Comparison of MS score and HScore for the diagnosis of adult-onset Still's disease-associated macrophage activation syndrome

We read with great interest the article by Minoia *et al*,[1] which reported MAS/sJIA (MS) score, a new scoring tool for diagnosis of systemic juvenile idiopathic arthritis (sJIA)-associated macrophage activation syndrome (MAS). This new diagnostic score has raised great interest and also some concerns.[2–5] Although Wang *et al*[2] tested the MS score in a group of Chinese patients with adult-onset Still's disease (AOSD)-associated MAS, the diagnostic capacity needs to be evaluated in future.

HScore was first developed for the diagnosis of reactive haemophagocytic syndrome, which resulted from mainly haematological malignancy or infection,[6] and was ever tested in patients with MAS, which resulted from different rheumatic diseases, with good performance.[7] Since there are no studies comparing the diagnostic capability of HScore and MS score, we conducted a study to compare the capacity of HScore and MS score for the diagnosis of AOSD-associated MAS.

Patients diagnosed with AOSD during January 2012 and October 2019 in our hospital were retrospectively analysed. As there is no gold standard for diagnosing AOSD-associated MAS, the diagnosis of MAS is mainly based on the profiles of clinical and laboratory data as well as agreement of more than four rheumatologists.

We included 174 patients with pure AOSD and 35 patients with AOSD-associated MAS. Clinical and laboratory data of these two groups of patients are detailed in table 1. Patients with AOSD-associated MAS were younger than those with pure AOSD (32±11.4 years vs 36.9±13.5 years, p=0.028). More deaths were observed among patients with AOSD-associated MAS (17.1% vs 3.4%, p=0.001). Regarding clinical manifestations, patients with AOSD-associated MAS had higher incidence of central nervous system involvement, decreased blood cells, haemorrhagic manifestations, hepatomegaly and enlarged lymph nodes (p<0.05), but comparable incidence of arthritis, eruption and abnormal liver function, compared with patients with pure AOSD. As for laboratory tests, patients with AOSD-associated MAS had a relatively lower level of white blood cell count, neutrophil count, lymphocyte count, platelet count, haemoglobin, fibrinogen and erythrocyte sedimentation rate (p<0.05) and a relatively higher level of ferritin, triglycerides and liver enzyme (p<0.05).

Patients with AOSD-associated MAS had higher HScore and MS score than those with pure AOSD (table 1) . ROC curve analysis (figure 1) revealed that the HScore had a stronger ability to diagnose AOSD-associated MAS compared with MScore (AUC=0.973 and 0.865 for HScore and MS score, respectively; p<0.001). HScore of ≥120 performed best (sensitivity 90.6% and specificity 89.6%), while MS score of ≥−0.25 performed best and yielded a sensitivity of 75% and a specificity of 73%.

Our results indicate that patients with AOSD-associated MAS had higher incidence of visceral involvement and more severe disease than patients with pure AOSD, and HScore seems to perform much better than MS score for the diagnosis of AOSD-associated MAS. MS score was tested by Wang *et al*[2] that it is suitable to detect MAS in patients with AOSD; however, its cut-off value should be modified from ≥−2.1 to ≥−1.08 and yielded a sensitivity of 94.1% and a specificity of 95.0%. The different performance of MS score in AOSD may result from different patients' selection. The diagnosis of MAS by Wang *et al*[2] was mainly based on the 2004 haemophagocytic lymphohistiocytosis (HLH-2004) diagnostic criteria, which is not suitable for early recognition of MAS,[8] indicating that the patients with MAS in Wang *et al*'s study might be in a relatively late stage. We believe that we included patients with MAS in a much earlier stage.

Table 1 Features of patients with AOSD with and without MAS*

	non-MAS (n=174)	MAS (n=35)	P values
Demographic			
Age, mean±SD (years)	36.9±13.5	32±11.4	0.028
Gender (F/M)	138/36	28/7	0.927
Deaths, n (%)	6 (3.4)	6 (17.1)	0.001
Clinical manifestations			
Arthritis, n (%)	119 (68.4)	25 (71.4)	0.723
Eruption, n (%)	123 (70.7)	28 (80)	0.262
Abnormal liver function, n (%)	143 (82.2)	33 (94.3)	0.073
Decreased blood cells, n (%)	1 (0.6)	26 (74.3)	<0.001
Central nervous system involvement, n (%)	0 (0)	7 (20)	<0.001
Haemorrhagic manifestations, n (%)	0 (0)	6 (17.1)	<0.001
Splenomegaly, n (%)	36 (20.7)	8 (22.9)	0.774
Hepatomegaly, n (%)	3 (1.7)	4 (11.4)	0.016
Enlarged lymph nodes, n (%)	107 (61.5)	28 (80)	0.037
Known underlying immunosuppression	1 (0.6)	13 (37.1)	<0.001
Temperature (°C)			
38.4–39.4	51 (29.3)	3 (8.6)	0.011
>39.4	123 (70.7)	32 (91.4)	0.011
Bone marrow Hemophagocytosis	1 (0.6)	17 (48.6)	<0.001
Laboratory features			
White cell count (×10^9/L)	14.2 (3.6–50.4)	6.3 (0.2–37.7)	<0.001
Neutrophil count (×10^9/L)	12.1 (1.13–48.13)	5.2 (0–36.3)	<0.001
Lymphocyte count (×10^9/L)	1.28 (0.4–4.71)	0.7 (0.15–3.08)	<0.001
Haemoglobin (g/L)	109 (53–141)	85 (63–134)	<0.001
Platelet count (×10^9/L)	295 (34–564)	81 (8–368)	<0.001
Ferritin (ng/mL)	1813 (25–42 138)	2000 (459–217 988)	0.007
Aspartate aminotransferase (U/L)	40 (7–555)	157 (17–2888)	<0.001
Alanine aminotransferase (U/L)	37 (5–539)	143 (11–2407)	<0.001
Triglycerides (mmol/L)	1.2 (0.4–3.8)	2.56 (0.7–19.3)	<0.001
Fibrinogen (g/L)	4.3 (0.9–8.1)	1.49 (0.31–5.59)	<0.001
ESR (mm/hour)	69 (3–132)	27 (1–126)	<0.001
CRP (mg/L)	83.0 (0.27–498.9)	75.6 (1.5–250)	0.772
Scores			
HScore, median (range)	68 (33-156)	196 (98–333)	<0.001
MS score, median (range)	−1.17 (−1.26 to 2.52)	1.05 (−1.26 to 26.55)	<0.001

*Values are expressed as n (%) or median (range).
AOSD, adult-onset Still's disease; CRP, C reactive protein; ESR, erythrocyte sedimentation rate; F, female; M, male; MAS, macrophage activation syndrome.

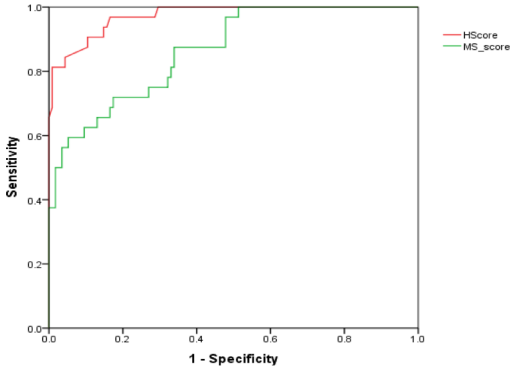

Figure 1 Roc curve of HScore and MS score. HScore=120, sensitivity=90.6%, specificity=89.6%. MS score=−0.45, sensitivity=75%, specificity=73%. AUC-HScore=0.973, AUC-MS score=0.865, p<0.001

The best cut-off value of HScore was 169, with a sensitivity of 93% and a specificity of 86% when it was developed.[6] The cut-off was set at 190.5 and yielded a sensitivity of 96.7% and a specificity of 98.4% when tested in a group of Turkish patients with MAS.[7] Our results indicate that HScore is suitable for detecting AOSD-MAS but with a lower cut-off value. Indeed, different patients' selection criteria, different disease status and different underlying diseases may result in quite different conclusions. Further studies are needed to validate these different scoring tools.

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Correction notice This article has been corrected since it published Online First. Table 1 has been amended.

Acknowledgements We thank our colleagues for their assistance in data collection and analysis.

Contributors LZ and TL designed the study; LZ, XY and XL collected the data; LZ analysed the data, performed statistical analysis and wrote the manuscript; TL and SL revised the manuscript. All authors read and approved the final manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, conduct, reporting or dissemination plans of this research.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; internally peer reviewed.

To cite Zhang L, Yang X, Li T-F, *et al*. *Ann Rheum Dis* 2022;**81**:e99.

Received 12 May 2020
Accepted 15 May 2020
Published Online First 1 July 2020

► http://dx.doi.org/10.1136/annrheumdis-2020-218033

Ann Rheum Dis 2022;**81**:e99. doi:10.1136/annrheumdis-2020-217917

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