Comparison of radiographic scoring methods in a cohort of RA patients treated with anti-TNF therapy

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Abstract

Objective. To compare the ability of the simple erosion narrowing score (SENS) to classify radiographic progression relative to the Sharp/van der Heijde score (SHS) in a prospective cohort of anti-TNF-treated RA patients.

Methods. Radiographs of the hands, wrists and feet of patients enrolled in a pharmacovigilance programme are performed every 2 years. These radiographs were read in chronological order by three rheumatologists and scored using the SHS. SENS scores were derived from the SHS. Additionally, one rheumatologist scored the radiographs using the SENS method only. Patients with radiographic progression in excess of the smallest detectable change were classified as progressors. The probability of agreement and $\kappa$-value between the SHS and SENS methods for determining progression was calculated.

Results. A sample of 25 patients was selected from the database. The annualized mean (S.D.) change in SHS score was 6.61 U (7.48 U) and in SENS score was 2.27 U (2.17 U). Five patients were classified as progressors using SHS and seven using SENS, with a probability of agreement of 84% ($\kappa = 0.565$).

Conclusion. The SENS method captures radiographic progression reliably compared with the more detailed SHS method. SENS is suitable for application in clinical practice or in observational cohorts.

Key words: rheumatoid arthritis, radiological assessment, simple erosion narrowing score.

Introduction

Clinical trial evidence has demonstrated that DMARDs and anti-TNF-α therapies slow or impede radiographic progression in RA, as summarized in a recent meta-analysis [1]. Randomized controlled trials typically employ intensive radiographic scoring methods that detail joint erosion and joint narrowing scores separately [2]. Readers require a significant amount of training, and the scoring itself is time consuming. This investment is justifiable when proving the efficacy of expensive therapeutic agents in trials where minimal radiographic progression is expected. This process, however, is not easily applied to large observational cohorts of patients followed over many years. Indeed, despite a significant number of prospective cohorts having been assembled to monitor the efficacy and safety of anti-TNF therapies in the real-world setting, radiographic data on relatively few cohorts have been published [3–7].

In 1999, van der Heijde proposed the simple erosion narrowing score (SENS), a simplified scoring system based on the same parameters and joints scored in the van der Heijde modification of the Sharp score (SHS) [8]. The initial publication describing this method used radiographs from a clinical trial comparing gold and MTX therapies. Validation studies for the SENS method have been performed on radiographs from the Trial of Etanercept and Methotrexate with Radiographic Patient Outcomes (TEMPO) [9] and Behandel Strategieën (BeST) trial [10] and from a selected sample of patients in the European Research on Incapacitating Disease and Social Support (EURIDISS) cohort, with a disease duration up to 4 years but with unspecified treatment or response [11]. The objective of our study was to validate the SENS method in determining radiographic progression in a cohort of patients exposed to anti-TNF therapies.

Methods

A prospective observational cohort of consecutive patients receiving anti-TNF therapies was created in the
year 2000. We collect efficacy and safety data for all enrolled patients. In addition, plain radiographs of the hands, wrists and feet are performed every 2 years. This pharmacovigilance programme is supported by Alberta Health and Wellness and approved by the University of Calgary Health Research Ethics Board. All patients participating in the programme provide informed consent for the collection and evaluation of clinical data in accordance with ethical standards described in the Declaration of Helsinki.

Digital radiographs of the hands, wrists and feet were read in chronological order by three rheumatologists and scored using the SHS [12]. The films were first scored independently by each reader. After that, the readers met to review films where discrepant erosion and narrowing scores had been assigned and reached consensus on the final score to be used in the analysis. SENS scores were derived from the SHS. Additionally, a fourth rheumatologist not trained in SHS or SENS scoring independently assessed the same radiographs using the SENS method. As opposed to applying a semiquantitative scale of 0–4 for joint space narrowing and 0–5 for erosions, the SENS simply dichotomizes whether an erosion is absent (score of 0) or present (score of 1), and whether joint space narrowing is absent (score of 0) or present (score of 1) [8]. The maximum possible score for the SENS method is 86 compared with 448 in the SHS.

We calculated an annualized mean score for radiographic progression as the difference in the number of SHS or SENS units over the time between baseline and follow-up radiographs. Patients with an annualized mean score change greater than the smallest detectable change (SDC) [13] were classified as progressors. The probability of agreement between the SHS and SENS methods for classifying progression and the $\kappa$-value were determined. All analyses were performed with STATA IC version 10.0 (StataCorp, College Station, TX, USA).

**Results**

A sample of 25 patients with serial digital radiographs of the hands, wrists and feet was selected for this study. The mean age of the sample was 57 years, 76% were female and the mean disease duration was 9 years. Anti-TNF exposure included infliximab (56%), etanercept (48%) and adalimumab (44%), and 75% were on concurrent DMARD therapy.

At baseline assessment, prior to the initial anti-TNF prescription, patients had significant disease activity and functional impairment with a mean (S.D.) DAS-28 of 6.08 (1.10) and a mean (S.D.) HAQ of 1.36 (0.69). These patients also had significant radiographic damage, with a mean (S.D.) SHS score at baseline of 93.0 (86.3; range 2–297) and a derived mean (S.D.) SENS score of 36.7 (25.0; range 2–77) (Fig. 1). The mean (S.D.) baseline SENS score assigned by the independent reader was 22.5 (23.7; range 0–68).

At follow-up (mean 2.1 years), 52% of patients achieved a good European League Against Rheumatism (EULAR) response and 44% were in DAS-28 remission. Despite this clinical response to anti-TNF therapy, the calculated annualized mean (S.D.) change in SHS score was 6.6 (7.5) and in the derived SENS score was 2.3 (2.27). The annualized mean (S.D.) change in the SENS score assigned by the independent reader was 2.7 (2.2). The SDC value was similar for the SENS score derived from the SHS score and the independent reader’s scores (3.013 vs 3.036). Classification of progression status using the SDC yielded five progressors using the SHS method and seven progressors using the SENS method. The probability of agreement between the SHS and SENS methods for determining progression was 84% ($\kappa = 0.565$), and between the readers using the derived and directly scored SENS method was 79% ($\kappa = 0.565$).

Progressors by the SHS method had a mean (S.D.) follow-up DAS-28 of 3.96 (2.02) compared with 2.53 (1.12) in non-progressors ($P = 0.05$). Similarly, progressors by the SENS method had a higher mean (S.D.) follow-up DAS-28 of 3.63 (1.97) compared with 2.50 (1.02) in non-progressors ($P = 0.09$). Sixty per cent (3/5) of SHS progressors required a change in therapy during the observation period compared with 30% (6/20) of SHS non-progressors. This is comparable with 43% (3/7) of SENS progressors and 33% (6/18) of SENS non-progressors.
Discussion

We have demonstrated that there is a high probability of agreement between the SHS and SENS methods for classifying radiographic progression in a cohort of anti-TNF-treated patients, whether the SENS be derived from the more detailed SHS by experienced readers or scored independently by a clinician with no formal radiographic scoring training. The SENS method is a simple way to score erosions and joint space narrowing of small joints of the hands, wrists and feet affected by RA. In a validation study comparing five scoring methods for hand radiographs, the SENS method had good cross-sectional and longitudinal interrater reliability as well as intrarater reliability, with intraclass correlation coefficients >0.9 [11]. It did, however, have less sensitivity to change compared with the Larsen, Larsen/Rau, Sharp and SHS scores. In a study directly comparing reliability and sensitivity to detect change to the SHS method, SENS had good results with no detectable ceiling effect [9].

Scoring by the SENS method requires less training and is less time consuming. In the original study, it took experienced readers ~25 min to score radiographs using the SHS method compared with 7 min for the SENS method [8]. Indeed, the average time to score a radiograph by the independent reader was ~7 min using the SENS method. The SENS method is thus more likely to be applied in clinical practice and in longitudinal cohorts of patients treated with advanced therapeutics.

Validation of the SENS method in our cohort study of patients with established RA is an important addition to the literature. The only other published cohort study used only hand radiographs, and included patients with relatively short disease duration [11]. The sensitivity to change of scoring methods may be different in patients with established disease where different slopes of radiographic progression or even a ceiling effect may be observed [11]. We also show that using the SDC calculated from the SENS score is reflective of the clinical experience in a cohort.

There is a need for observational cohorts to report radiographic data in addition to treatment efficacy and sustainability, clinical outcomes and adverse events. This will allow rheumatologists to assess whether disease activity mirrors radiographic outcomes longitudinally in the clinical setting. We propose that the SENS method is suitable for this purpose.

**Rheumatology key message**

- The SENS is a valid radiographic scoring method for observational cohorts.

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