Endomyocardial Radial Strain Imaging and Left Ventricular Relaxation Abnormalities in Patients With Hypertrophic Cardiomyopathy or Hypertensive Left Ventricular Hypertrophy

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Background: Asymmetrical septal hypertrophy and impaired left ventricular (LV) diastolic function are common echocardiographic features of hypertrophic cardiomyopathy (HCM). However, it is difficult to differentiate nonobstructive HCM from hypertensive LV hypertrophy (H-LVH).

Methods and Results: Standard echocardiography and tissue Doppler imaging were performed in 14 patients with HCM, 16 patients with H-LVH, and 21 control subjects. Endomyocardial radial strain, systolic strain rate (SR), and the early diastolic SR at the posterior and septal segments of the LV short axis were calculated. Endomyocardial peak strain (ε) and the absolute value of peak early diastolic SR at the posterior segment were significantly smaller in patients with HCM than in those with H-LVH, whereas the thickness of the LV posterior wall did not differ between these 2 groups. Multivariate analysis of discrimination, including the ratio of interventricular septal thickness and posterior wall thickness (IVST/PWT), ε, and SR parameters, between HCM and H-LVH patients revealed that ε at the LV posterior segment was the highest discriminant parameter (discriminant coefficient: –14.6, P=0.012). The ε at the posterior segment significantly correlated with early diastolic mitral annular velocity.

Conclusions: Endomyocardial radial strain imaging may prove informative for discriminating between HCM and H-LVH. (Circ J 2009; 73: 2294–2299)

Key Words: Hypertension; Hypertrophic cardiomyopathy; Left ventricular hypertrophy; Strain

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Endomyocardial Radial Strain Imaging and Left Ventricular Relaxation Abnormalities in Patients With Hypertrophic Cardiomyopathy or Hypertensive Left Ventricular Hypertrophy

Hypertrophic cardiomyopathy (HCM) is characterized by regional hypertrophy, especially asymmetrical ventricular septal hypertrophy, and left ventricular (LV) diastolic dysfunction.1,2 The mechanisms responsible for the myocardial ischemia associated with HCM remain unclear, and it is difficult to differentiate nonobstructive HCM from hypertensive LV hypertrophy (H-LVH). We previously showed that longitudinal strain rate (SR) imaging is able to discriminate HCM from H-LVH.3

Radial fiber thickening varies across the different layers of the myocardial wall and is more pronounced in the endomyocardium than in the epicardium.4 The endomyocardium moves faster than the epicardium during myocardial contraction, reflecting the rate of increase in wall thickness (WT). The endomyocardium and mid-wall of the LV play important roles in ventricular function.5–7 Measurement of strain and the SR derived from tissue Doppler imaging (TDI) allows quantitative assessment of regional myocardial wall motion, reflecting both systolic and diastolic LV function.3,8,9 especially the endomyocardial region.10

We have now investigated the utility of endomyocardial radial strain and SR derived from TDI for assessment of regional myocardial dysfunction in patients with HCM or H-LVH.

Methods

Study Subjects
We studied 14 consecutive patients with nonfamilial HCM and 16 patients with H-LVH (Table 1). The diagnosis of HCM was based on conventional echocardiographic demonstration of a nondilated and hypertrophic LV (maximum LVWT >13 mm) in the absence of other cardiac or systemic diseases that might lead to LVH;11 it was confirmed by cardiac catheterization, angiography, and endomyocardial biopsy. The diagnosis of H-LVH was based on conventional echocardiographic demonstration of a hypertrophic LV (maximum LVWT >12 mm) in the absence of other cardiac or systemic diseases with the exception of long-term hypertension (systolic blood pressure ≥140mmHg or diastolic blood pressure ≥90mmHg, or both). All patients were in normal sinus rhythm and had a normal LV ejection fraction.
On completion of the standard echocardiographic measurements, color TDI was performed. Digital data were transferred for off-line analysis with the software incorporated in the Aplio system. The early diastolic mitral annular (Ea) velocity was determined by placing a tissue Doppler sample volume at the septal mitral annulus in the apical 4-chamber view, and the E/Ea was calculated. Endomyocardial radial strain and SR were calculated at the posterior and septal segments of the LV short axis. The region of interest (ROI: 4x4 mm) was continuously positioned within the interrogated segment shown in Figure 1 with the use of automatic tracking and the correction by manual tracking throughout a cardiac cycle. If the ROI swerved away from the myocardium, tracking was repeatedly modified manually in all subjects.

Lagrangian strain can be estimated by the velocity gradient, as follows:

$$\text{Strain} = \frac{d(\int v \, dt)}{dx}$$

Endomyocardial peak strain ($\varepsilon$), peak systolic SR (SR$_{sys}$), and peak early diastolic SR (SR$_{e}$) were measured.

Two examiners who were unaware of the clinical status of the subject performed the echocardiographic analysis independently of each other.
Figure 2. Examples of radial strain and strain rate at the posterior segment with ECG in HCM patients, H-LVH patients, and control subjects. ECG, electrocardiogram; HCM, hypertrophic cardiomyopathy; H-LVH, hypertensive left ventricular hypertrophy.

Figure 3. Comparison of ε, SRsys, and absolute value of SRdia among HCM patients, H-LVH patients, and control subjects. ε, endomyocardial peak strain; HCM, hypertrophic cardiomyopathy; H-LVH, hypertensive left ventricular hypertrophy; SRsys and SRdia, endomyocardial peak systolic and peak early diastolic strain rate, respectively.
Reproducibility
Intraobserver reproducibility was assessed with a single observer on 2 separate occasions and interobserver reproducibility for 6 patients was assessed by independent observers. Intraobserver or interobserver reproducibility was calculated as the absolute difference between the measurements divided by the average of the 2 measurements or the 2 observations.

Statistical Analysis
Data are presented as means±SD. Differences among 3 groups were evaluated by analysis of variance with Fisher’s protected least significant difference adjustment for multiple comparisons. The relations between measured parameters were assessed by linear regression analysis. The cutoff values for differentiation between HCM and H-LVH were determined with a receiver-operator characteristic curve. Sensitivity, specificity, and predictive accuracy were determined and expressed as percentages. The discriminant probability was calculated by a discriminant analysis based on stepwise forward selection method. A P value <0.05 was considered statistically significant. All statistical analyses were performed with SPSS, version 12 (Chicago, IL, USA).

Results
Representative strain and SR imaging for the 3 groups of study subjects are shown in Figure 2. IVST, LV posterior WT, and the IVST/PWT ratio were greater in patients with HCM than in control subjects, and IVST and LV posterior WT were also greater in patients with H-LVH than in control subjects (Table 1). IVST was greater in patients with HCM than in those with H-LVH, but the LV posterior WT did not differ between patients with HCM and those with H-LVH. The left atrial dimension was greater in patients with HCM than in either those with H-LVH or the control subjects. The peak Ea velocity was smaller and the E/Ea was greater in patients with HCM than in control subjects. The peak Ea velocity was smaller and the E/Ea was greater in patients with HCM than in either those with H-LVH or the control subjects. Neither the LVEF, the ratio of the peak E velocity to the peak late transmural filling velocity nor the deceleration time of the peak E velocity differed significantly among the 3 groups.

The ε and absolute value of SR\textsubscript{A\textsubscript{sys}} at both the posterior and septal segments were smaller in patients with HCM than in either those with H-LVH or the control subjects, whereas these indices in H-LVH patients were smaller than in the control subjects (Figure 3). The SR\textsubscript{A\textsubscript{sys}} at both the posterior and septal segments was smaller in patients with HCM or H-LVH than in control subjects, but did not differ between the 2 groups of patients.

The ε at the posterior segment significantly correlated with the peak Ea velocity, but not with LVEF, in all study subjects (Table 2). The ε at the posterior segment also significantly correlated with LV posterior WT in all subjects, but not in the 2 groups of patients combined. Similarly, the ε at the septal segment significantly correlated with the peak Ea velocity and IVST in all subjects.

Intraobserver reproducibility was 5.6, 7.1, and 6.9%, for ε, SR\textsubscript{A\textsubscript{sys}} and SR\textsubscript{A\textsubscript{sys}}, respectively. Similar results were obtained for interobserver reproducibility, with values of 7.6, 9.1, and 8.8%, respectively.

Multivariate analysis of discrimination, including IVST/PWT ratio, ε, and SR parameters, between HCM and H-LVH patients revealed that ε at the LV posterior segment was the highest discriminant parameter (Table 3). The IVST/PWT ratio and ε at the LV posterior and septal segments were selected by multivariate analysis based on a stepwise forward selection method. The discriminant score was 71.1%, 72.7%, and 65.2%, respectively: the discriminant score by the combination of the IVST/PWT ratio, and the ε at the LV posterior segment was 84.7%, and that by the combination of the IVST/PWT ratio and ε at the LV posterior segment was 80.6%. Receiver-operator characteristic curve analysis identified the optimal cutoff value of ε, SR\textsubscript{A\textsubscript{sys}} at the posterior segment, and the IVST/PWT ratio.

### Table 2. Correlations Among the Echocardiographic Data for All Subjects

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Posterior segment</th>
<th>Septal segment</th>
</tr>
</thead>
<tbody>
<tr>
<td>ε</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>IVST</td>
<td>–0.53(\ast)</td>
<td>–0.36(\ast)</td>
</tr>
<tr>
<td>LVPWT</td>
<td>0.30</td>
<td>0.08</td>
</tr>
<tr>
<td>LVMI</td>
<td>–0.51(\ast)</td>
<td>–0.35(\ast)</td>
</tr>
<tr>
<td>Peak Ea velocity</td>
<td>0.44(\ast)</td>
<td>0.34(\ast)</td>
</tr>
<tr>
<td>SR\textsubscript{A\textsubscript{sys}}</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>IVST</td>
<td>–0.34(\ast)</td>
<td>–0.58(\ast)</td>
</tr>
<tr>
<td>LVPWT</td>
<td>0.26</td>
<td>0.13</td>
</tr>
<tr>
<td>LVMI</td>
<td>–0.44(\ast)</td>
<td>–0.47(\ast)</td>
</tr>
<tr>
<td>Peak Ea velocity</td>
<td>0.57(\ast)</td>
<td>0.39(\ast)</td>
</tr>
</tbody>
</table>

\(\ast\)P<0.05; \(\ast\)P<0.001.
ε, endomyocardial peak strain; SR\textsubscript{A\textsubscript{sys}} and SR\textsubscript{A\textsubscript{sys}}, endomyocardial peak systolic and absolute value of peak early diastolic strain rate, respectively. Other abbreviations see in Tables 1, 2.

### Table 3. Multivariate Discriminant Analysis for Differentiation of Patients With HCM From Those With H-LVH

<table>
<thead>
<tr>
<th>Discriminant coefficient</th>
<th>95%CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVST/PWT</td>
<td>4.24</td>
<td>-0.84–9.34</td>
</tr>
<tr>
<td>ε at PWT</td>
<td>-14.6</td>
<td>-25.4–3.67</td>
</tr>
<tr>
<td>SR\textsubscript{A\textsubscript{sys}} at PWT</td>
<td>0.49</td>
<td>-1.76–2.74</td>
</tr>
<tr>
<td>SR\textsubscript{A\textsubscript{sys}} at IVST</td>
<td>-0.11</td>
<td>-0.99–0.76</td>
</tr>
<tr>
<td>ε at IVST</td>
<td>-2.84</td>
<td>-20.1–14.4</td>
</tr>
<tr>
<td>SR\textsubscript{A\textsubscript{sys}} at IVST</td>
<td>-1.64</td>
<td>-5.12–1.84</td>
</tr>
<tr>
<td>SR\textsubscript{A\textsubscript{sys}} at IVST</td>
<td>-0.98</td>
<td>-2.74–0.78</td>
</tr>
</tbody>
</table>

Abbreviations see in Tables 1, 2.

### Table 4. Receiver-Operator Characteristic Curve Analysis for Differentiation of Patients With HCM From Those With H-LVH

<table>
<thead>
<tr>
<th>Cutoff value</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVST/PWT</td>
<td>1.29</td>
<td>85.7</td>
<td>75.0</td>
</tr>
<tr>
<td>ε at PWT</td>
<td>0.55</td>
<td>71.4</td>
<td>87.5</td>
</tr>
<tr>
<td>SR\textsubscript{A\textsubscript{sys}} at PWT</td>
<td>3.05</td>
<td>61.5</td>
<td>93.8</td>
</tr>
<tr>
<td>ε at IVST</td>
<td>0.32</td>
<td>66.7</td>
<td>66.7</td>
</tr>
<tr>
<td>SR\textsubscript{A\textsubscript{sys}} at IVST</td>
<td>1.71</td>
<td>63.6</td>
<td>73.3</td>
</tr>
</tbody>
</table>

Abbreviations see in Tables 1, 2.
PWT ratio for discrimination between HCM and H-LVH, and the sensitivity, specificity, and predictive accuracy are shown in Table 4.

Discussion

We found that (1) the ε and absolute value of SRd at the posterior segment were significantly smaller in patients with HCM than in those with H-LVH, whereas the LV posterior WT did not differ between these 2 groups; (2) the ε and absolute value of SRd at the septal segment were also significantly smaller in patients with HCM than in those with H-LVH; and (3) the ε at the LV posterior segment was the highest discriminant parameter between HCM and H-LVH. Our findings suggest that endomyocardial radial strain and SR may provide important information for discriminating HCM from H-LVH.

Strain Imaging in Patients With LVH

In addition to the differences in strain and SR between patients with HCM and those with H-LVH described above, both strain and the absolute value of SR were smaller in patients with H-LVH than in control subjects. The diagnosis of HCM is based on conventional echocardiographic findings, but there is substantial overlap in the extent of LVH and asymmetrical septal hypertrophy between patients with HCM and those with H-LVH. Previous studies have shown that TDI is able to quantify LV myocardial abnormalities. SR imaging based on TDI is a newly developed echocardiographic modality and an emerging technique for assessment of myocardial systolic and diastolic function. The superiority of SR imaging for evaluating regional myocardial properties has been demonstrated. With the use of multivariate analysis, we have now shown that the combination of the IVST/PWT ratio, and ε at the LV posterior and septal segments is a good predictor of this condition. Endomyocardial radial strain imaging may thus yield information about regional dysfunction in patients with LVH.

Relation Between Strain Imaging and WT

Whereas the LV posterior WT did not differ between patients with HCM and those with H-LVH in the present study, the ε at the posterior segment was significantly smaller in patients with HCM than in those with H-LVH. We also showed a significant correlation between strain imaging and WT. Heterogeneity in LVWT have previously been associated with regional and global LV diastolic dysfunction in HCM. Regional relaxation abnormalities have been shown to contribute to impaired global LV relaxation. Regional systolic function has also been related to LVWT in HCM patients. In addition, previous studies based on magnetic resonance imaging revealed heterogeneity of regional systolic function in HCM. Park et al showed that regional asynchrony and regional heterogeneity derived from strain imaging, which were associated impaired global LV relaxation, improved after nonsurgical resection of the basal septum in HCM patients. These findings might support the relation between strain imaging and WT found in our study. Strain imaging may prove valuable as a predictor of HCM diagnosis during follow-up of patients with LVH.

Relation Between Endomyocardial Radial Strain and LV Relaxation

The ε at both the posterior and septal segments significantly correlated with the peak Ea velocity. The peak Ea velocity has the potential to provide a load-independent assessment of diastolic function and is closely related to LV relaxation and the LV filling pressures. Moreover, the ε/Ea is a potential predictor of the patients with HCM who are at risk of adverse outcome and of their survival after acute myocardial infarction. A magnetic resonance imaging study demonstrated that the extent of myocardial fibrosis has a significant correlation with both the LVEF and peak filling rate. The ε is a systolic parameter, whereas elastic recoil, which is determined by the LV end-systolic volume, is an important determinant of the relaxation rate. LV systolic performance is thus dependent on LV diastolic performance. Previous studies have suggested that indexes of systolic function are altered substantially earlier than those of diastolic function. The importance of diagnosis and treatment of diastolic heart failure is increasingly evident. The present data are consistent with those of our previous study using longitudinal SR imaging. Both radial and longitudinal strain imaging may thus provide insight into the pathophysiology of HCM.

Study Limitations

The problem of angle dependence is common to all quantitative Doppler-based techniques. In the present study, care was taken to maintain the ultrasonic beam perpendicular to the interrogated segment in order to minimize the influence of the insonation angle. The sensitivity was modest with regard to the differentiation of patients with HCM from those with H-LVH using strain and SRs. A further limitation of the present study is the lack of a large validation population. Additional prospective studies are warranted to determine whether relaxation insufficiency related to regional systolic function might be corrected by pharmacological or mechanical intervention.

Conclusions

The combination of the endomyocardial radial strain derived from TDI and the IVST/PWT ratio may be a good tool for discriminating between HCM and H-LVH.

References

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