

Evaluating diagnostic criteria for macrophage activation syndrome in patients with adult onset Still's disease. Response to: 'Comparison of MS score and HScore for the diagnosis of adult-onset Still's disease associated macrophage activation syndrome' by Zhang *et al*

We thank Zhang *et al*¹ for their interest in our MAS/sJIA (MS) score for diagnosis of macrophage activation syndrome (MAS) in systemic juvenile idiopathic arthritis (sJIA).² Considering that sJIA and adult-onset Still's disease (AOSD) are nowadays thought to constitute a continuum of a single disease entity^{3,4} and that they share a similar risk for MAS, it is worth evaluating whether the proposed diagnostic tools are suitable to detect MAS in both illnesses.

Zhang *et al*¹ compared the diagnostic performance of the MS score with that of the HScore⁵ in their retrospective series of 209 patients with AOSD, 35 of whom had MAS. The HScore is aimed at identifying a broad range of reactive haemophagocytic syndromes and has been developed in a cohort of adult patients, most of whom had infection or haematological malignancy.

By means of a receiver operating characteristic curve analysis, Zhang *et al*¹ found that the HScore had a better capacity to capture MAS than the MS score, with an area under the curve (AUC) of 0.973 and 0.865, respectively ($p < 0.001$). A cut-off value ≥ 120 in the HScore yielded a sensitivity of 90.6% and a specificity of 89.6%, whereas the best results for the MS score (sensitivity of 75% and specificity of 73%) were obtained with a cut-off value ≥ -0.25 .

Although the authors' conclusion that the HScore performs better than the MS score in diagnosing AOSD-associated MAS is justified by the results of the analyses, their findings contrast with those reported by Wang *et al*,⁶ who found that an MS cut-off score of ≥ -1.08 led to achieving a sensitivity of 94.1% and a specificity of 95% and an AUC of 0.98 in their patients with AOSD.

This discordance may depend on differences in the characteristics of patient populations. As compared with the cohort of Zhang *et al*¹, patients with MAS included in the study of Wang *et al*⁶ had a lower frequency of active arthritis (31.6% vs 71.4%), central nervous system dysfunction (1.7% vs 20%) and haemorrhagic manifestations (1.7% vs 17.1%), and a higher frequency of splenomegaly (83.3% vs 22.9%). There are also remarkable diversities between the AOSD patients with MAS in the series of Zhang *et al*¹ and the patients with sJIA-associated MAS enrolled in our study that led to the development of the MS score.^{2,7} Our patients had a higher frequency of hepatomegaly (70% vs 11.4%) and splenomegaly (57.9% vs 22.9%), a lower frequency of lymphadenopathy (51.4% vs 80%), and a higher median value of ferritin (5253 ng/mL vs 2000 ng/mL).⁷

Beside these disparities, there are some caveats that hamper a thorough evaluation of the results of Zhang *et al*.¹ In table 1, the figures for some items that are part of the HScore, namely known underlying immunosuppression, temperature and bone marrow haemophagocytosis, are missing. Furthermore, the cut-off value for the MS score mentioned in the legend to figure 1

(-0.45) is different from that included in the manuscript text (-0.25).

In conclusion, the report of Zhang *et al*¹ highlights the urgent need to harmonise the diagnostic tools used to diagnose MAS in AOSD and sJIA. In order to obtain reliable and widely applicable results, this objective should be pursued by conducting multinational and multicentre prospective studies based on a uniform and standardised investigational protocol.

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REFERENCES

- Zhang L, TF L, Liu X, *et al*. Comparison of MS score and HScore for the diagnosis of adult-onset Still's disease associated macrophage activation syndrome. *Ann Rheum Dis* 2020. doi: 10.1136/annrheumdis-2020-217917.
- Minoia F, Bovis F, Davi S, *et al*. Development and initial validation of the MS score for diagnosis of macrophage activation syndrome in systemic juvenile idiopathic arthritis. *Ann Rheum Dis* 2019;78:1357–62.
- Inoue N, Shimizu M, Tsunoda S, *et al*. Cytokine profile in adult-onset still's disease: comparison with systemic juvenile idiopathic arthritis. *Clin Immunol* 2016;169:8–13.
- Nirmala N, Brachat A, Feist E, *et al*. Gene-Expression analysis of adult-onset still's disease and systemic juvenile idiopathic arthritis is consistent with a continuum of a single disease entity. *Pediatr Rheumatol Online J* 2015;13:50.
- Fardet L, Galicier L, Lambotte O, *et al*. Development and validation of the HScore, a score for the diagnosis of reactive hemophagocytic syndrome. *Arthritis Rheumatol* 2014;66:2613–20.
- Wang R, Li T, Ye S, *et al*. Application of MS score in macrophage activation syndrome patients associated with adult onset still's disease. *Ann Rheum Dis* 2019;annrheumdis-2019-216286.
- Davi S, Minoia F, Pistorio A, *et al*. Performance of current guidelines for diagnosis of macrophage activation syndrome complicating systemic juvenile idiopathic arthritis. *Arthritis Rheumatol* 2014;66:2871–80.