Correspondence on ‘2023 ACR/EULAR antiphospholipid syndrome classification criteria’

The release of the eagerly anticipated 2023 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) Antiphospholipid Syndrome (APS) Classification Criteria marks a significant milestone since the revision of the Sapporo criteria in 2006. The updated criteria, characterised by a compulsory entry requirement and the application of an additive weighted system, have been rigorously validated in two distinct cohorts, demonstrating a remarkable specificity of 99% and a commendable sensitivity of 84%.

To ensure comprehensive validation across diverse ethnic groups, we conducted a study involving 965 potential patients with APS of Asian descent in China. Among them, 436 patients are clinically diagnosed as APS by our experienced rheumatologists (CY and JT), establishing the gold standard. In our cohort, 367 patients were classified as APS by the new criteria, while 479 patients were included as APS by the revised Sapporo criteria. Notably, the new criteria displayed a heightened specificity of 98% (95% CI 97% to 99%) compared with the revised Sapporo APS criteria’s 90% (95% CI 87% to 92%), although with a slightly lower sensitivity of 82% (95% CI 78% to 85%) compared with 98% (95% CI 96% to 99%).

The incorporation of well-defined microvascular domain items into the criteria has led to the reclassification of nine ‘no APS’ patients as APS due to their presentation with thrombocytopenia, cardiac valve involvement and livedo racemosa. Additionally, we have identified patients with APS who concurrently exhibited both macrovascular and microvascular manifestations, including antiphospholipid antibody (aPL)iniepathy, pulmonary haemorrhage and adrenal haemorrhage. This underscores the remarkable precision and effectiveness of the new criteria. It is important to acknowledge that thrombocytopenia and positive aPLs are common clinical features in systemic lupus erythematosus (SLE) and are integrated into the 2019 EULAR/ACR classification criteria for SLE. Consequently, the inclusion of thrombocytopenia raises concerns about potential APS overdiagnosis in these complex clinical scenarios.

Conversely, 78 out of 436 patients with APS (18%) did not meet the new criteria. Among them, 30 (38%) scored less than 3 points in the clinical domains. Many of these patients had experienced either ≥3 consecutive early fetal losses or late fetal losses but were assigned only one point under the new criteria, despite having moderate-to-high titre aPL positivity. While the new criteria aimed to redefine pregnancy morbidity to better identify patients with obstetric APS, this redefinition has raised concerns about managing obstetric patients with persistent moderate-to-high aPL positivity. They may not meet the APS criteria due to low clinical domain scores, which prompts questions about the appropriateness of initiating combination treatment with low-dose aspirin and anticoagulants for such patients.

Furthermore, among the patients not meeting the new criteria, 58 individuals (74%) exhibited only aCL and/or aβ2GP1 IgM positivity, resulting in low laboratory domain scores. Remarkably, many of them had moderate-to-high aPL levels. The new criteria assign weights to aPL positivity, but it appears to conflict with the previous definition of the aPL risk profile. Specifically, patients with APS with moderate–high levels of both aCL and aβ2GP1 IgM (double aPL positivity) are categorised as having a high-risk aPL profile, necessitating the reinforcement of thrombosis prevention and treatment strategies. However, these patients may not be classified as APS according to the new criteria. Additionally, our previous study suggested that aCL/aβ2GP1 IgM isotypes maintain high specificity (97%) for aCL IgM and aβ2GP1 IgM in the diagnostic evaluation. In our cohort, 83 seronegative APS, who consistently test negative for criteria aPLs, still cannot be classified as APS since neither ‘non-criteria’ aPLs nor new detection methods for aPLs were incorporated into the new criteria with the goal of enhancing the uniformity of the laboratory domain. Enhancing the standardisation of aPLs detection platforms and broadening the range of aPLs hold substantial significance in the identification of patients with these characteristics.