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Editorial

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Editorial

Measurement of arterial stiffness in antiphospholipid syndrome: a step forward in cardiovascular risk stratification?

This editorial refers to the article 'Arterial stiffness tested by pulse wave velocity and augumentation index for cardiovascular risk stratification in antiphospholipid syndrome' by Evangelatos *et al.* 2024;63:1039–47.

Advances in non-invasive vascular assessment techniques over the last few decades now allow the monitoring of the entire sequence of steps that lead from a normal arterial vessel through its initial atherosclerotic degeneration to atherothrombotic occlusion [1–3]. The first hit in this succession of events is the functional deterioration of endothelium triggered by chronic exposure to an array of noxious stimuli, including classical cardiovascular (CV) risk factors and inflammatory mediators [4, 5].

Endothelial dysfunction associates primarily with a reduction of nitric oxide (NO) release, with the consequent impairment of arterial vasodilation that is typically studied non-invasively as flow-mediated vasodilation (FMD) of the brachial artery. The progressive atherosclerotic degeneration of the arterial wall then translates into a reduction of the viscoelastic properties of large (elastic) and medium (muscular) size arteries that can be detected by the measurement of arterial stiffness [6].

The standard reference method for the non-invasive assessment of arterial stiffness is the measurement of carotid-femoral pulse wave velocity (cfPWV), which evaluates the elastic properties of the aorta. The most relevant triggers of enhanced stiffness are arterial hypertension and ageing, but all CV risk factors, and in particular systemic inflammation, enhance cfPWV. Increased arterial stiffness has been shown to be a predictor of future CV events [6, 7].

Another validated method, although less widely employed, is applanation tonometry, which studies radial pulse morphology measuring the systolic blood pressure increase generated by peripheral arterial reflection waves through the calculation of the augmentation index (AIx) [8]. This method allows measurement of the stiffness of elastic and muscular arteries the compliance of which is mediated in part by NO and correlates with FMD [9]. There is some evidence that alterations of AIx are predictive of subsequent CV events [10].

Among inflammatory conditions impairing endothelial function, rheumatological disorders occupy an important place, and indeed for several of them reduced FMD and enhanced arterial stiffness have been reported [11, 12]. In particular, the AIx was found to be altered in primary antiphospholipid syndrome, systemic sclerosis, rheumatoid arthritis and polymyostis, and to correlate with cfPWV [11].

Given that arterial stiffness is increased in patients at enhanced CV risk and predicts subsequent arterial events, its measurement might theoretically improve risk stratification and thus patient management. However, although indisputably able to detect early arterial damage, current CV prevention guidelines do not recommend the measurement of AIx and/or of cfPWV for CV risk stratification [13], except in people with arterial hypertension in whom an abnormal cfPWV may represent a marker of hypertension-mediated organ damage, and hypertension-mediated organ damage may modify the CV risk estimate in stage 1–2 arterial hypertension [14].

The most recent European Society of Cardiology Guidelines on CV disease prevention include among potential risk modifiers only coronary artery calcium scoring and carotid ultrasound for plaque determination, while all other non-invasive vascular assessment techniques, including the measurement of arterial stiffness, are not recommended [13].

Evangelatos and coworkers measured arterial stiffness in a relatively large series of patients with antiphospholipid syndrome (APS) as a possible aid in the stratification of the atherothrombotic risk [15]. They measured cfPWV and AIx in 110 APS patients and compared it with an equal number of age- and sex-matched diabetic patients and of healthy controls and showed that APS patients display enhanced AIx compared with healthy controls, similar to diabetic patients, and that this associates with some CV risk factors, like enhanced age and mean arterial pressure, and concluded that the measurement of arterial stiffness may improve CV risk stratification in APS [15]. This study has several merits, among which are the inclusion of a relatively large series of APS patients, the measurement of arterial stiffness in all subjects by one experienced operator thus reducing variability, the simultaneous vascular ultrasound assessment for atherosclerotic plaques, and the presence of a significant fraction of APS patients at low–intermediate CV risk who might indeed benefit from CV risk restratification. However, it also has limitations, including the lack of a follow-up assessing the incidence of CV events depending on baseline AIx values or the

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lack of a control group of APS patients without CV risk factors. Concerning the latter point, as the authors mention, a previous study examining arterial stiffness in APS patients showed a significant association between altered AIx and impaired flow-mediated vasodilation. Therefore, given that previous studies have shown that APS patients without CV risk factors present a normal endothelial function [16], clarifying whether it is the presence of CV risk factors [7] or of APS itself that is responsible for enhanced arterial stiffness would help in understanding the pathophysiology of this syndrome.

Thus, while the study by Evangelatos *et al.* addresses an important clinical issue, in the absence of prospective studies on the predictive value of cfPWV and AIx for major cardiovascular events in patients with APS, alterations of arterial stiffness may only provide useful pathophysiological insight in atherogenesis in this patient group or may be used as a surrogate end point in atherosclerosis intervention studies.

In conclusion, the search for the improvement of CV risk prediction in APS patients is still ongoing and, as Evangelatos and coworkers conclude, prospective studies in well-defined APS patient categories, possibly assessing the incidence of CV events at follow-up, are needed to further examine the utility of arterial stiffness markers in CV risk stratification and management of APS patients.

Data availability

Data are available upon reasonable request by any qualified researchers who engage in rigorous, independent scientific research, and will be provided following review and approval of a research proposal and Statistical Analysis Plan (SAP) and execution of a Data Sharing Agreement (DSA). All data relevant to the study are included in the article.

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