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EDITORIAL

Exhausted atrial reserve by tissue Doppler echocardiography: a risk marker in heart failure with reduced ejection fraction

Otto A. Smiseth*

Division of Cardiovascular and Pulmonary Diseases, Department of Cardiology and Institute for Surgical Research, Oslo University Hospital and Center for Heart Failure Research, Center for Cardiological Innovation, and University of Oslo, Rikshospitalet, 4956 Nydalen, N-0424 Oslo, Norway

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Implantable cardioverter defibrillators (ICDs) are widely used in the prevention of ventricular arrhythmias and their efficiency to prolong life is well documented in long-term follow-up studies. On the other hand, defibrillators may cause complications, and as shown recently, the 12-year cumulative incidence of adverse events was 20% for inappropriate shock, 6% for device-related infection, and 17% for lead failure.[1] Furthermore, a large fraction of patients with an ICD implant never receive appropriate shock therapy.[2,3] As stated in the article by Biering-Sørensen *et al.*,[4] there is a need for further refinement of selection criteria for ICD.

Traditionally, left ventricular (LV) ejection fraction (EF) is used as a measure of LV systolic function, and is so far the only measure of LV contractile function which is incorporated into clinical practice guidelines for treatment with ICD.[5] However, the ability of EF to predict outcome is limited, and supplementary or alternative methods to quantify LV function are needed.[6]

The study of Biering-Sørensen *et al.*[4] investigated the ability of tissue Doppler imaging to predict ventricular tachycardia, ventricular fibrillation, and cardiovascular mortality in patients with ischaemic cardiomyopathy who received ICD as primary prevention. They showed that global mitral annular velocity during atrial contraction (a′) was an independent predictor, and events were four times more common in the lowest quartile of a′ than in the highest. Neither LVEF nor other echocardiographic indices of systolic or diastolic function were significantly different in patients who developed events compared with those who did not. Biering-Sørensen *et al.*[4] propose to measure a′ as a novel risk marker in patients with heart failure and reduced LVEF. This is an important extension of the concept that abnormal diastolic function measured as restrictive LV filling is a strong prognostic marker.[7] Restrictive filling by Doppler echocardiography is characterized by a tall mitral early velocity (E), which decelerates rapidly, and is followed by abnormally low velocity (A) during atrial contraction. The elevated mitral E-velocity is a reflection of high left atrial pressure, and the elevated transmitral pressure gradient causes rapid early-diastolic LV filling. When the rapid inflow enters a stiff, diseased ventricle, there is rapid flow deceleration and therefore a short E-deceleration time. Elevated diastolic pressure implies that the pressure–volume coordinates operate on the stiff portion of the LV pressure–volume curve, and therefore when the atrium contracts, there is a marked rise in LV pressure, but little blood enters the ventricle. This principle is demonstrated in *Figure 1*, which illustrates how the contribution from atrial contraction to LV filling decreases when LV diastolic pressure is elevated. The mitral annular a′ measured by TDI in the LV long-axis represents the velocity of LV myocardial lengthening caused by atrial systole. Therefore, the progressive decrease in a′ with severe heart failure reflects a reduction in the contribution from active atrial contraction to LV filling. When the magnitude of a′ is markedly reduced, it implies that the compensatory increase in LV preload that results from atrial contraction is exhausted. This might be the fundamental mechanism behind a low a′ as a marker of high risk of cardiovascular events. *Figure 2* shows schematically how progression of heart failure may lead to decrease in a′. In a dilated ventricle with markedly elevated diastolic pressure, atrial contraction makes very little contribution to LV filling, indicating that the potential for activation of the Frank–Starling mechanisms is nearly exhausted. Importantly, the relationship between low a′ and risk is not present at earlier stages of heart failure since the response of a′ to ventricular dysfunction is biphasic with an increase in a′ in early stage LV dysfunction characterized by an impaired relaxation type filling pattern. The ability of a′ to predict high risk is valid only when there is marked reduction in LV systolic function.[4]

An interesting observation by Biering-Sørensen *et al.*[4] is a non-uniformity of a′ between different parts of the LV wall and how

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* Corresponding author. Tel: +47 23070000/+47 23073271; Fax: +47 23073530. E-mail: otto.smiseth@ous-hf.no

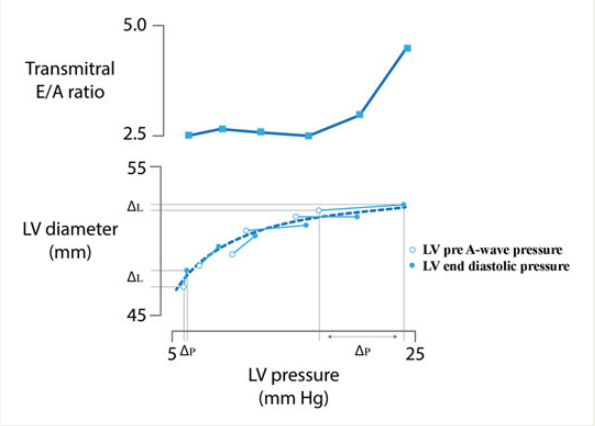

Figure 1 Experimental study showing in the upper panel that the transmitral E/A velocity ratio increases when LV end-diastolic pressure is elevated. The lower panel illustrates that LV diameter approaches a maximum when LV diastolic pressure exceeds 15–20 mmHg, and therefore the increase in LV diameter with atrial contraction (ΔL) becomes very small. The pressure increase with atrial contraction (ΔP), however, increases markedly when LV pre-A-wave pressure is elevated. Modified from Myreng *et al.*,[8] with permission.

this may reflect altered geometry in the diseased ventricle. They propose that due to flattening (higher radius of curvature) of the septum and inferior wall, there is higher wall stress according to the La Place principle and therefore most marked reduction of a′ in these walls. More detailed analysis of local radii of curvature and wall stress should be done to further explore this potential mechanism.

A limitation of the method proposed by Biering-Sørensen *et al.*[4] is that measuring a′ at six sites is time consuming and not in keeping with common clinical practice, which is to measure at the septal and lateral annulus or just at the septal side.[9] Potentially, the measurement of left atrial volume, rather than diameter, could make atrial size a predictor together with a′. Furthermore, the potential role of reduced atrial contractility as a mechanism of reduced a′ needs to be considered. The study of Biering-Sørensen *et al.*[4] is limited by its retrospective design and moderate sample size. Finally, there is a need for studies of the reproducibility of measuring a′ in clinical routine. A limitation of the proposed approach to use a′ as a risk predictor is that about 25% of all heart failure patients have atrial fibrillation. It should be explored in future trials whether a short E-deceleration time as a marker of restrictive filling may serve as a predictor in patients with atrial fibrillation who are candidates for ICD.

In summary, the suggestion by Biering-Sørensen *et al.*[4] to use a′ as a predictor of risk in patients with ischaemic cardiomypathy who are

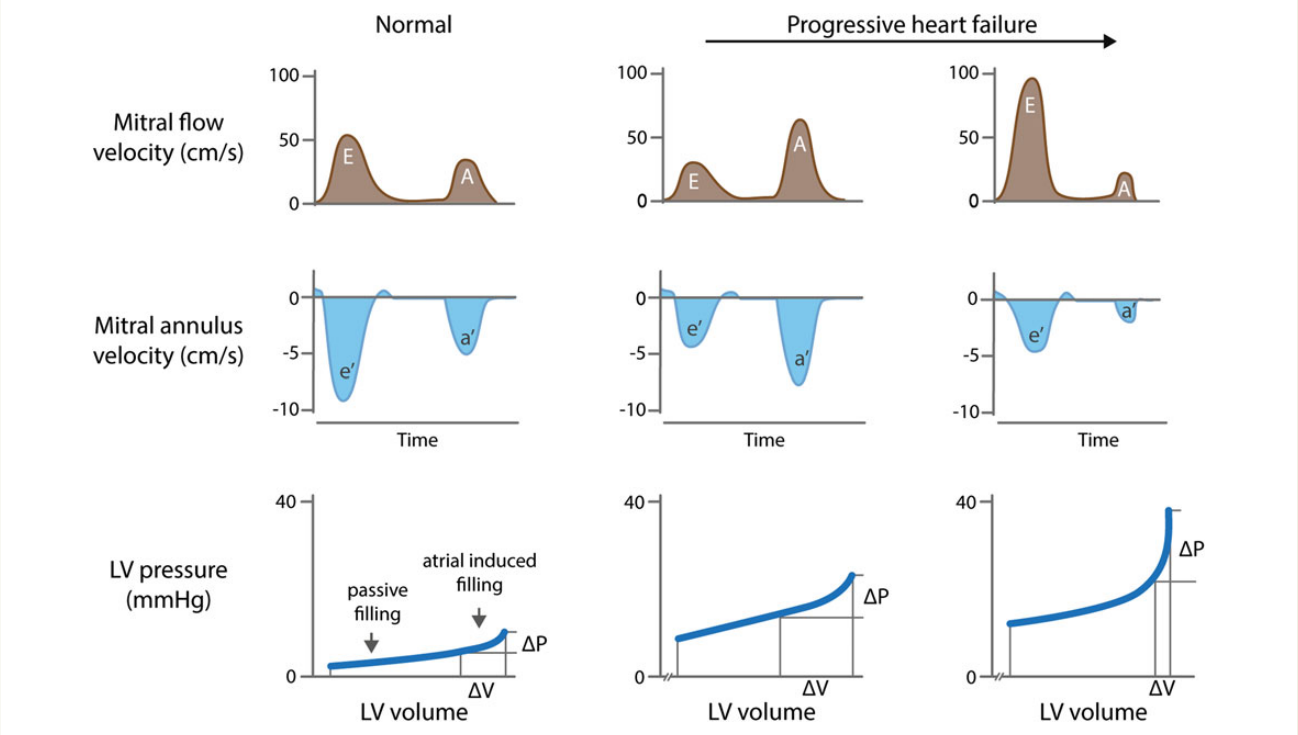

Figure 2 Schematic illustration showing mitral flow velocities (upper panels) and mitral annular velocities (middle panels) in a normal heart and in progressive degrees of heart failure. The lower panels illustrate LV diastolic pressure–volume curves and indicate changes in LV volume (ΔV) and pressure (ΔP) with atrial contraction. The panels to the right illustrate that in severe heart failure there is little further increase in LV volume with atrial contraction, but a marked rise in LV pressure, and a small A and small a′.

candidates for ICD is interesting and should be explored in larger prospective trials. Not only a single marker such as a′ but also other indices of diastolic function as well as global longitudinal strain as a measure of systolic function should be included in future trials. Importantly, at the present time, no other cardiac imaging marker than EF has proven to be effective when deciding upon ICD therapy. Therefore, EF is still the guide when selecting patients for ICD therapy and should be used until other markers are proven to provide added value in appropriately designed prospective trials.

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