

LABORATORIO E FATTORI PREDITTIVI

CLINICAL RELEVANCE OF ISOLATED ANTI-PHOSPHATIDYLSERINE/PROTHROMBIN ANTIBODY POSITIVITY.

A. Hoxha¹, P. Žigon^{2|3}, L. Katja^{2|3}, S. Čučnik^{2|4}, Ž. Rotar^{2|5}, S. Gavasso¹, P. Zerbinati¹, G. Gobbo¹, P. Simioni¹.

¹University of Padua, Internal Medicine Unit, Thrombotic and Hemorrhagic Centre, Department of Medicine-DIMED, Padua; ²University Medical Centre Ljubljana, Department of Rheumatology, Ljubljana; ³University of Primorska, Faculty of Mathematics, Natural Sciences and Information Technologies, Koper; ⁴University of Ljubljana, Faculty of Pharmacy, Ljubljana; ⁵University of Ljubljana, Faculty of Medicine, Ljubljana) Slovenia.

Background and aims: Anti-phosphatidylserine/prothrombin antibodies (aPS/PT) are non-criteria antiphospholipid antibodies (aPL) strongly associated with thrombosis and pregnancy complications related to antiphospholipid syndrome (APS). The latest ACR/EULAR classification criteria for APS aim to classify APS with an increased specificity of up to 99%, but also recommend exploring the relevance of other aPL tests, such as aPS/PT, to guide future updates. In this study, we aimed to assess the clinical relevance of a single aPS/PT-positivity.

Material and Methods: Sixty-nine patients prospectively followed between January 2011 and December 2024 were enrolled from the University Medical Centre Ljubljana (UMCLJ) and the University of Padua (UniPD). IgG and IgM antibodies against cardiolipin (aCL), β 2-glycoprotein I (anti- β 2GPI) and aPS/PT antibodies were tested at UMCLJ using in-house ELISAs (1) and at UniPD using commercial assays from Orgentec Diagnostika, Mainz, Germany, and INOVA Diagnostics Inc., San Diego, CA, USA, respectively (2). Lupus anticoagulant (LAC) was determined using a three-step procedure in accordance with the ISTH guidelines.

Results:

The combined cohort comprised 69 patients (11 men, mean age at diagnosis 45.5 ± 16.1 years, range 10-77 years) who were persistently single aPS/PT positive, confirmed by at least two measurements between 2014 and 2024. Importantly, 27 of 69 (39%) patients achieved a clinical domain score of more than 3 weight points (WP), thus fulfilling the clinical domain of the new classification criteria. Among them, 11 patients were LAC-negative and therefore did not meet the labo-

ratory criteria (<3 WP), whereas 16 patients had persistent LAC positivity and met the new criteria (Table 1). In the LAC-negative group, the mean clinical domain weight was 4.5 compared to 5.4 in the LAC-positive group, which was not a statistically significant difference (Figure 1). Eight out of eleven (73%) LAC-negative patients and twelve out of sixteen (75%) LAC-positive patients had an underlying autoimmune disease, mostly SLE.

Seven LAC-negative patients experienced venous thromboembolism (VTE), one with a high-risk VTE profile, three experienced arterial thrombosis (AT), two with a high-risk CVD profile, one had established microvascular manifestations and three had obstetric manifestations, two of which were PEC, three patients had cardiac valve manifestations and three had thrombocytopenia.

Nine LAC-positive patients experienced VTE, one with a high-risk VTE profile, six experienced AT, all without a high-risk CVD profile, two had established and three suspected microvascular manifestations and four had obstetric manifestations; none of them were PEC. Four patients had cardiac valve manifestations, and five had thrombocytopenia.

Conclusion: Single aPS/PT positivity is associated with all six clinical domains included in the 2023 ACR/EULAR APS classification criteria, even independently of LAC positivity. The association of aPS/PT with newly added clinical domains, known to be linked to damage accrual, makes aPS/PT a tool for risk stratification in APS.

Figure 1: Clinical relevance of single aPS/PT positivity. Created in <https://BioRender.com>

Email: ariela.hoxha@unipd.it

