumatology (SFR) for managing RA [23] and of the EULAR for defining a core dataset in RA [24], patients who fail to meet the clinical and laboratory ACR/EULAR criteria but who have typical radiographic erosions can be classified as having RA, and the adverse prognostic significance of structural damage progression warrants adding a biologic to the treatment regimen. These recommendations support the need for a simple but consensual score that can be used in everyday practice by clinicians who have experience with recognizing typical radiographic RA lesions but have not been trained in determining the SvHS.

In our study, the SRS values correlated well with the SvHS values at baseline, supporting its use for the initial diagnosis of RA. For the change over the first year, the SRS also correlated well with the SvHS and may therefore be suitable for assessing disease progression in daily practice. The SRS has been used previously to compare the value of tender joints vs clinical synovitis for predicting structural damage in RA [25]. Since the change over time is characterized as absent (score of 0) or as worsening (score of 1), the SRS is well-suited for identifying associations between clinical signs (e.g. synovitis or tenderness) and radiographic changes.

The early SRS change performed similarly to the early SvHS change for predicting SvHS progression between 1 and 5 years. If rapid progression is defined as a total SvHS increase >5 points per year, i.e. 20 points between years

1 and 5, the SRS change of at least 1 point over the first year had 66.7% sensitivity, 69.9% specificity, 14.5% PPV and 96.5% NPV. Corresponding values for the SvHS change over the first year were 55.6%, 77.7%, 16% and 95.8%, respectively. The SRS thus seems to perform as well as the SvHS for identifying patients at risk for rapid structural progression. The SRS scoring system cannot score improvement of the bony changes, but improvement is rarely seen. The exception is for patients under biologic DMARD treatment in whom improvement of the JSN has been observed in previous studies [26]. A way to overcome this lack is to calculate a new 'baseline' score taking the improvement into account.

A comparison of times required by experienced readers to score seven sets of radiographs of the hands and feet in one patient showed 25 min (3 min 34 s per set) with the SvHS and 7 min (1 min per set) with the SENS [27]. In our study, 1 min 40 s was required to score one set of radiographs using the SRS. Thus, the SRS requires far less time than the SvHS but more time than the SENS. At baseline, the SRS is semi-quantitative and the SENS binary, explaining that the latter is faster to determine. Similar to the SENS, the SRS does not require specific training, as an ability to identify the typical erosions and JSN caused by RA is sufficient.

Further studies are needed to validate use of the SRS in daily practice. In the ESPOIR cohort, it would be of interest to evaluate correlations between SRS changes and changes in treatment regimens. Furthermore, additional simplification might be possible by determining which joints are most informative and scoring only those.

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