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INVITED EDITORIAL

The left atrium: an old 'barometer' which can reveal great secrets

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In patients with heart failure (HF), left atrial (LA) function plays a central role in maintaining optimal cardiac output despite impaired left ventricular (LV) relaxation and reduced LV compliance.[1] It has been demonstrated that the Frank–Starling mechanism is also operative in the left atrium and that LA output increases as atrial diameter increases, which contributes to maintain a normal stroke volume. In a non-compliant left ventricle, as the left atrium is exposed to the pressures of the left ventricle during diastole, LA pressure rises to maintain adequate LV filling. The resulting increase in LA wall tension, through myocyte stretch, induces myolysis, fibrosis, and apoptosis, and leads to progressive LA enlargement, which tends to prevent passive transmission of pressure to the pulmonary circulation.[2,3]

Clinically, LA enlargement is most commonly expressed by the maximum LA volume obtained at end-systole when LA chamber is at its greatest dimension. It should be noted that left atrium is not a symmetrically shaped three-dimensional (3D) structure, and that LA enlargement is not a uniform process. Therefore, measurement of the left atrium by M-mode echocardiography is likely to be an insensitive assessment of any change in size of the left atrium. Conversely, LA volume by two-dimensional (2D)/3D echocardiography provides a more accurate and reproducible estimate of the size of the left atrium.[4]

Because a large number of individuals with LV dysfunction are in a pre-clinical phase of the disease,[5] increased LV filling pressures (E/e′) could only be expressed during exercise. The causes of increased E/e′ with exercise are not well characterized. In a group of patients with a resting a E/e′ <15, Hammoudi *et al.*[6] showed that the patients with increased LV filling pressures at exercise echocardiography (E/e′ >13 in 12% of the population) were those with larger LA volumes at rest. A LA volume index >33 mL/m^2, a cut-off already shown associated with increased risk of developing symptomatic HF,[7] predicted abnormal exercise LV filling pressures with a high sensitivity (91%) and a good specificity (78%), while a LA volume index <26 ml/m^2 was a marker of normal exercise echocardiogram. Therefore, abnormal exercise LV filling pressures could be suspected in patients with enlarged left atria. The LA volume is thus a good expression of the cumulative/chronic exposure to abnormal LV filling pressures over time. Whether LA volume could be used to identify patients in whom an exercise echocardiography should be ordered needs to be further addressed.

Increased LA volume may be accompanied/preceded by a progressive impairment in LA function and both may occur before symptom development and may adversely affect prognosis.[8] Dysfunction of the left atrium could be an early sign of LA pathological process. Left atrial function has three components: reservoir, conduit and active contractile functions. Reservoir function occurs during LV systole, the conduit function results from the blood transiting from the pulmonary veins into the left atrium during early diastole and finally, the active contractile function arrives in late diastole to increase LV filling. Left atrial function has been initially described by volumetric method in several diseases.[9] In recent years, tissue Doppler-derived strain imaging has also been documented to adequately assess regional and global LA function in normal subjects, in increased afterload states and in HF. Two-dimensional speckle tracking-derived strain, an angle independent tool, overcomes the main drawbacks of tissue Doppler imaging and thus provides more accurate quantification of LA function.[10]

Compared with normal subjects, the different components of LA function—reservoir, conduit and active contractile functions—have been shown to be altered in various cardiovascular diseases.[9,11] Left ventricular systolic and diastolic dysfunction, elevated filling pressure, LV hypertrophy, mitral regurgitation, and intrinsic atrial myopathy are all potential contributors to ongoing LA remodelling/dysfunction.[12] In a group of patients with HF, preserved LV ejection fraction and elevated *N*-terminal pro-brain natriuretic peptide (NT-proBNP) derived from the PARAMOUNT trial (The Prospective comparison of ARNI with ARB on Management Of heart failUre with preserved ejectioN fraction), Santos *et al.*[13] also reported an impairment of LA reservoir and pump (active contractile) function compared with controls. Interestingly, reduction in LA reservoir function (LA positive strain during LV systole), as assessed by 2D speckle tracking, occurred regardless of LA size (LA volume) or history of atrial fibrillation. Therefore, volumetric methods and strain imaging are not interchangeable approaches to assessment of LA function. Impairment in LA function may thus precede/promote LA dilatation, which in turn may

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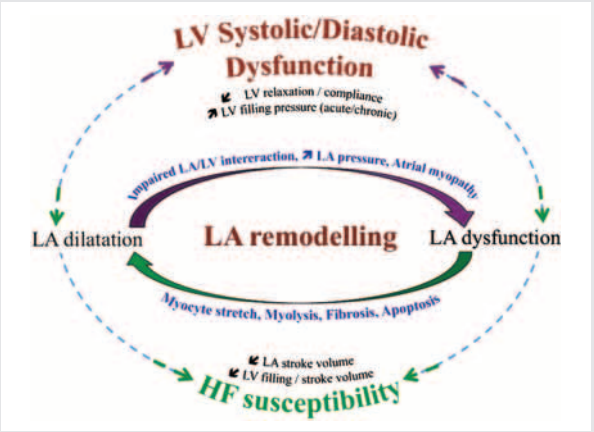

Figure 1 Relationship between left atrial (LA) remodelling, left ventricular (LV) function and heart failure (HF).

contribute/accentuate LA dysfunction and reduce the contribution of the LA to LV filling/LV stroke volume (*Figure 1*).

There is a close interdependence between LV and LA function. Left atrial reservoir function is influenced by LV contraction through the descent of LV base during systole, LA relaxation and stiffness, LA conduit function is dependent on LV relaxation and preload, and LA booster pump function is influenced by LV compliance, LV filling pressures, and intrinsic LA contractility.[1] In the PARAMOUNT trial, lower LA systolic strain (reservoir function) was associated with higher prevalence of previous HF hospitalization and history of atrial fibrillation, as well as worse LV systolic function (global longitudinal strain), LV hypertrophy and LA remodelling.[13] In contrast, LA reservoir function was not correlated with E/e′, an estimate of LV filling pressures, or NT-proBNP. The relative contribution of LA phasic function to LV filling is dependent upon the LV filling properties and therefore varies with level of diastolic dysfunction and of pre-A (LA contraction) LV end-diastolic pressure. In the PARAMOUNT trial, all patients had elevated NT-proBNP, which is known to be associated with increased basal LV filling pressures and higher E/e′, leading to lower early filling gradients and reduced LA reservoir function. Conversely LA systolic strain was significantly associated with reduced LV global longitudinal strain but not with LV ejection fraction, implying that subtle changes in LA/LV function occur early in the disease process. Moreover, reduced LA systolic strain was associated with higher prevalence of previous HF hospitalization and history of atrial fibrillation, suggesting that LA dysfunction may also be a marker of severity in HF with preserved LV ejection fraction. Whether early LA dysfunction is a cause or a consequence of HF, what its prognostic relevance is, and whether it could be used to monitor the evolution of HF remain to be determined in further studies.

In the study of Hammoudi *et al.*[6] concerning patients with normal E/e′ at rest, the LA function was not examined. Accordingly, the potential relationship between impaired LA function, enlarged left atrium and exercise-induced increase in LV filling pressures (E/e′) was not confirmed. Intuitively, LA dilatation can contribute to ongoing LA dysfunction with a negative feedback loop: the more severe the dilatation, the more pronounced the dysfunction. Previous studies have shown that LA dysfunction is linked to HF symptoms, exercise capacity and increased onset of atrial fibrillation, even without LA dilatation.[14,15] However, further studies are warranted to know whether LA dysfunction is an early sign of LA remodelling (before significant dilatation) related to fluctuating LA pressure or a risk marker of progression to HF in patients with normal resting E/e′ and relatively preserved LA size.

Conflict of interest: none declared

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