

# Comparison of Disease Activity Score-28 Based on Erythrocyte Sedimentation Rate and C-reactive Protein Level in Rheumatoid Arthritis

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The original Disease Activity Score (DAS) was calculated based on the Ritchie articular index and 44 swollen joint count, and has been used as a tool for monitoring disease activity in patients with rheumatoid arthritis (RA) [1]. The DAS based on 28 joints (DAS28) is calculated from four components: number of tender joints, number of swollen joints, visual analogue scale score of the patient's global health, and erythrocyte sedimentation rate (ESR) [2]. As ESR is an inflammation marker, this version is referred to as DAS28-ESR. The DAS28-ESR score was developed through a modification of the original DAS for reasons of convenience [2]. DAS28-ESR has been widely used and validated in clinical practice and trials for monitoring RA disease activity and determining the treatment response using the European League Against Rheumatism (EULAR) response criteria [3]. ESR is affected by age, sex, anemia, fibrinogen levels, hypergammaglobulinemia, and plasma viscosity, and reflects the disease activity of the past few weeks [4]. On the other hand, C-reactive protein (CRP) is less confounded by these factors, and reflects the more short-term changes in disease activity [5]. DAS28 based on CRP (DAS28-CRP) was developed through the modification of DAS28-ESR [2], and DAS28-CRP has been proposed as a substitute for DAS28-ESR because of the faster response of CRP to inflammatory changes than that of ESR.

DAS28-CRP and DAS28-ESR have been considered comparable and interchangeable when assessing patients with RA. The EULAR, American College of Rheumatology, and Asia Pacific League of Associations for Rheumatology recommendations for managing RA do not specify whether

DAS28-CRP or DAS28-ESR should be used [6]. Consequently, it has been considered that the values of DAS28-CRP and DAS28-ESR are interchangeable. Although a positive correlation was found between DAS28-CRP and DAS28-ESR values, this correlation does not necessarily indicate that the two scores agree with each other. DAS28-CRP values have been developed to produce equivalent results to those of DAS28-ESR. However, DAS28-CRP is not as well established as DAS28-ESR, because its validity is inferred through a comparison with DAS28-ESR [7,8]. DAS28-CRP and DAS28-ESR values may not be interchangeable. The difference between DAS28-CRP and DAS28-ESR in assessing RA activity and EULAR response may be caused by the difference between CRP and ESR [5].

The DAS28-CRP values are lower than the DAS28-ESR values in assessing RA activity [9]. Using the DAS28-ESR cutoffs for DAS28-CRP for high disease activity underestimates the number of patients with high disease activity [10], thus, DAS28-CRP may need lower cutoffs for categorizing disease activity than DAS28-ESR. Nevertheless, these values are used interchangeably in clinical trials. Whether the criteria of disease activity and the response criteria for DAS28-ESR could be applied to DAS28-CRP needs to be validated, because the validated threshold values for DAS28-CRP have not been determined yet, and the discordance between DAS28-CRP and DAS28-ESR could result in different treatment decisions in patients with RA. A global cohort showed that a DAS28-CRP of 4.6 corresponds to 5.1 for DAS28-ESR [10]. As this is substantially lower than the DAS28-ESR cutoff of 5.1, us-

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ing 5.1 as the cutoff for DAS28-CRP underestimates the disease activity in RA. The DAS28-CRP cutoff values that are equivalent to DAS28-ESR for remission and low disease activity were  $<2.4$  and  $\leq 2.9$ , respectively, rather than  $<2.6$  and  $\leq 3.2$  [10]. A Japanese study reported a much lower high-disease-activity cutoff value of 4.1 for DAS28-CRP and showed lower remission and low-disease-activity cutoff values (2.3 and 2.7, respectively) [11].

In a previous issue of this journal, Choi [12] demonstrated that the cutoff value of DAS28-CRP needs to be reduced to 4.5 for high disease activity, in a cross-sectional study with 1,117 patients with RA from the Korean Biologics Registry. Seventy-eight percent of patients had high disease activity as defined by DAS28-ESR  $>5.1$ , whereas the DAS28-CRP cutoff of  $>5.1$  defined only 43.0% patients as having high disease activity. Thus, the author proposed the optimal cutoff value (4.5) of DAS28-CRP for high disease activity for Korean patients to be used interchangeably, which is consistent with the recommendation by Fleischmann et al. [10], who used a global cohort. However, this study examined the DAS28-CRP value corresponding to the DAS28-ESR value only for high disease activity. Further study is needed to determine the DAS28-CRP value corresponding to the validated DAS28-ESR cutoff for remission and low disease activity in Korean patients with RA.

In conclusion, DAS28-CRP underestimates disease activity and overestimates response according to the EULAR response criteria compared with DAS28-ESR. Therefore, DAS28-CRP needs different cutoffs from those used for DAS28-ESR. Those DAS28-CRP cutoffs then need to be validated in longitudinal or other cohorts to establish the definition of high disease activity based on the new DAS28-CRP value applicable to the Korean population.

## CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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