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Clinical Insights

Atrial cardiomyopathy: Pathophysiology and clinical implications

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The term atrial cardiomyopathy appears sporadically in the medical literature, and generally has been used in conjunction with atrial fibrillation (AF), or as "atrial fibrotic cardiomyopathy", a pathological determinant of AF, caused by a primary cardiomyopathic process, independent of the arrhythmic disorder [1,2].

The definition of atrial cardiomyopathy as: "*Any complex of structural, architectural, contractile or electrophysiological changes affecting the atria with the potential to produce clinically-relevant manifestations*" was proposed for the first time in a consensus document produced in 2016 by the European Heart Rhythm Association (EHRA), Heart Rhythm Society (HRS), Asia Pacific Heart Rhythm Society (APHRS), and Sociedad Latino americana de Estimulacion Cardiaca y Electrofisiología (SOLAECE), in collaboration with the American College of Cardiology (ACC) and the American Heart Association (AHA) [3]. A histologically based classification is used in this experts' consensus documents, with the acronym EHRAS (for EHRA/HRS/APHRS/SOLAECE), including four classes: (I) principal cardiomyocyte changes, (II) principally fibrotic changes, (III) combined cardiomyocyte-pathology/fibrosis, (IV) primarily non-collagen infiltration (with/without cardiomyocyte changes) [3].

This is the first histopathological classification of atrial cardiomyopathy, that might be useful primarily to describe pathological changes of the atria, to correlate these changes to the results of imaging procedures, and, in the future, to help defining a tailored management of patients with AF. However, an important limitation of this purely descriptive classification is the absence of progression in severity from EHRAS class I to EHRAS class IV, in contrast with other clinically useful classifications, such as the New York Heart Association functional class (NYHA class) [3]. Moreover, the different atrial cardiomyopathies (lone AF, atrial amyloidosis, muscular dystrophies, congestive heart failure, obstructive sleep apnea, AF-induced remodeling, drug-induced, myocarditis, high blood pressure, obesity, age, diabetes and valvular heart disease) can have features of multiple EHRAS classes, with the only exception of atrial amyloidosis in the IV class [2,3].

Regardless of the limits of the classification, we believe that the detection of atrial cardiomyopathy may have potential important practical clinical implications: (1) to guide ischemic stroke prevention in patients with or (2) without AF, (3) to guide antiarrhythmic therapy, rhythm maintenance and rate control in AF patients [2].

In recent years there has been growing interest in better evaluating left atrial dilation and myocardial fibrosis, causing left atrial dysfunction and electromechanical conduction delay, as a substrate for AF. Indeed, the 2020 ESC Guidelines for the diagnosis/management of AF [4] included for the first time a structured characterization of AF, with clinical assessment of stroke risk, symptom status, burden of AF, and evaluation of substrate, with a clear indication to detect atrial cardiomyopathy, for the optimal management of AF patients [4,5]. The guidelines state that the diagnosis of atrial cardiomyopathy could be based on easily accessible parameters (e.g. etiology, prothrombotic state, and abnormal left atrial -LA- volume/function) [4].

Easily accessible parameters at transthoracic echocardiography (TTE), such as abnormal LA volume/function, integrated with the currently used clinical scores could substantially improve thromboembolic risk prediction in AF. This in particular in patients at intermediate risk according to the CHA_2DS_2VASc (congestive heart failure, arterial

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hypertension, age > 75 years, diabetes mellitus, stroke/transient ischemic attack, vascular disease, age 65–74 years, sex category) score: CHA_2DS_2VASc classes 1 if males and 2 if females [6,7].

Among the TTE measurements, the parameter of choice for this purpose could incorporate a combination of LA size and function. The LA strain is increasingly used to assess LA (LA reservoir, conduit and contractile function), although it remains subject to limited availability and inter-vendor variability [6]. P-wave to A′ duration on tissue Doppler imaging (PA-TDI, reflecting total atrial conduction time) is also a surrogate marker of LA function [8]. The evaluation of LA emptying fraction (LAEF) by the easy measurement of LA maximal and minimal LA volumes [(LA maximal volume – LA minimal volume) / LA maximal volume x 100], using 2D and, even better, 3D echocardiography, may also be a good estimate of the global capacity of LA to fill the left ventricle (LA ejection fraction). This index probably represents more than a simple surrogate of LA strain and could be therefore utilized and further investigated [6]. Studies have demonstrated that LAEF is reduced in patients with AF [6]. Future prospective studies are needed to confirm the prognostic power of LA functional (in combination with LA size) assessment in predicting thromboembolic risk in AF patients. The European Association of Cardiovascular Imaging has planned an international multi-center registry designed to explore the possible additional value of standard and advanced TTE parameters to CHA_2DS_2VASc score in AF patients [9].

There is also suggestion that atrial remodeling, evaluated with LAEF, not only can predispose to AF, but itself may be associated with an increased risk of systemic thromboembolism. In this perspective, AF is not only a risk factor for thromboembolism for but also a marker of atrial cardiomyopathy, which could explain sometimes the lack of temporal relationship observed between detected AF and stroke [10–15]. It should also be noted that, in patients with chronic heart failure, the CHA_2DS_2VASc score is predictive of thromboembolic risk in the absence of AF history [16]. Moreover, the CHA2DS2-VASc score correlates with the presence of LA spontaneous echo contrast (sludge) in patients with rheumatic mitral stenosis and, again, without AF history. These patients are at risk of LA thrombus formation and systemic thromboembolism, despite sinus rhythm [17].

The concept that a “diseased atrium” is fundamental to the pathogenesis of thrombus formation and ischemic stroke should be considered and emphasized [18,19]. If atrial cardiomyopathy is considered as a stroke risk factor, independent of AF, it could be used to identify patients with sinus rhythm who might have thromboembolic events that could be prevented by oral anticoagulation. This hypothesis would need to be tested in prospective randomized trials.

Detection of atrial cardiomyopathy could also improve the evaluation of the duration of anticoagulant therapy after ablation, and also the identification of individuals for whom ablation therapy will fail, considering the frequent risk of long-term recurrences after the procedure. Indeed, failure of ablation procedures may be caused by progression of atrial cardiomyopathy [2]. However, the real impact of atrial cardiomyopathy on the success of catheter ablation has not been clearly elucidated, likely because specific cardiomyopathies may differentially affect ablation procedures [3]. A cardiovascular risk factor intervention (correction of obesity, optimal treatment of arterial hypertension) can also improve outcomes after ablation by prevention/reversal of atrial remodeling and atrial cardiomyopathy [2,3]. Finally, detection of atrial cardiomyopathy might be useful for guiding the selection of the appropriate antiarrhythmic drugs, rhythm maintenance and rate control therapy, by identifying patients who are likely to experience therapy failures [2,3].

In conclusion, the practical clinical value of the detection of atrial cardiomyopathy may be extremely important but remains to be better elucidated. A great effort is needed in evaluating specific atrial cardiomyopathy imaging/etiologic features in large-scale multi-center trials. At the same time, further studies are also needed to validate the EHRAS classification and to assess its practical role in the management of patients with or without AF.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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