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## Cardiac involvement in the antiphospholipid syndrome

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**Introduction:** Antiphospholipid syndrome (APS) is a systemic autoimmune disease, associated with a hypercoagulable state and fetal loss and with other clinical manifestations including cardiac involvement. The antiphospholipid syndrome has been associated with multiple cardiac abnormalities. Cardiac manifestations of APS are valve abnormalities (valve thickening and vegetations), occlusive arterial disease (atherosclerosis and myocardial infarction), intracardiac emboli, ventricular dysfunction, and pulmonary hypertension. Antiphospholipid antibodies (aPL) may have a role in the accelerated atherosclerotic arterial disease observed in APS, related to their ability to induce endothelial activation. aPL have been incriminated in the pathogenesis of heart valve lesions in APS patients. Markers of endothelial cell activation are up-regulated with prominent deposition of aPL in heart valves, suggesting aPL deposition initiates an inflammatory process that recruits complement leading to the valve lesion. Autoantibody-mediated endothelial cell activation probably plays a role in sustaining a proadhesive, proinflammatory, and procoagulant phenotype. The heterogeneity of APS clinical manifestations is likely linked to the varied effects that aPL can induce on endothelial cells and to the different functions that endothelial cells display depending on the anatomic localization.

**Objectives:** The aim of this study was to investigate association between cardiac manifestations in patients with antiphospholipid syndrome (APS) with type of antiphospholipid antibodies (aPL).

**Methods:** Among the 446 patients from the Serbian National APS Registry, 330 met the criteria for primary APS (PAPS), 126 were diagnosed with secondary APS (SAPS) in scope of SLE, and 10 presented APS in scope of some other autoimmune rheumatic disorder. Of these patients, 333 (218 with PAPS and 115 with SAPS) were included into this prospective study. Antiphospholipid antibody (aPL) analysis included detection of aCL (IgG/IgM),  $\beta$ 2GPI (IgG/IgM) and LA and served to evaluate associations with distinct cardiac manifestations.

**Results:** Presence of aCL IgG was more common ( $p=0.001$ ) in SAPS and LA in PAPS patients ( $p=0.002$ ). In all patients echocardiography study was performed in order to reveal presence of vegetations, pseudoinfective endocarditis, intracardiac thrombus and valve thickening or dysfunction. Data considering acute myocardial infarction, unstable angina, coronary artery bypass grafting (CABG) or percutaneous coronary artery angioplasty (PTCA) as well as manifestations of chronic or acute heart failure were also collected. There was no statistically significant difference between overall cardiac manifestations and the type of aPL. There were 27.7% SAPS patients and 9.3% PAPS patients with valve vegetations ( $p=0.000$ ). Pseudoinfective endocarditis was observed in 12.8% SAPS patients and 3.1% in PAPS patients ( $p=0.004$ ). 30% of the patients with high levels of aCL IgG antibodies ( $>100$  PLU/ml) had valve thickening and dysfunction, as compared to 4.1% without valve abnormalities ( $p=0.002$ ). Highly statistically significant difference was revealed considering presence of aCL-IgG and aCL-IgM antibodies and pseudoinfective endocarditis ( $p=0.004$ ,  $p=0.003$  respectively) and presence of aCL-IgG and valvular dysfunction ( $p=0.023$ ). Valvular manifestations in our cohort were significantly related to titers of aCL antibodies. The level of aCL IgG ( $p=0.005$ , Pearson  $+0.138$ ) were in positive correlation with presence of pseudoinfective endocarditis. Our study showed that patients with SAPS had higher prevalence of valvular lesions, and that higher levels of aCL IgG were associated with their appearance. Opposite, patients with PAPS were more often presented with coronary artery disease, although without statistical significance.

**Conclusion:** Certain aPL type and levels are associated with distinct cardiac manifestation, suggesting their predictive role. There is strong link between some cardiac manifestations in APS patients, suggesting complexity and evolutionary nature of APS.

### Biography

Ljudmila Stojanovich is Research Professor, and the Scientific Director in the Bezanijska Kosa, University Medical Center of Belgrade University. Her research focuses on Systemic Lupus Erythematosus, Antiphospholipid Syndrome, and Vaccination in patients with Autoimmune Rheumatic diseases. She is an author of three monographs and of about 250 articles on various aspects of Rheumatic disorders, published in international journals and in conference proceedings. She is in Editorial Boards /Reviewer in the "Current Contents" or "Science citation index", like LUPUS, Cellular and Molecular Neurobiology, The Journal of Vaccine, The Journal of Rheumatology, Allergologia et Immunopathologia and others. She is a member of number International Project, like of "the European Forum on Antiphospholipid Antibodies", "Multicenter Studies Antiphospholipid Antibodies, Infections and Autoimmune Diseases". She is the member of steering group committee (composed of experts representing 11 European countries) of European League Against Rheumatism (EULAR) for the recommendations for vaccination in patients with autoimmune inflammatory rheumatic diseases.

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