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Prognostic Power of Mitral Annulus Indices of Left Ventricular Diastolic Function

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Left ventricular (LV) diastolic function (LVDF) is an important determinant of exercise tolerance in patients with normal and depressed ejection fraction (EF). Several studies have also shown that noninvasive Doppler measurements of LV relaxation and filling pressures are predictors of outcome in several patients with cardiovascular (CV) disorders, including patients with HFrEF, HFpEF, atrial fibrillation, acute myocardial infarction (MI), mitral regurgitation, end-stage renal disease, and hypertension.[1] Importantly, the change in LVDF can identify patients with normal EF who subsequently die or develop heart failure symptoms.[2,3]

Whereas most of the published literature includes reports from single-center studies, there are community-based reports that have shown similar results.[4,5] The study in this issue by Kuznetsova et al. extends these observations by examining data from 793 subjects who were part of the Flemish Study on Environment, Genes and Health Outcomes (FLEMENGHO). After a median follow-up close to 5 years, mitral annulus early diastolic velocity (e′) by tissue Doppler (TD) was an independent predictor of fatal and nonfatal CV events (CVEs) with an impressive net reclassification improvement of 54.2% for CVEs and 64% for cardiac events (CEs).[6] In addition, CEs and CVEs were observed significantly more frequently in patients with elevated LV filling pressures (LVFPs; assessed by E/e′ ratio). The conclusions are based largely on data from subjects with normal EF, because only 6 patients had an EF of ≤50%.

Aside from the main findings noted above, there are other interesting observations. Mitral annulus e′ velocity predicted outcome after adjusting for age, gender, EF, and other CV risk factors. A progressive decrease was observed in e′ velocity in patients with more advanced grades of diastolic dysfunction. This was coupled with a 4-fold higher risk of CEs in patients with elevated LVFPs. Figure 2 shows that the largest increment in events was observed when e′ was <12.5 cm/s and when the E/e′ ratio was >7.5.[6]

The investigators are to be congratulated for several aspects of the study design and execution, including a solid number of enrolled subjects and losing only 2.2% to follow-up. In addition, the investigators followed a comprehensive protocol for assessment of LVDF, acquired TD signals from 4 annular sites, used spectral pulse Doppler technique for annular velocities (as opposed to color-coded TD, which is not the recommended approach for acquisition of e′ velocity for the assessment of LVDF), performed an analysis that was blinded to clinical data, and were able to classify LVDF based on their algorithm in the vast majority of patients (99.5%).

However, there are also some limitations: Some are related to the Doppler methodology and classification and others have to do with the events included for predicting outcome using TD velocities. Though the imaging protocol allowed for the acquisition of mitral inflow, pulmonary vein signals, and TD velocities, it does not appear that the tricuspid regurgitation signal by continuous wave Doppler was acquired. This parameter can help estimate pulmonary artery systolic pressure, which has been shown to predict outcome in several populations, including patients with heart failure. The choice of an average E/e′ ratio >8.5 to identify patients with elevated LVFPs likely resulted in including several subjects with normal, as opposed to raised, filling pressures. The latter group of patients usually have an average E/e′ ratio ≥13.[1] The investigators tried to substantiate their classification based on an E/e′ ratio >8.5 by looking for a left atrial (LA) volume index (LAVI) ≥28 mL/m^2 and a pulmonary vein atrial reversal signal duration that exceeded mitral A (atrial filling velocity) duration by at least 10 ms. Whereas the approach of using multiple measurements to assess LVDF is a valid one, both cut-off values are still not sufficient to identify elevated LVFPs. For LAVI, this is ≥34 mL/m^2, and for difference in duration between pulmonary vein atrial reversal and mitral A velocities, the cutoff is 30 ms.[1] The result of the approach adopted by the investigators is the attenuation of the predictive power of

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the E/e′ ratio. This point of view is reinforced by several previous studies, which noted strong and independent prognostic power for the E/e′ ratio that ranged between 12.5 and 15.0.[1]

Diastolic dysfunction in patients with normal EF leads to pulmonary congestion symptoms, which limit exercise tolerance, and, with diuretic treatment, can lead to reduced cardiac output. Both of the above-mentioned mechanisms explain the development of heart failure, LA enlargement, atrial fibrillation, and embolic consequences of atrial fibrillation, such as arterial embolism, stroke, and transient ischemic attacks. The diseases that cause LV diastolic dysfunction can also contribute to the occurrence of coronary artery disease (CAD) and events related to CAD, such as MI and coronary revascularization. In addition, with increased LV diastolic pressures resulting from diastolic dysfunction, LV perfusion can be compromised, thus contributing to myocardial ischemia. In this study, the investigators included some events where it is difficult to explain how LVDF would contribute to their occurrence. This includes cor pulmonale (n=1), aortic aneurysms (n=2), and revascularization of peripheral arteries (n=7). In addition, the investigators do not provide us with the details of how the presence of CAD was confirmed in the 15 patients with this outcome (Table 2).[6]

In conclusion, this study is a welcome addition to the existing literature on the use of TD indices of diastolic function for prediction of outcome in patients without apparent cardiac disease. Additional studies are needed to explore the utility of the existing and new methodology for predicting outcome and detecting changes in cardiac function in response to treatment and risk factor modification.

Disclosures

None.

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