

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-

Received : December 1, 2017, **Accepted :** December 1, 2017

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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 ≤ 2.9 , respectively, rather than <2.6 and ≤ 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.

REFERENCES

1. van der Heijde DM, van 't Hof MA, van Riel PL, Theunisse LA, Lubberts EW, van Leeuwen MA, et al. Judging disease activity in clinical practice in rheumatoid arthritis: first step in the development of a disease activity score. *Ann Rheum Dis* 1990;49:916-20.
2. Prevoo ML, van 't Hof MA, Kuper HH, van Leeuwen MA, van de Putte LB, van Riel PL. Modified disease activity scores that include twenty-eight-joint counts. Development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. *Arthritis Rheum* 1995;38:44-8.
3. Fransen J, van Riel PL. The disease activity score and the EULAR response criteria. *Clin Exp Rheumatol* 2005;23(5 Suppl 39):S93-9.
4. Talstad I, Scheie P, Dalen H, Rölli J. Influence of plasma proteins on erythrocyte morphology and sedimentation. *Scand J Haematol* 1983;31:478-84.
5. van Leeuwen MA, van Rijswijk MH, van der Heijde DM, Te Meerman GJ, van Riel PL, Houtman PM, et al. The acute-phase response in relation to radiographic progression in early rheumatoid arthritis: a prospective study during the first three years of the disease. *Br J Rheumatol* 1993;32 Suppl 3:9-13.
6. Smolen JS, Landewé R, Breedveld FC, Dougados M, Emery P, Gaujoux-Viala C, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs. *Ann Rheum Dis* 2010;69:964-75.
7. Tamhane A, Redden DT, McGwin G Jr, Brown EE, Westfall AO, Reynolds RJ 4th, et al. Comparison of the disease activity score using erythrocyte sedimentation rate and C-reactive protein in African Americans with rheumatoid arthritis. *J Rheumatol* 2013;40:1812-22.
8. Castrejón I, Ortiz AM, García-Vicuña R, Lopez-Bote JP, Humbría A, Carmona L, et al. Are the C-reactive protein values and erythrocyte sedimentation rate equivalent when estimating the 28-joint disease activity score in rheumatoid arthritis? *Clin Exp Rheumatol* 2008;26:769-75.
9. Song GG, Lee YH. Comparison of disease activity score 28 using C-reactive protein and disease activity score 28 using erythrocyte sedimentation rate in assessing activity and treatment response in rheumatoid arthritis: a meta-analysis. *J Rheum Dis* 2016;23:241-9.
10. Fleischmann RM, van der Heijde D, Gardiner PV, Szumski A, Marshall L, Bananis E. DAS28-CRP and DAS28-ESR cut-offs for high disease activity in rheumatoid arthritis are not interchangeable. *RMD Open* 2017;3:e000382.
11. Inoue E, Yamanaka H, Hara M, Tomatsu T, Kamatani N. Comparison of disease activity score (DAS)28- erythrocyte sedimentation rate and DAS28- C-reactive protein threshold values. *Ann Rheum Dis* 2007;66:407-9.
12. Choi IA. Comparison of the disease activity score-28 based on the erythrocyte sedimentation rate and C-reactive protein in rheumatoid arthritis. *J Rheum Dis* 2017;24:287-92.