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Ultrasound beam angle-independent evaluation of left ventricular filling pressure using three-dimensional speckle-tracking echocardiography

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E/e' is a major parameter in the algorithm for estimating left ventricular filling pressure (LVFP) by echocardiography.[1] However, E and e' can be affected by Doppler beam malalignment. Moreover, regional e' is used as an extrapolation of global LV relaxation. These limitations may cause the estimation of LVFP to be inaccurate in some conditions. In the multicentre Euro-Filling study, E/e' was weakly correlated with LV end-diastolic pressure but was not an independent parameter correlated with end-diastolic pressure in patients with an ejection fraction (EF) < 50%.[2]

Three-dimensional speckle-tracking echocardiography allows the simultaneous evaluation of LV volume and global myocardial strain. The early diastolic filling rate (FRe), derived from the rate of LV volume change (dV/dt), is theoretically expected to reflect transmitral E, and the early diastolic global strain rate (SRe) correlates with the time constant of global LV relaxation better than e'.[3] Furthermore, FRe and SRe are independent of the ultrasound beam angle because they are not measured by the Doppler method. Therefore, FRe/SRe may be used to estimate LVFP, even under conditions where the use of E/e' is limited. In canine models, we have reported that FRe/SRe correlates well with simultaneously measured LVFP and provides a better estimate of LVFP than E/e'[4,5]; however, the utility of FRe/SRe in the clinical setting remains unclear.

A single-centre prospective study was conducted by enrolling 107 patients with various diseases who underwent two-dimensional and three-dimensional echocardiography (Aplio i900 or Artida, Canon Medical Systems, Otawara, Japan) within 24 hours before and after LVFP (mean pulmonary artery wedge pressure or LV pre-A pressure) was measured by a catheter. Elevated LVFP was defined as ≥ 12 mmHg. Three-dimensional speckle-tracking analysis was performed by offline software, and SRe was derived from area strain (i.e., percentage change in a segmental endocardial surface area). [4,5] Since FRe/SRe is not dimensionless like E/e' but has units of volume, we also calculated the FRe/SRe index, which

is normalized to the body surface area. All echocardiographic data were measured by observers blinded to the pressure data. The relationship between each echocardiographic parameter and LVFP as well as the diagnostic accuracy of elevated LVFP, which was derived from the area under the curve (AUC) of the ROC curve, were evaluated in all patients and in the subgroup with EF < 50%.

FRe/SRe could be analysed in 96 of the 107 patients (90%). The median LVFP was 10 mmHg (minimum 2 mmHg, maximum 28 mmHg), and 33 patients (34%) were evaluated as having elevated LVFP. In all patients, E/A and E/e' showed weak correlations with LVFP; in contrast, FRe/SRe and the FRe/SRe index demonstrated moderate but better correlations with LVFP. In the low-EF subgroup, FRe/SRe and the FRe/SRe index preserved similar correlations to the all-patient analysis; however, the correlations of E/A and E/e' were exacerbated (Figure).

In all patients, FRe/SRe and the FRe/SRe index tended to show better AUCs than E/e'. The optimal cut-off values to identify elevated LVFP were 125.6 mL for FRe/SRe and 76.2 mL/m^2 for the FRe/SRe index. In the low-EF subgroup, the AUCs of the FRe/SRe and the FRe/SRe index remained the same as those in the all-patient analysis, but that of E/e' worsened (Figure).

FRe/SRe is a new parameter designed to estimate LVFP using three-dimensional speckle-tracking echocardiography based on the E/e' concept.[4,5] Once LV endocardial borders have been traced, the software semiautomatically calculates FRe/SRe. Another advantage is that there is no time lag between FRe and SRe measurements, unlike that between E and e' measurements. The most important feature is that FRe/SRe is acquired without using the Doppler method. Therefore, this parameter can work even when accurate measurements by the Doppler method are difficult to obtain.

In our results, the diagnostic accuracy of E/e' worsened in the low-EF subgroup. One of

the reasons seems to be due to difficulties in Doppler beam alignment. Doppler beam malalignment is likely to occur in this subgroup because an LV with reduced contraction is prone to be enlarged by remodelling. This result implies that accurately determining the true transmitral E values is more difficult than one might think and suggests that E may be underestimated in some cases. Even when the Doppler beam is completely adjusted on two-dimensional colour flow mapping, the actual main transmitral flow can be out of plane in the two-dimensional mapping in a dilated LV.[5] Another reason E/e' did not work could lie in e'. Since e' is measured from only septal and lateral mitral annuli, it does not always reflect global LV relaxation. Moreover, Doppler beam malalignment arises for e'.

In the clinical setting, the assessment of FRe/SRe was feasible and allowed a more accurate estimation of LVFP than E/e'. This ultrasound beam angle-independent method may overcome the weakness associated with the angle dependence of the Doppler method.

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Conflict of interest

T.A and S.N. are authors of a patent (WO 2013147262A1) related to this work but have waived their patent rights. All other authors have no conflicts of interest to disclose related to this work.

Data availability

The data underlying the research results described in this paper will be shared on reasonable request to the corresponding author.

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Figure legend

Figure (A) Early diastolic filling rate (FRe) (orange point) and early diastolic global strain rate (SRe) (yellow point) analysed from three-dimensional speckle-tracking echocardiography in a representative case. **(B and C)** The relationship between each echocardiographic parameter and left ventricular (LV) filling pressure, and ROC curve analysis for the diagnosis of elevated filling pressure in all patients and patients with EF < 50%. *P* values for areas under the curve (AUC) are in comparison to the line of no information. *CI*, confidence interval.