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Original article

Prevalence and concordance of early and sustained remission assessed by various validated indices in the early arthritis "ESPOIR" cohort

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ABSTRACT

Objectives: To assess the prevalence of remission in early arthritis, to evaluate the concordance across different criteria sets in defining this state, and to look for predictive factors for early and sustained remission.

Methods: Patients from the ESPOIR cohort were followed-up every 6 months. We analysed early remission and sustained remission in 3 groups of patients: patients having rheumatoid arthritis (RA) according to 2010 ACR/EULAR criteria, undifferentiated arthritis (UA), and the whole cohort. Remission was defined according to ACR/EULAR criteria, 28 Joint Disease Activity Score (DAS28 < 2.6), and Simplified Disease Activity Index (SDAI ≤ 3.3). Agreement was evaluated by k-coefficient. Predictive factors for sustained remission at 1, 3 and 5 year in RA patients were analyzed.

Results: Eight hundred and nineteen patients were included. Early remission rates in the RA/UA/ESPOIR groups were observed in respectively 29.2% (181/682), 51.4% (55/123) and 32.7% (239/813) of patients by DAS28; 15.7%, 29.1% and 18% by SDAI; and 11.2%, 29.1% and 12.8% by ACR/EULAR criteria. Agreement between classifications of remission was low for DAS28 vs. ACR/EULAR (k = 0.44), high for SDAI vs. ACR/EULAR (k = 0.78), and moderate for SDAI vs. DAS28 (k = 0.54). Lower baseline disease activity scores, non-menopausal status and younger age were the best predictive factors for sustained remission, with consistent results across the 3 definitions of remission.

Conclusion: Our study showed that the rate of early and sustained remission in early arthritis is dependent on the definition used, with a variable degree of agreement across criteria sets, but with consistent predictive factors of favourable outcome in patients finally diagnosed with RA.

1. Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory joint disease that is characterized by joint inflammation leading to joint destruction. This causes decreased functional capacity, work disability, and reduced quality of life [1]. Studies evaluating tight control and treat-to-target strategies advocate that remission should be reached as soon as possible and should ideally be maintained during the course of the disease [2,3]. Since a cure has not yet been established for rheumatoid arthritis (RA), the best achievable state in patients with RA is remission. However, the best way to define remission is still under debate. Categories of high, moderate, and low disease activity as well as remission have been identified for the most commonly used indices: the disease activity score using 28 joint counts (DAS28) [4], and Simplified Disease Activity Index (SDAI) [5]. The American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) recently proposed new definitions of remission in RA for clinical trials, which could also be used as the primary outcome of clinical trials and real life practice [6,7]. Testing these new remission criteria in RA cohorts was encouraged to determine their practicality for daily use [6]. Recently, a validation of these criteria using the ESPOIR study showed that patients in ACR/EULAR remission in ESPOIR had a high rate of later radiographic and functional stability, and suggests that these definitions of remission are valid in clinical practice settings [8].

Better knowledge about prevalence and prognostic factors for remission might improve patient care according to their individual profile. Only a few studies have examined sustained remission in usual clinical settings [9–11]. In the literature, definitions of sustained remission in RA vary considerably in both measurement and duration, and whether discontinuation of antirheumatic treatment is a prerequisite remains also debated.

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The aim of this study was to assess the prevalence of remission during the initial follow-up of a cohort of patients with early inflammatory arthritis, to evaluate the concordance across different criteria sets in defining this state, and to look for predictive factors for early and sustained remission in RA patients.

2. Methods

2.1. Source data

The ESPOIR cohort is a nationwide prospective cohort study of adults in France conducted under the auspices of the French Society of Rheumatology [12]. The study was approved by the Institutional Review Board of the Montpellier University Hospital, which was the coordinating center. Prior to inclusion, written informed consent was obtained from each participant.

This cohort has included 813 patients with early arthritis between December 2002 and March 2005. Forteen participating investigational centres located across French territory had participated. Each center included a substantial number of patients, ranging from 35 to 83. In each of those centres, each staff physician as well as the private rheumatologists accustomed to refer patients were incited and reminded on a regular basis that patients were expected for inclusion in ESPOIR, and although no strict rule had been imposed, all efforts were made to systematically offer this opportunity to patients with early arthritis potentially fulfilling inclusion criteria.

Patients were eligible for inclusion in the cohort if they had a definite clinical diagnosis of RA or a diagnosis of undifferentiated arthritis (UA) with a potential for progressing to RA. Thus, these patients had at least two swollen joints, present for more than 6 weeks but less than 6 months, and were naïve for DMARDs and corticosteroids at inclusion. The baseline clinical, immunological, and radiological features of the 813 included patients were published [13,14]. Diagnosis of RA was defined after 1 year of follow-up, according to 2010 ACR/EULAR criteria for RA.

2.2. Study design

The baseline assessment included a standardized interview, a general physical examination, and laboratory tests. Each patient was asked to undergo an evaluation by an office-based rheumatologist every 6 months for 2 years and once a year thereafter.

2.3. Outcome measurement

We analyzed early remission (at 6 months follow-up) in 3 different groups of patients: patients who were diagnosed as having RA according to 2010 ACR/EULAR criteria (RA) at month 12, undifferentiated arthritis (UA) after 1 year of follow-up, and the whole cohort.

The characteristics of patients, which included the swollen joint count (SJC), the tender joint count (TJC), patient's and evaluator's global assessments of disease activity (PGA and EGA, respectively) on a visual analog scale (in cm), smoking status, comorbidity, presence of extra-articular features, ESR, CRP, RF and HAQ were described and compared according to fulfilment or not of remission according to the following definitions:

- 28 Joint Disease Activity Score (DAS28 < 2.6) [4];
- Simplified Disease Activity Index (SDAI $\leq$ 3.3) [5];
- the 2011 ACR/EULAR Boolean remission criteria [6].

For this study, sustained remission at 1 year was defined by remission state in both 6 months- and 1 year visits; sustained remission at 3 years was defined by remission state in all consecutive 6 months-, 1- and 3-year visits; and sustained remission at 5 years was defined by remission state at all consecutive 6 months-, 1-, 3-, and 5-year time points.

2.4. Measurements

Clinical assessment included demographic data: age, gender, menopause, smoking status and comorbidities. Biochemical measurements included rheumatoid factor, anti-CCP antibody and C-reactive protein (CRP; mg/L) were also assessed.

2.5. Radiological data

Radiographs of the hands, wrists and feet in the postero-anterior view were performed for each patient at baseline, 6 and 12 months. Images were centralised and scored according to modified total Sharp score (mTSS) [15] by an experienced rheumatologist who was blinded to the patient's other data, in known chronological order. For each patient, an erosion score, a joint-narrowing score and a total radiographic score were assessed [16].

2.6. Statistical analysis

The statistical analysis was performed in three steps. Firstly, descriptive statistics were calculated for baseline characteristics in three groups of patients: patients who were diagnosed as having RA according to 2010 ACR/EULAR criteria (RA), undifferentiated arthritis (UA) after 1 year of follow-up, and the whole cohort. For variables that were normally distributed, the mean $\pm$ standard deviation (SD) was reported. For dichotomous variables, the number (%) of patients was listed relative to the total number of patients for whom information was available about the characteristic under investigation. Agreement across available criteria sets was evaluated by k-coefficient. In the second step, three logistic regression models using three definitions of the dependent variable "remission yes/no" were developed at 6 months, 1 year, 3 years and 5 years in the patients who were diagnosed as having RA according to 2010 ACR/EULAR criteria (RA) at 1 year. The first definition of remission was the DAS28 < 2.6. The second definition of remission used the ACR/EULAR remission criteria set. The third definition of remission was based on SDAI $\leq$ 3.3. Categorical variables were analysed using Chi-square or Fisher's tests, depending on sample size restrictions, and the odds ratios (OR) with 95% confidence intervals (95% CI) were calculated. Factors found to be significant to the $P < 0.15$ level in univariate analysis were included to the multivariate model. At last, characteristics of patients in DMARD-free sustained remission at 1 year, 3 years and 5 years according to DAS28 were calculated: For variables that were normally distributed, the mean $\pm$ SD was reported. For dichotomous variables, the number (%) of patients was listed relative to the total number of patients for whom information was available about the characteristic under investigation.

Statistical analyses were performed using SAS V.8.2. *P*-values < 0.05 were regarded as significant.

3. Results

3.1. Demographic, clinical and biological characteristics of the 3 groups of patients

Table 1 shows the baseline characteristics of the patients. The mean age was 48.5 $\pm$ 12.2 years, 46.5 $\pm$ 13.7, and 48.1 $\pm$ 12.6 for