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Editorial

Heart valve involvement in antiphospholipid syndrome: More than you think!

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In this issue of the International Journal of Cardiology, Tufano et al. show that left ventricular (LV) diastolic abnormalities are more frequently seen in patients with antiphospholipid syndrome (APS) than in controls.

APS is a group of clinical manifestations (vascular thrombosis either arterial, venous or microvascular; and pregnancy morbidity) associated with persistent antiphospholipid antibodies (aPL). These aPL are detected using three traditional assays namely lupus anticoagulant test, anticardiolipin and anti-β_2-glycoprotein I antibodies. APS is defined when at least one clinical manifestation and one laboratory test are present. While it has been confirmed that this syndrome can induce thrombosis in the cardiovascular system (e.g. coronary thrombosis, ventricular thrombus), association of APS and LV diastolic dysfunction and its risk factors still have to be clarified.

Multiple risk factors for developing LV diastolic dysfunction (e.g. moderate to severe valvular disease, systemic hypertension or pulmonary hypertension, myocardial infarction or myocarditis) [1,2] are more frequent in APS patients with or without systemic lupus erythematosus than in the general population; however it was unclear if LV diastolic dysfunction was due to aPL or to the latter additional risk factors. To avoid this bias in Tufano's study, patients with coronary artery disease, valve disease and heart failure were excluded. In multivariate analysis, authors found that lupus anticoagulant was independently associated with LV diastolic dysfunction parameters after adjusting on several confounders such as age, body mass index and LV mass index. Previous data support these results, since LA is considered as the most clinically relevant aPL test that is highly associated with manifestations of APS such as thrombosis, pregnancy morbidity or other cardiac manifestations [1,2].

Most of previous studies [3,4] have identified an impaired left ventricular diastolic dysfunction in APS patients vs. controls while other did not [5]. Methods for the identification of LV diastolic dysfunction vary significantly among studies (mitral inflow velocity, E/A ratio, LV isovolumic relaxation time…). In the study of Tufano et al. diagnosis of LV diastolic dysfunction was done using recent ASE/EACVI recommendations [6]. Since older criteria were used so far, no direct comparison of frequency can be made. In comparison with controls, frequency of grade I LV diastolic dysfunction was much higher (7.2% vs. 20.3%). This underlines the importance of a comprehensive TTE screening of heart involvement in APS patients including LV diastolic dysfunction using recent ASE/EACVI criteria.

The identification of the full spectrum of clinical manifestations of APS is still underway. Indeed, international criteria for definite APS published in 1999 and updated in 2006 included vascular thrombosis and pregnancy complications only (fetal loss, placental insufficiency). Other manifestations including non-thrombotic cardiac complications were not included because of lacking and conflicting data in the literature regarding their association with aPL. Recently, meta-analyses demonstrated an epidemiological link between heart valve disease [1], pulmonary hypertension [2] and aPL positivity. Furthermore, rising evidence support the concept of an APS vasculopathy: Besides the durable hypercoagulable state due to APS (acquired thrombophilia) which causes macro- and micro-vascular thrombosis, published data confirmed the negative impact of aPL on vascular wall cells i.e. endothelial and smooth muscle cells. Indeed, Canaud et al. demonstrated that the mTORC pathway was impaired in APS patients with renal involvement causing endothelial proliferation [7]. Furthermore, numerous studies identified a vasculopathy in APS patients presenting with non-criteria manifestations such as livedo or non-thrombotic neurological manifestations (transient ischaemic attack, cognitive dysfunction, demencia) [8] We may hypothesize that this vasculopathy could be systemic and impair several organs including the heart. Further studies will be needed to identify which underlying mechanisms mediated by aPL cause LV diastolic dysfunction.

Recently new aPL tests have been developed to identify high-risk patients. Indeed anticardiolipin antibodies and also at a lesser extent

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anti-β_2-glycoprotein I antibodies identify both pathogenic and non-pathogenic/non-specific aPL. Basic research allowed to develop new biomarkers identifying pathogenic aPL [9]. It would be interesting to know whether these specific antibodies can identify high risk patients for developing heart involvement.

Since up to 30% of asymptomatic APS patients have subclinical myocardial abnormalities identified by cardiac MRI [10], could new imaging techniques help us identifying LV diastolic abnormalities more precisely. Furthermore, regarding the therapeutic approaches for these asymptomatic patients, we still do not know which treatments would slow the progression of heart involvement.

To conclude, this study contributes to the understanding of the whole spectrum of APS. As we are trying to solve the "APS puzzle", new therapeutic targets emerge.

Conflict of interest

None.

Fundings

None.

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