

# Order of tricuspid and mitral valve opening as an index of left ventricular filling pressure and prognosis

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**This editorial refers to ‘Visual echocardiographic scoring system of the left ventricular filling pressure and outcomes of heart failure with preserved ejection fraction’, by M. Murayama et al., pp. 616–626.**

Heart failure is defined as the inability to deliver the required amount of oxygenated blood to the body or only to do so under elevated filling pressure.<sup>1</sup> Diastolic dysfunction with elevated filling pressure, will eventually damage the heart and is associated with a poor prognosis.<sup>2</sup> This also applies to patients with heart failure and preserved ejection fraction (HFpEF), who typically have elevated left ventricular (LV) filling pressure and mortality rate comparable to heart failure patients with reduced ejection fraction.<sup>3</sup> Assessment of elevated LV filling pressure is therefore of high clinical interest. A consensus document of the European Association of Cardiovascular Imaging provides recommendations for how to assess diastolic function in patients evaluated for potential HFpEF.<sup>2</sup> A number of echocardiographic parameters may be used to evaluate LV filling pressure, but there is a continuous search to find better parameters.<sup>2,4</sup>

Recently, a new marker of LV filling pressure was proposed based on the timing and order of tricuspid and mitral valve opening.<sup>5,6</sup> In the normal heart, tricuspid valve opening (TVO) occurs slightly prior to mitral valve opening (MVO).<sup>7,8</sup> The atrioventricular valves open when the ventricle is still relaxing and ventricular pressure is still falling. When ventricular pressure falls below atrial pressure, the valve opens. In cases when filling pressure and thus atrial pressure is elevated, isovolumic relaxation time (IVRT) is cut short as the pressure crossover, and hence valve opening, occur earlier during relaxation,<sup>9</sup> a mechanism which is similar for the tricuspid and the mitral valve. Hence, when LV filling pressure is elevated, mitral valve opening will occur at an earlier time-point, and may coincide or even precede

tricuspid valve opening. Murayama et al.<sup>6</sup> therefore proposed a visually assessed time difference between MVO and TVO scoring system (VMT) where TVO occurring first, was given 0 point; simultaneous opening, 1 point, and MVO first, 2 points. However, heart failure may be associated with concomitant elevation of right and left ventricular filling pressure. Elevated right atrial pressure (RAP) may cause TVO to occur before or simultaneous with MVO despite elevated LV filling pressure. Thus, an additional point was added when elevated RAP was indicated by a large cava diameter with reduced collapsibility. This resulted in a VMT score from a minimum of 0 for TVO occurring first and no signs of elevated RAP to a maximum of 3 where MVO occurred first with signs of elevated RAP. They found that a VMT score  $\geq 2$  was associated with elevated LV filling pressure assessed as pulmonary artery wedge pressure  $\geq 15$  mmHg.

The results showed an overall sensitivity of 78% and specificity of 93% to identify elevated LV filling pressure.<sup>6</sup> This indicates that patients with VMT  $\geq 2$ , in almost all cases have truly elevated LV filling pressure while many patients in whom TVO occurs before or simultaneous with MVO, may also have elevated filling pressure, i.e. false negatives. There may be several reasons why TVO occurs prior to MVO despite elevated LV filling pressure. While a high left atrial pressure tends to shorten IVRT, slowed relaxation prolongs IVRT and delays time of MVO.<sup>9</sup> Slowed relaxation is common in HFpEF,<sup>10</sup> and in the subgroup of HFpEF patients, sensitivity was only 36% and specificity 97%, though these results should be regarded with caution as there were only 44 patients with ejection fraction  $\geq 50\%$  in that study.<sup>6</sup> However, this is qualitatively similar with other studies where echocardiographic parameters have less accuracy for stratifying LV filling pressure in HFpEF patients.<sup>11,12</sup> Thus, classification of filling pressure in particularly HFpEF patients remains a challenge.

The opinions expressed in this article are not necessarily those of the Editors of the *European Heart Journal - Cardiovascular Imaging* or of the European Society of Cardiology.

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In this edition of the journal, the same group has applied the VMT score retrospectively on 310 HFpEF patients and evaluated cardiac death and heart failure hospitalization after 2 years as primary outcome.<sup>13</sup> Patients with VMT  $\geq 2$  had worse outcome, and the VMT score still showed incremental value also after adjusting for other variables. Patients with VMT  $\geq 2$  showed more signs of poor function and were thus sicker, which is consistent with their previous study that patients meeting this cut-off truly have a high filling pressure. Notably, both the previous<sup>6</sup> and the new study<sup>13</sup> showed that VMT score performed well to stratify patients with atrial fibrillation. This is interesting because these patients tend to have monophasic LV inflow, which makes use of conventional LV filling pressure parameters problematic. In both studies, the authors find that the EACVI recommendations for evaluation of LV filling pressure<sup>4</sup> results in a large number of unclassified patients due to lack of accessible parameters and that the VMT score then is able to stratify these patients and thus improve the overall classification results. This is similar to our findings where we used left atrial strain as an additional parameter for classification of LV filling pressure.<sup>12</sup> Left atrial strain could be used to stratify the remaining unclassified patients from the recommendation algorithm,<sup>4</sup> thereby allowing classification of practically all patients at similar accuracy.

Assessment of the TVO and MVO sequence, seems an interesting parameter, however, it may be technically challenging. The authors reported cases where the sequence was changed during consecutive beats. Probably standard respiratory conditions must be used as particularly RAP is highly influenced by respiration. Murayama *et al.*<sup>6</sup> reported an inter-observer agreement  $\kappa$ -value of 0.81. Possibly dedicated imaging at adequate frame-rate or other imaging features, e.g. M-mode through the valves in parasternal images, could improve the assessment. Sugahara *et al.*<sup>5</sup> used dual Doppler echocardiography to measure onset of inflow in both ventricles simultaneously to assess the time difference. However, the inter-observer variability seemed relatively high. Furthermore, imaging of the right ventricle and tricuspid valve may be particularly challenging in obese patients, and feasibility of the method should be investigated in more detail. Further studies of the method's strengths and weaknesses are therefore required.

**Conflict of interest:** O.A.S. is co-inventor of 'Method for myocardial segment work analysis' and has filed patent on 'Estimation of blood pressure in the heart'.

## Data availability

No new data were generated or analysed in support of this research.

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