Value of assessment of left atrial volume and diameter in patients with heart failure but with normal left ventricular ejection fraction and mitral flow velocity pattern

Chikako Yoshida, Shinji Nakao, Akiko Goda, Yoshiro Naito, Mika Matsumoto, Misato Otsuka, Miho Shimoshikiryo, Akiyo Eguchi, Masaaki Lee-Kawabata, Takeshi Tsujino, and Tohru Masuyama*

Cardiovascular Division, Department of Internal Medicine, Cardiovascular Division, Hyogo College of Medicine, 1-1 Mukogawa-cho, Nishinomiya 663-8501, Japan

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Aims We assessed the comparative value of measurements of tissue Doppler early diastolic mitral annular velocity (E'), left atrial diameter (LAD), and left atrial volume (LAV) in patients with possible heart failure (HF) but with normal left ventricular (LV) ejection fraction (EF) and mitral flow velocity pattern.

Methods and results We determined LAV and LAD indexes in addition to the ratio of peak early diastolic mitral flow velocity (E) to E' (E/E' ratio) in 91 patients with all three of the followings: HF, LV EF of greater than 55%, and normal mitral E/A ratio between 0.8 and 1.5. Twenty healthy subjects were used as controls. E/E' ratio was abnormal (>1.5) in 38 of the 91 patients (sensitivity=44%). LAV index was 32 mL/m² or greater in 71 of the 91 patients (sensitivity=78%), while LAD index was 27 mm/m² or greater in 81 of 91 patients (sensitivity=89%). The area under the curve by receiver–operator curve analyses was 0.995 for LA volume index, 0.998 for LAD index, and 0.885 for E/E' ratio.

Conclusion LAV and LAD indexes are more useful in detecting with HF and normal EF patients than E'-related parameters.

KEYWORDS
Left atrium volume; Mitral flow; E'/E; Diastole; Heart failure

Introduction
Diagnosis of heart failure (HF) has been made on the basis of signs and symptoms. HF occurs even in the absence of left ventricular (LV) systolic dysfunction, and parameters—LV diastolic filling or the mitral flow velocity pattern (MFVP)—have been demonstrated to be useful to assess outcome of the therapy, prognosis of HF, etc. MFVP changes with the advance of the disease process from the normal to the relaxation abnormality pattern, and in turn to the pseudonormal pattern and finally to the restrictive pattern. It is often difficult to assess whether MFVP is pseudonormal or truly normal in patients with possible HF, but with preserved LV ejection fraction (EF). Thus, other complementary indexes are necessary to assess MFVP pseudonormal or normal.

Measurement of tissue Doppler early diastolic mitral annular velocity (E') has been shown useful to complement the interpretation of MFVP, but the accuracy of this measure is not perfect.

Left atrial (LA) enlargement has been proposed as a barometer of diastolic burden and a predictor of common cardiovascular outcomes, such as atrial fibrillation, stroke, congestive HF, and cardiovascular death.† Left atrium changes in size in the condition of HF; therefore, assessment of LA size may be useful to judge MFVP pseudonormal or normal. The objective of this study is to assess the value of measurements of left atrial size and E'-related parameters in patients with preserved LV EF.

Methods
Subjects
We retrospectively analysed 7180 consecutive echocardiographic studies that were performed in Hyogo College of Medicine.
echo cardiography laboratory between 01 January 2005 and 31 October 2005. We selected those who fulfilled the following criteria: Framingham study HF criteria, LVEF of greater than 55%, pulmonary artery systolic pressure as estimated with simplified Bernoulli equation of 35 mmHg or greater, and E/A ratio between 0.8 and 1.5. Exclusion criteria were atrial fibrillation, congenital heart diseases, prosthetic valve, valvular heart diseases, atrio-ventricular block, post open cardiac surgery, respiratory disease, or renal dysfunction. Consequently, the study population consisted of 91 patients. There were 41 women and 50 men. Mean age was 68 ± 12 years. We separately collected 20 healthy subjects as controls. Any of them had no cardiovascular symptom or sign, and normal electrocardiographic and echocardiographic findings. There were 9 women and 11 men. Mean age was 63 ± 13 years.

**Echo studies**

M-mode, 2D, and Doppler echocardiographic studies were performed in all subjects. We determined LVEF using a method proposed by Quinones and his colleagues in 1981. MFVP was recorded with the sample volume positioned at the level of the mitral tips to determine the peak early diastolic filling velocity (E) and its ratio to the peak filling velocity at atrial contraction (E/A ratio). In order to complement the diastolic filling parameters, we obtained tissue Doppler mitral annular velocity pattern at the septal site to determine peak early diastolic velocity of the mitral annulus movement (E), and 2D echograms of the left atrium to determine LA diameter and volume.

Two-dimensional echocardiography was used to determine LA diameter. Specifically, this was measured as an antero-posterior distance in the parasternal long-axis view utilizing the inner edge in the inner edge method at end systole when the LA chamber is at its greatest dimension. LA volume was determined using the biplane Simpson’s method. For the Simpson’s method, maximal area was measured with a planimeter for four- and two-chamber views by tracing the endocardial border, excluding the confluence of the pulmonary veins and LA appendage, and the length was measured from the mid-line of the plane of mitral annulus to the opposite superior aspect of the left atrium. Automatic volume calculation was performed using the software for the modified Simpson’s disc summation method resident in the echo machine. Body surface area was used to adjust for the body size.²

In this study, LV mass was calculated from diastolic ventricular septal wall thickness (SWTd, cm), LV dimension (LVDd, cm), and LV posterior wall thickness (PWTd, cm), using the following equation:

\[ \text{LV}(g) = 0.80 \times 1.04 \times ( \text{SWTd} + \text{LVDd} + \text{PWTd} )^2 - ( \text{LVDd} )^2 + 0.6 \]

**Statistical analysis**

Data are presented as mean ± SD. Continuous variables were analysed by Student’s t-test. Differences were considered significant at \( P < 0.05 \). Receiver–operator curves (ROCs) were used to compare the efficacy of diagnostic tests (the Somer’s D statistic). Statistical analysis was performed using SPSS software (Dr. SPSS for Windows).

**Results**

E/E ratio is normal if the value is <8. If the value is greater than 15, we may take the pattern to be abnormal or indicating significant LV diastolic dysfunction. If the value was between 8 and 15, the pattern may be judged as borderline. We applied these criteria to the 91 patients. Results are shown in Figure 1 and LV diastolic dysfunction (E/E' >15) was detectable in 40 patients of the 91 patients (sensitivity=44%).

![Figure 1](image1.png)  
Assessment of the left atrial volume index, left atrial diameter index, and E/E' for detecting abnormality.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Characteristics of the normal controls and the patients with heart failure but with normal left ventricle ejection fraction and mitral flow velocity pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal controls</td>
</tr>
<tr>
<td>Age (years)</td>
<td>63 ± 13</td>
</tr>
<tr>
<td>Gender</td>
<td>9F, 11M</td>
</tr>
<tr>
<td>LVDD (mm)</td>
<td>45 ± 4</td>
</tr>
<tr>
<td>LVDS (mm)</td>
<td>28 ± 4</td>
</tr>
<tr>
<td>EF (%)</td>
<td>68 ± 6</td>
</tr>
<tr>
<td>E (cm/s)</td>
<td>56 ± 19</td>
</tr>
<tr>
<td>A (cm/s)</td>
<td>63 ± 14</td>
</tr>
<tr>
<td>E/A</td>
<td>0.94 ± 0.43</td>
</tr>
<tr>
<td>DcT</td>
<td>215 ± 48</td>
</tr>
<tr>
<td>LVMi (g/m²)</td>
<td>76 ± 14</td>
</tr>
<tr>
<td>LAD index (mm²/m²)</td>
<td>20 ± 3</td>
</tr>
<tr>
<td>LAV index (mL/m²)</td>
<td>14 ± 4</td>
</tr>
<tr>
<td>E/E'</td>
<td>9 ± 3</td>
</tr>
</tbody>
</table>

LVDD, left ventricular dimension, end-diaostole; LVDS, left ventricular dimension, end-systole; DcT, deceleration time; LVMi, left ventricular mass index; LAD index, left atrial dimension index; LAV index, left atrial volume index; EF, ejection fraction.  
* P < 0.05 vs. control.

Left atrial volume (LAV) index was larger in the patients than in the normal controls (Table 1). LAV index was 32 mL/m² or greater in 71 of the 91 patients (sensitivity=78%). Left atrial diameter (LAD) index was 27 mm/m² or greater in 81 of 91 patients (sensitivity=89%) (Figure 1).

We compared accuracy of the E/E', LAV index, and LAD index for detecting abnormality by receiver–operator curve (ROC) analyses (Figure 2). The area under the curve was 0.885 for E/E' ratio, 0.995 for LAV index, and 0.998 for LAD index, respectively.

**Discussion**

When LVEF is preserved, it is often difficult to assess whether MFVP is pseudonormal or truly normal in patients with possible HF. Values of additional measurements of E/E' ratio, LAD index, and LAV index were compared with one another in this study. We judged 71 of 91 patients abnormal by LAV index (sensitivity=78%), 81 of 91 patients by LAD index (sensitivity=89%), and 40 of 91 patients by E/E' ratio (sensitivity=44%). Thus, LAD and LAV indexes appeared to be superior to E/E' ratio in the assessment of normality of the MFVP.
There is a close relation between pressure and volume in any cardiac chamber, and LA dilation is considered due to LA pressure overload. LA pressure overload is usually secondary to increased LA afterload which is caused by mitral valve stenosis or LV dysfunction. With increased stiffness of the left ventricle, LA pressure rises to maintain adequate LV filling, and the consequent increased atrial wall tension may well lead to LA chamber dilatation. Thus, LA volume may well increase in patients with diastolic HF independent of LV systolic function. The structural changes of the left atrium may express the length of exposure to abnormal filling pressures and thus may provide predictive information beyond that of diastolic function grade, which is determined from evaluating multiple load-dependent parameters and therefore reflective of the instantaneous LV diastolic function and filling pressures. In fact, LAV index was much larger in those with diastolic HF than in the normal subjects. On the other hand, LAV and LAD indexes were superior to E/E' for detecting diastolic HF. This finding may be comparable with Abhayaratna’s description that LA volume is useful for monitoring long-term haemodynamic control, whereas Doppler and tissue Doppler assessment of instantaneous filling pressure is better suited for dynamic control, whereas Doppler and tissue Doppler assess-  

LAV index

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LAD index

LA enlargement has been considered to be more accurately assessed with LAV index than with LAD index. Thus, we expected LAV index should be superior to LAD index in the detection of abnormality in our patients. Surprisingly, LAD index was even superior to LAV index in the sensitivity, while there was no significant difference in the area under ROC curve between the indexes. The left atrium is an asymmetrical cavity, and LA dilatation might not have been evenly distributed in all planes. In fact, it may not be dilated in the anteroposterior direction so easily as in the other directions because of the pulmonary vein; however, we have no data to support this idea. Gottdiener et al. showed that the left atrium may enlarge more in the anteroposterior direction than in the superoinferior direction in the condition of HF. This observation may at least partially support the aforementioned idea. Alternatively, the small difference between the LAV and LAD indexes may be explained by some unknown characteristics of our patient population, because it was shown that the LAD might be more affected by some clinical and echocardiographic measurements than the LAV index. Although we excluded patients with atrial fibrillation and valvular heart diseases, inclusion of some patients with trivial mitral regurgitation might have affected the results. We do not claim that the LAD index is superior to the LAV index, but it is noted that even a simple measurement of LAD index may be helpful to assess the abnormality in patients with possible diastolic HF. To assess LA geometry, LAV is more sensitive parameter than LA area and LAD, but LAD is most simple and significant parameter for predicting cardiovascular disease and congestive HF and detecting diastolic HF.

Study limitations

Eight limitations of the study are noted. First, diagnosis of HF was based on the Framingham study HF criteria in this study; therefore, there should have been inherent misdiagnosis in some of our patients. Special care was taken particularly because all of our patients had normal LVEF and normal MFVP. Second, we estimated LA volume only with two-dimensional echocardiography. Use of other methods such as computed tomography, magnetic resonance imaging, and three-dimensional echocardiography might have provided better accuracy than that in this study. Third, any data of LV filling pressure were not available in our patients; therefore, the mechanism of the LA enlargement is only speculative. Forth, we selected 20 healthy persons as a normal control. Inclusion and determination of the control group are important in the interpretation of ROC. Thus, we also paid attention to the values of sensitivity that were determined using established normal values.
Fifth, those with atrial fibrillation were excluded from this study. Long-standing atrial fibrillation enlarges the left atrium by itself; therefore, measurement of LA size cannot be used to assess normality of the MFVP in patients with atrial fibrillation. Sixth, LV filling pressure was not measured because of ethical issues. Seventh, EF was measured by the Quinones method and not by the modified Simpson’s method in this study. Finally, we measured tissue Doppler mitral annular velocity pattern only at the septal wall. The presence of LV asynergy may certainly affect $E_0$, but there were no patients with asynergy in this study.

Conclusion

When we assess patients with possible HF but with normal LVEF and normal MFVP, additional measurements of LAV or LAD index is useful to assess whether the patient is truly normal or not. If the patient had greater than normal LAV index, he or she may suffer from diastolic HF.

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Conflict of interest: none declared.

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