

The Optimal Tool for Assessment of Organ Damage in Antiphospholipid Syndrome

To the Editor:

We read with great interest the article by Grika, *et al*, a retrospective analysis of the morbidity, mortality, and organ damage in patients with antiphospholipid syndrome (APS), with or without systemic lupus erythematosus (SLE)¹. The authors conclude that “APS occurs among young individuals and it is a cause of increased morbidity, with one-fourth of the patients progressing to organ damage in a mean time of 10 years from disease onset”¹. Given that the number of studies analyzing the organ damage in patients with APS is limited and that no damage index exists specifically validated for patients who are aPL-positive, the study is timely and important. Our group also has been interested in assessing and quantifying organ damage in patients with APS, and thus we would like to highlight some of the challenges in studying organ damage in patients who are aPL-positive.

The organ damage in the study by Grika, *et al* was evaluated using the Systemic Lupus International Collaborating Clinics (SLICC)/American College of Rheumatology (ACR) Damage Index (DI; the higher SLICC/ACR DI score was associated with increased mortality), which has been designed and validated for SLE to identify nonreversible organ damage, not related to active inflammation, lasting at least 6 months². In our analysis of the utility of the SLICC/ACR DI in patients who are aPL-positive, we also showed that (1) the SLICC/ACR DI score increases with additional aPL and/or SLE-related damage; and (2) the SLICC/ACR DI identifies most, but not all, of the aPL-related organ damage³. The top 2 limitations of SLICC/ACR DI use in patients who are aPL-positive were (1) not being able to record aPL-related “damage” (livedo reticularis/racemosa, adrenal infarcts requiring chronic treatment, diffuse pulmonary hemorrhage resulting in chronic symptoms, permanent inferior vena cava filter placement, multiple sclerosis-like disease, and/or white matter changes); and (2) the definition of the 2 SLICC/ACR DI items (“venous thrombosis with swelling, ulceration, OR venous stasis for at least 6 months”; “skin ulceration [excluding thrombosis] for more than 6 months”). In our analysis, we created an experimental category for aPL-related damage, assigning the above damage items 1 point each; we also scored all venous events and skin ulcers as 1 point.

In another retrospective study, we demonstrated that functional prognosis is poor in an important minority of patients with primary APS for > 10 years; one-third of patients with primary APS had organ damage and one-fifth were functionally impaired⁴. In that study, we defined organ damage as permanent loss of the normal function of an organ system because of a clinical manifestation of APS, and functionally impaired as any patient who was unable to perform everyday activities self-identified as important to maintain quality of life⁴.

A recent cross-sectional study by Amigo, *et al* also aimed at the development and validation of a new physician-reported chronic DI in APS patients (DIAPS)⁵, after an expert panel identified 47 items that reflected irreversible aPL-related damage. The study demonstrated content, criterion, and construct validity; and DIAPS had a good correlation with

EuroQol⁶, a standardized non-disease-specific instrument for describing and valuing health-related quality of life by evaluating various factors (e.g., mobility, self-care, usual activities, pain/discomfort, and anxiety/depression).

Given the significant morbidity as well as social and financial implications associated with increased organ damage in patients with APS, it is clear that there is a need for a more accurate way to assess aPL-related organ damage in patients who are aPL-positive, with or without SLE. Meanwhile, physicians should be aware that while the SLICC/ACR DI can provide a crude estimate of APS-related organ damage, in persistently aPL-positive patients with SLE it should be interpreted cautiously because it can overestimate SLE-related damage and underestimate aPL-related damage.

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