Left Atrium as an Active Component of the Pathophysiology in HCM

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Hypertrophic cardiomyopathy (HCM) is a genetic cardiomyopathy that causes left ventricular hypertrophy (LVH) and myocardial fibrosis. HCM is a disorder without a distinct ethnic or gender pattern of distribution. Its prevalence is estimated at 0.16-0.29% (1:625-1:344 individuals) in the general population. The screening of HCM is usually conducted by echocardiography, but when more sensitive imaging methods or genetic testing are used, a much higher estimate of 0.6% (1:167) has been reported.

Left ventricular outflow tract obstruction (hypertrophic obstructive cardiomyopathy; HOCM) in HCM patients is known to be associated with a high incidence of heart failure, various arrhythmias such as atrial fibrillation (AF), thromboembolic events, and sudden death. Since the signature of HOCM is very characteristic, it is easily diagnosed, and the risk stratification and treatment are also well established. Compared to HOCM, patients without ventricular obstruction (non-HOCM) usually have normal systolic function and are thought to have a stable clinical course. However, some non-HOCM patients also experience heart failure, AF, and even death because of diastolic dysfunction and high LV filling pressures. Identifying non-HOCM patients with a poor prognosis is a major unmet need in clinical settings.

The left atrium (LA) acts as a reservoir during systole (LA reservoir function reflects the ability of the LA to fill), as a conduit during early diastole (LA conduit function reflects the contribution of the LA to early LV filling), and as an active pump during late diastole (LA booster function reflects LA contractile function). The thin left atrial wall is sensitive to changes in LV filling pressures. Therefore, left atrial function is a strong marker of the severity and chronicity of diastolic dysfunction.

Many studies have described the diagnostic and prognostic importance of LA size and pressure both in the general population as well as in selected clinical conditions such as heart failure with preserved ejection fraction (HFpEF). In this issue of International Heart Journal, Shin, et al. examined the prognostic impact of LA minimal volume (LAVmin) on clinical outcome in a total of 167 consecutive non-HOCM patients. They found LAVmin was an independent risk factor for composite outcome (HF hospitalization, stroke, mortality) in patients with non-HOCM. They also found that LAVmin was superior to LAVmax, which has previously been reported as an important indicator of left ventricular diastolic function and predictor of clinical outcome in HCM patients. The result that LAVmin is superior to LAVmax in non-HOCM patients is a result that is reasoned because early in 2012, Russo, et al. reported that LAVmin measured by real-time 3D echocardiography is more strongly correlated to LV diastolic function (E/e’) and LV filling pressure than LAVmax. This suggests that LAVmin may be a good marker of LA remodeling caused by LV diastolic function. One of the important limitations of the study by Shin, et al. is that they used 2D echocardiography instead of 3D echocardiography. Previous studies have shown that 3D echocardiography is more accurate for the measurement of LA volume than 2D echocardiography. Therefore, if we use 3D echocardiography in non-HOCM patients, LAVmin may have a prognostic impact and may be useful for risk stratification, even in the very early stage of the disease.

The modalities and technologies for the assessment of LA pathophysiology are rapidly advancing (Figure). In addition to 3D imaging of LA using echocardiography or cardiovascular magnetic resonance, echocardiographic speckle-tracking strain is also a technology in the spotlight because it can noninvasively measure the functional components of the LA, including reservoir, conduit, and contractile strain. LA reservoir strain, in particular, has strong prognostic value in HFpEF. In their study about the prognostic utility of LA strain, Freed, et al. reported that abnormal indices of LA mechanics (particularly LA reservoir strain) are powerful clinical and prognostic factors in HFpEF. In HCM patients, Fujimoto, et al. have shown...
that loss of LA active function (evaluated by LA strain) was independently associated with increased cardiac events.21) When recent insights about LA physiology and function are taken together, it creates a paradigm shift that the LA is no longer simply being a passive marker of disease severity, but an active component of the heart failure in HCM patients. Several questions still remain to be answered. Can LA dysfunction identify non-HOCM patients with a poor prognosis at an early stage, before they develop more overt forms of heart failure? And which parameter is suitable for the assessment of early LA dysfunction?

Although the striking pathologic features of the LV in HCM patients have attracted our attention for decades, it is now time to focus more on the LA. After we increase our understanding of the characteristics and pathophysiology of the LA, unloading therapy of LA and improvement of LA function may be important future therapeutic targets in HCM patients.

Disclosures

Conflicts of interest: None.

References

16. Shih SH, Jang JH, Baek YS, et al. Prognostic impact of left atrial minimal volume on clinical outcome in patients with non-