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Original Article

Comparative study of DAS 28 ESR and DAS 28 CRP among rheumatoid arthritis patients in India

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ARTICLE INFO

Article history:
Received 11 August 2015
Accepted 30 October 2015
Available online 22 January 2016

Keywords:
Rheumatoid arthritis
Disease activity
DAS 28 CRP
DAS 28 ESR

ABSTRACT

Background: The Disease Activity Score (DAS) in rheumatoid arthritis (RA) involving 28 joints and using erythrocyte stimulation rate (ESR) is used frequently. But the inability of DAS 28 ESR to reflect short-term changes in disease activity has given rise to DAS 28 using C-reactive protein (CRP). The objective of the present study was to compare DAS 28 CRP with DAS 28 ESR.

Methods: 294 patients of RA diagnosed as per ACR EULAR 2010 revised classification criteria for RA were included. New cutoff values of remission, low, moderate and high disease activity using DAS 28 CRP were defined.

Result: There was a good correlation between DAS 28 ESR and DAS 28 CRP. On classifying the disease activity of the subjects according to new cutoff values of DAS 28 CRP, there was substantial agreement with classification according to DAS 28 ESR.

Conclusion: DAS 28 CRP may be considered as an alternative to DAS 28 ESR.

1. Introduction

Disease Activity Score (DAS) is a frequently used scoring system for classifying disease activity in rheumatoid arthritis (RA). It is a widely accepted tool, not only for clinical research purposes, but for therapeutic decision-making and prognostication as well. Since the development of DAS in 1990, it has gained immense importance, and undergone several modifications.[1,2] At present, DAS based on 28 joints (DAS 28) is in vogue, and is more convenient than the original 44 joints.[3] The DAS 28 score combines number of swollen and tender joints, in addition to a measure of general health, and the acute phase reactants, with scores ranging from 0 to 9.4. The acute phase reactants used for calculating the DAS 28 are erythrocyte sedimentation rate (ESR) and less commonly, C-reactive protein (CRP). DAS 28 ESR values are categorized as follows: >5.1, high disease activity; ≤3.2, low disease activity; and <2.6, remission.[4] European League Against Rheumatism (EULAR) response criteria have been defined for DAS 28 ESR, and have been widely used ever since.[4] The original DAS 28 based on ESR has been extensively used and validated.[5] However, recent studies encourage the application of DAS 28 using CRP (DAS 28 CRP) compared to DAS 28 using ESR (DAS 28

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http://dx.doi.org/10.1016/j.injr.2015.10.006

ESR).[6,7] ESR usually reflects disease activity of the past few weeks, whereas CRP tends to reflect more short-term changes in disease activity.[7] Therefore, CRP is expected to be more sensitive to short-term changes in the disease activity. Moreover, ESR can be influenced by confounding factors such as age, sex, fibrinogen levels, hyper-gammaglobulinemia, rheumatoid factor, and anemia.[6] The criteria for disease activity have not been extensively validated while using DAS 28 CRP. Some investigators have used the same cut-offs as DAS 28 ESR, while some have determined cutoffs for their population. EULAR response criteria for DAS 28 ESR have been applied to DAS 28 CRP as well.[8] The primary objectives of the present study was to validate DAS 28 CRP in the Indian population, and appraises the extent of correlation and agreement between DAS 28 ESR and DAS 28 CRP. The secondary objective was to define new cutoffs for DAS 28 CRP in our population.

2. Patients and methods

A cross-sectional study was conducted in the Rheumatology Clinic of Medical College Hospital, from June 2010 to May 2012. A total of 294 patients (92 males and 202 females) with RA were included in this study. Patients were diagnosed to have RA by the rheumatologists according to American College of Rheumatology European League Against Rheumatism (ACR-EULAR) 2010 classification criteria for RA. All patients included in the study signed an informed consent form according to the declaration of Helsinki. Ethical approval was obtained from the Institutional Ethics Committee. Patients with diseases other than RA were excluded from the study. Demographic and disease related characteristics of the participants were collected. A CRP test with a lower detection level of 1.0 mg/l was used. The CRP (mg/l) test was calibrated using a standardized method (CRM 470 of the International Federation of Clinical Chemistry). ESR (mm/h) was measured by the Westergren method.

2.1. Calculation and evaluation of disease activity

The DAS 28 indices, both with ESR and CRP, were calculated as follows (http://www.das-score.nl):

$$\text{DAS28-ESR} = 0.56*\sqrt{(\text{TJC28})} + 0.28*\sqrt{(\text{SJC28})} + 0.70*\ln(\text{ESR}) + 0.014*(\text{GDAP})$$

$$\text{DAS28-CRP} = 0.56*\sqrt{(\text{TJC28})} + 0.28*\sqrt{(\text{SJC28})} + 0.36*\ln(\text{CRP} + 1) + 0.014*(\text{GDAP}) + 0.96$$

DAS 28 ESR values were categorized as follows: >5.1 high disease activity (HDA), >3.2 to ≤5.1 moderate disease activity (MDA), ≤3.2 low disease activity (LDA) and <2.6 remission.

Three trained Rheumatologists were involved with performing the swollen and tender joint counts of the patients. Agreement was substantial ($\kappa = 0.71$ and $\kappa = 0.68$) for high and moderate disease activity where as moderate ($\kappa = 0.59$ and $\kappa = 0.53$) for remission and low disease activity, respectively.[9]

2.2. Statistical analysis

Statistical analysis was done by using SPSS version 20.0. Correlation coefficient between the scores of DAS 28 ESR and CRP was calculated, and correlations with other disease-activity parameters such as CDAI and SDAI were also assessed.

2.3. Validation analyses for DAS 28 CRP

Criterion validity for DAS 28 CRP was assessed against DAS 28 ESR. Bland–Altman plots were created by plotting the differences between DAS-28 ESR and DAS-28 CRP values against the mean of the two DAS 28 values. Limits of agreement and their 95% CIs were calculated following the methods of Bland and Altman.[10]

2.4. Construct validity

Appraisal of changes in disease activities of the patients over time was beyond the scope of this work owing to cross-sectional design.

2.5. Defining new cut-offs for DAS 28 CRP

Receiver operating characteristic (ROC) curve analysis was used to find out the cutoff values for DAS 28 CRP, taking the cutoffs of DAS 28 ESR as gold standard. Area under the curve (AUC) with 95% confidence intervals (CIs) was determined, and p value less than 0.05 was considered statistically significant.

2.6. Cross-classification of DAS 28 ESR and CRP categories

Cross-classification into disease activity categories was done based on existing cutoffs for DAS 28 ESR and new cutoffs for DAS 28 CRP. Binary kappa (κ) for agreement was assessed for the patients in each of the DAS 28 categories.[9] Percentages for exact agreement (PEA), percentages of close (in immediate adjacent categories) agreement (PCA) and category-specific percentage agreement (CAT SP) was also calculated, as per the formulae elaborated by Hensor et al.[11]

Lastly, the effects of other variables namely, age, gender and disease duration on the DAS 28 ESR and CRP scores, as well as interactions of the variables themselves were assessed after logarithmic transformation to normalize the distributions.

3. Results

The demographic and disease activity parameters of the study population are shown in Table 1. Mean DAS 28 CRP was less than that of DAS 28 ESR. There was distinct female preponderance (202, 68.7%). As the distributions of DAS 28 ESR and DAS 28 CRP values in our population were found to be non-Gaussian, Spearman's correlation was done. There was high degree of correlation between the DAS 28 ESR and DAS 28 CRP values (Spearman's correlation coefficient 0.941, $p < 0.01$). Correlations with other disease activity parameters are shown in Table 2.