Relationship Between Regional and Global Left Ventricular Systolic and Diastolic Function in Patients With Coronary Artery Disease Assessed by Strain Rate Imaging

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Background  The relationship between regional and global left ventricular function has not been evaluated. The present study aimed to assess whether regional myocardial contraction and relaxation reflect global left ventricular systolic and early diastolic function, respectively.

Methods and Results  The study involved 45 patients with coronary artery disease (CAD). Conventional echocardiography was performed, and segmental peak strain rate (SR) in the systole (Ssr) and early diastole (Esr) were obtained from tissue Doppler imaging in each of 18 segments of the left ventricular myocardium from the apical views. The Esr was significantly correlated with Ssr in all studied segments (r=0.55, p<0.0001). The average values of SR indices in each patient were defined as Ssr index and Esr index, which were derived by dividing the summed value of the Ssr or Esr by the number of respective assessable segments. A significant positive relationship was observed between the Ssr index and left ventricular ejection fraction (r=0.85, p<0.0001). Also, there was a positive correlation between the Esr index and mitral flow E (r=0.68, p<0.0001).

Conclusions  Regional myocardial contraction and relaxation, as assessed by SR imaging, were closely related in patients with CAD. Furthermore, regional myocardial contraction and relaxation are important factors affecting global left ventricular systolic and early diastolic function. (Circ J 2007; 71: 517–523)

Key Words:  Coronary artery disease; Left ventricular myocardial function; Strain rate imaging

G lobal left ventricular systolic and diastolic functions in patients with coronary artery disease (CAD) are traditionally assessed as important clinical and prognostic parameters. Several studies have recently demonstrated, by using non-invasive techniques including echocardiography, magnetic resonance imaging and radionuclide ventriculography, that the assessment of regional myocardial function provides important diagnostic and prognostic information in addition to that provided by global assessment alone.3–6 It has been shown that the indices of global left ventricular systolic and diastolic functions are associated with each other, but the relationship between regional myocardial contraction and relaxation remains unknown.

Echocardiographic tissue Doppler strain rate (SR) imaging is a new means of information about regional myocardial function that uses tissue velocity data to calculate velocity gradients between 2 distinct points along an ultrasound beam. It is therefore theoretically less susceptible than tissue velocity imaging to cardiac translational motion and to myocardial tethering. Thus, SR imaging might be able to analyze regional myocardial function more appropriately than tissue velocity imaging.7–11 Wall motion score is a parameter of regional left ventricular systolic function and the wall motion score index, which is an average of wall motion scores among assessable segments, and correlates with left ventricular ejection fraction (LVEF)12,13. In contrast, whether SR indices of regional myocardial function are associated with whole left ventricular function has not been clarified.

The present study aimed to assess the relationship between regional myocardial systolic and diastolic function in patients with CAD using SR imaging. We also evaluated whether SR imaging findings of regional myocardial contraction and relaxation reflect global left ventricular systolic and early diastolic function, respectively.

Methods

Study Population  Fifty patients with CAD were eligible for recruitment into the present study. Patients with heart failure, valvular or congenital heart disease were excluded. All patients were successfully treated with a prior balloon angioplasty and intracoronary stenting, and had no ischemic myocardial segments defined as a reversible myocardial perfusion defect as indicated by exercise or adenosine triphosphate stress technetium-99m tetrofosmin single-photon emission computed tomography. Of these patients, 5 were excluded because of inadequate echocardiographic image quality.
Table 1 shows the final study population of 45 patients (28 men and 17 women; mean age 67±7 years). Twenty-five patients had angina pectoris and no segmental wall motion abnormalities. Twenty had evidence of prior myocardial infarction established from chest pain, enzymatic evaluation, serial electrocardiographic changes and segmental wall motion abnormalities in the distribution of the affected coronary artery. All patients were in sinus rhythm. A total of 20 age-matched healthy participants (13 men and 7 women; mean age 65±5 years) with no evidence of cardiac disease served as control subjects. Written informed consent was obtained from all patients to participate in the study.

**Table 1 Patient Characteristics**

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>67±7</th>
</tr>
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<tbody>
<tr>
<td>Male</td>
<td>28 (62%)</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
</tr>
<tr>
<td>Angina pectoris</td>
<td>25 (56%)</td>
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<tr>
<td>Old myocardial infarction</td>
<td>20 (44%)</td>
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<tr>
<td>Risk factors</td>
<td></td>
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<tr>
<td>Diabetes mellitus</td>
<td>19 (42%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>22 (49%)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>24 (53%)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>16 (36%)</td>
</tr>
<tr>
<td>Medical therapy</td>
<td></td>
</tr>
<tr>
<td>Nitrates</td>
<td>35 (78%)</td>
</tr>
<tr>
<td>Calcium antagonist</td>
<td>10 (22%)</td>
</tr>
<tr>
<td>ß-blockers</td>
<td>9 (20%)</td>
</tr>
<tr>
<td>ACEI</td>
<td>24 (53%)</td>
</tr>
<tr>
<td>ARB</td>
<td>15 (33%)</td>
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</table>

n=45. Data are expressed as mean±SD or number (%). ACEI, angiotensin-converting enzyme-inhibitors; ARB, angiotensin receptor blockers.

An M-mode trace obtained just below the mitral valve leaflets was derived from the parasternal short-axis view. We measured left ventricular end-diastolic and end-systolic diameters and calculated fractional shortening. Left ventricular end-diastolic and end-systolic volumes were derived from apical 2- and 4-chamber views using the biplane modified Simpson’s rule, and the LVEF was calculated. Left ventricular filling variables were obtained from pulsed-wave Doppler recordings of the transmitral flow velocity. A sample volume was placed at the tips of the mitral valve leaflets. Doppler velocity recordings of 3 cardiac cycles on a paper at a speed of 100 mm/s were digitized and the variables were averaged. We then determined the peak early diastolic velocity (E), peak atrial systolic velocity (A), their ratio (E/A ratio) and the deceleration time of the E wave (DT).

**Tissue Doppler Imaging and SR Measurements**

Apical 2-chamber, 4-chamber and long-axis views of color 2-dimensional tissue Doppler images were acquired during end-expiration at a frame rate of 100 to 140 frames per second. Tissue Doppler digital data were stored and analyzed offline (EchoPac, GE Vingmed). Three consecutive cardiac cycles were recorded and averaged for each measurement. Sample volumes were placed in the inner half of the myocardium on the basal, mid, and apical segments of the left ventricle at the anteroseptum, anterior, lateral, posterior, inferior, and posteroseptum walls in the apical views. Thus, the left ventricle was divided into 18 segments. A sample volume that was 6.0 mm wide and 8.0 mm in length was used in all studies. The position of the sample volume was manually adjusted frame-by-frame to maintain its same position within the myocardium throughout the cardiac cycle. The SR profiles showed 1 negative and 2 positive waves during systole and diastole, respectively, and we measured peak systolic (SSR) and peak early diastolic SR (ESR) in each segment (Fig 1). Each patient had 18 values of SSR and ESR, and average values of SSR and ESR were defined as SSR index and ESR index, which were derived by dividing the summed value of the SSR or ESR by 18.
Esr by the number of assessable segments, respectively. If all 18 segments could not be assessed with tissue Doppler imaging, only assessable segments were included in this analysis. In addition, all assessable segments were divided into 3 groups according to regional systolic wall motion abnormalities and were based on the recommendations of the American Society of Echocardiography. Thus, segments were classified into normokinesis (Group I), hypokinesis (Group II) and akinesis or dyskinesis (Group III).

Statistical Analysis
All data were statistically analyzed by using StatView 5.0 software (SAS Institute Inc, Cary, NC, USA) and are expressed as mean ± SD. Comparisons of differences in subgroups were analyzed by using the Student’s t-test with the Bonferroni correction. Relationships between 2 variables were analyzed by using linear regression and are expressed as Pearson correlation coefficients. A difference was considered significant when the probability value was <0.05.

Results
We obtained SR values from 695 (586 in group I, 77 in group II, 32 in group III) out of 810 possible segments. We excluded 115 segments from the analysis because of noise (92 in group I, 16 in group II, 7 in group III). Although Ssr and Esr values in groups II and III were lower compared to those in group I, 109 segments (81%) in group II and III were feasible to be analyzed. Furthermore, no significant differences were observed in each group regarding the proportion of assessable segments (86% in group I, 83% in group II, 80% in group III). All 18 segments could be assessed in 6 patients; the remaining 39 patients had 2.9 ± 0.9 unassessable segments (range 1 to 4 segments). Table 2

<table>
<thead>
<tr>
<th>Hemodynamic and Echocardiographic Measurements</th>
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<tbody>
<tr>
<td>HR (beats/min)</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
</tr>
<tr>
<td>LVIDd (mm)</td>
</tr>
<tr>
<td>LVIDs (mm)</td>
</tr>
<tr>
<td>FS (%)</td>
</tr>
<tr>
<td>LVEF (%)</td>
</tr>
<tr>
<td>Mitral flow E (cm/s)</td>
</tr>
<tr>
<td>Mitral flow A (cm/s)</td>
</tr>
<tr>
<td>Mitr flow E/A</td>
</tr>
<tr>
<td>DT (ms)</td>
</tr>
<tr>
<td>Ssr index (1/s)</td>
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<td>Esr index (1/s)</td>
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n=45.
Data are expressed as mean ± SD.
HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; LVIDd, left ventricular end-diastolic diameter; LVIDs, left ventricular end-systolic diameter; FS, fractional shortening; LVEF, left ventricular ejection fraction; E, peak early diastolic velocity; A, peak atrial systolic velocity; DT, the deceleration time of the E wave; Ssr index, summed value of peak systolic strain rate divided by number of assessable segments for each patient; Esr index, summed value of peak early diastolic strain rate divided by number of assessable segments for each patient.
shows the hemodynamic and echocardiographic measurements. In all of the 45 patients, mitral flow A exceeded mitral flow E, resulting in a mitral flow E/A of less than 1.0 (ie, impaired relaxation pattern).

Fig 2 shows representative SR profiles from each group. SSR was significantly decreased in groups I, II and III (1.61±0.53, 0.73±0.25 and 0.43±0.27/s, respectively; all p<0.0001; Fig 3). ESR also significantly decreased in a similar order to that of SSR (2.16±0.87, 1.21±0.42 and 0.67±0.21/s, respectively; all p<0.0001; Fig 3). ESR significantly correlated with SSR in all studied segments (r=0.55, p<0.0001; Fig 4). In the control subjects, the SSR value was 1.67±0.32/s (1.63±0.24/s in basal, 1.74±0.22/s in mid, and 1.64±0.32/s in apical segments), and the ESR value was 2.21±0.37/s (2.23±0.21/s in basal, 2.14±0.19/s in mid, and 2.18±0.30/s in apical segments).

Relationship Between Regional and Global Left Ventricular Function

A significant positive relationship was observed between the SSR index and the LVEF in all 45 patients (r=0.85, p<0.0001; Fig 5). There was also a positive correlation between the ESR index and mitral flow E (r=0.68, p<0.0001; Fig 5). These significant relationships between the SSR index and the LVEF, and the ESR index and mitral flow E were also observed in patients with angina pectoris (n=25; r=0.87, p<0.0001, and r=0.67, p<0.0001, respectively), and old myocardial infarction (n=20; r=0.84, p<0.0001, and r=0.70, p<0.0001, respectively).

Reproducibility

The reproducibility of the SR measurements was evaluated as interobserver and intraobserver variability in 30 segments (10 in basal, mid and apical segments each) that were randomly selected by 2 independent observers. The interobserver variability was assessed by a second observer who was blinded to the values obtained by the first observer. The intraobserver variability was assessed by an observer who was blinded to the results of the previous measurements, and they also repeated the analysis at a different time. The interobserver and intraobserver variability is expressed as the absolute difference divided by the mean value of the measurements. The interobserver variabilities for SSR and for ESR were 7.1±5.0 and 10.8±8.2%, respectively, and the intraobserver variabilities for these indices were 9.2±8.0 and 11.4±8.6%, respectively.

Discussion

The present study demonstrated a close relationship between regional left ventricular myocardial contraction and relaxation as measured by SSR and ESR in patients with CAD. Both the SSR and ESR indices are global left ventricular indices and were obtained from quantitative assessments of regional wall motion using SR imaging. We found from their significant correlation that the SSR index is an alternative to LVEF. Furthermore, impaired regional left ventricular myocardial relaxation is an important factor that affects the reduction of left ventricular early diastolic filling because the ESR index and the mitral flow E are positively correlated.
Evaluation of Regional Myocardial Relaxation Using SR Imaging Parameters

Regional myocardial diastolic function has been quantified by radionuclide methods and by angiography. Echocardiographic tissue Doppler SR imaging is a new means of providing information regarding regional myocardial function. The SR imaging is equivalent to the velocity gradient between a point of interest and an adjacent point with a small offset. It equals the rate of regional myocardial deformation. The SR imaging can be determined by an algorithm that calculates spatial differences in tissue velocities between neighboring myocardial regions. Therefore, the major advantage of SR imaging is theoretically less susceptible than tissue velocity imaging to cardiac translational motion and myocardial tethering. This means that SR imaging might be more appropriate than tissue velocity imaging for analyzing regional myocardial function.

Several studies have suggested that SR imaging provides good parameters for evaluating regional myocardial function in diastole as well as in systole. Hoffmann et al. reported that normal contracting segments had higher peak early diastolic SR than dysysynergic segments, and that dobutamine stimulation caused an increase in peak early diastolic SR in dyssynergic viable myocardial segments, whereas non-viable segments were less responsive to dobutamine. We used ESR to represent the maximal velocity gradient of longitudinal wall lengthening in early diastole, as it is considered to be closely related to regional myocardial relaxation. Therefore, the reduced ESR suggested impaired regional myocardial relaxation.

Relationship of Regional Left Ventricular Myocardial Contraction and Relaxation

Regional left ventricular myocardial relaxation measured as ESR in the present study, was closely related to regional myocardial contraction, measured as SSR. Other studies have shown that whole left ventricular indices of contraction and relaxation are mathematically related. Several experimental studies have also demonstrated a relationship between contraction and relaxation in animal papillary muscle under various inotropic states. However, the relationship between regional myocardial systolic and diastolic function in humans has not been well characterized. Left ventricular myocardial relaxation occurs just after the end of active systole and is characterized by the active uptake of calcium ions into the sarcoplasmic reticulum. Several studies indicate that the ventricle exerts a suction effect that actively contributes to the generation of the early diastolic transmitral pressure difference that acts to fill the ventricular chamber, and that the magnitude of this suction effect is related to the elastic potential energy stored in the myocardium when the end-systolic volume achieved by the contracting ventricle is below equilibrium volume. Courtois et al. have shown that the peak early diastolic filling rate is closely related to left ventricular contractility and afterload in the normal left ventricle, suggesting that the storage of elastic energy at the end systole and subsequent recoil during early diastole are closely related to early diastolic mitral flow. These relationships are consistent with the notion that the process of early diastolic function is intimately related to systolic function and that the normal heart fills during early diastole under the influence of rapid ventricular expansion via elastic recoil. In the present study, we demonstrated using SR imaging that regional myocardial contraction is significantly associated with regional myocardial relaxation in patients with CAD.

Relationship Between Regional and Global Systolic Function

Wall motion score is a measurement of regional left ventricular systolic function and is derived by grading the wall motion of individual left ventricular segments. The wall motion score index is an average of wall motion scores among assessable segments and can be used as an alternative to LVEF for assessing global left ventricular systolic function. In fact, Galasko et al. and Moller et al. have reported that the wall motion score index closely correlates with LVEF. Furthermore, the wall motion score index at predischarge after an initial acute myocardial infarction is superior to the ejection fraction in predicting morbidity and mortality. However, the visual assessment of wall motion is qualitative and dependent on operator experience. In contrast, SR indices can be used as quantitative measurements of regional wall motion because they can be obtained from regional myocardial velocities by tissue Doppler echocardiography. In the present study, to elucidate quantitatively the relationship between regional and global left ventricular systolic function, we evaluated the SSR index as a marker of global systolic function derived from the assessment of regional systolic function for each patient. Our results showed that the SSR index closely correlated with LVEF, indicating that the SSR index is quantitative and likely to be a clinically useful index of global left ventricular systolic function.

Relationship Between Regional and Global Diastolic Function

Several investigators have found that there is a relationship between regional and global diastolic function using radionuclide angiography, contrast ventriculography and echocardiography. Bowon et al. reported that the severity of impairment of global left ventricular diastolic filling is related to the magnitude of asynchronous left ventricular diastolic function in patients with CAD, when radionuclide angiography is used. Our previous study demonstrated using SR imaging that improved global left ventricular early diastolic filling is associated with the degree of improvement in impaired regional myocardial relaxation in ischemic segments after successful percutaneous coronary intervention in patients with stable angina pectoris. To determine whether the impaired regional myocardial relaxation contributes to the reduced left ventricular early diastolic filling, we evaluated the ESR index derived from the assessment of regional myocardial relaxation as a marker of global left ventricular relaxation for each patient. The results showed a close correlation between the ESR index and mitral flow E, suggesting that the severity of reduction in left ventricular early diastolic filling is associated with the extent and degree of impairment in regional myocardial relaxation.

Study Limitations

SR measurements are angle-dependent and susceptible to noise. To minimize these effects, we measured 3 consecutive cardiac cycles, averaged the results for each measurement and maintained a small angle between the ultrasound beam and the left ventricular axis. Some investigators have reported that the reproducibility of SR measurements varies from 1 to 24% between and within observers. We found a modest interobserver and...
Thus, to assess the degree of diastolic dysfunction in patients.\textsuperscript{34} Thus, to assess the degree of diastolic dysfunction in significant value to the clinical management of cardiac pa-
standard echocardiographic measurements, and adds a sig-
power for cardiac mortality compared with clinical data and early diastolic function provides incremental predictive from the systolic evaluation alone. Wang et al showed that the diastolic assessment is independent from that derived
intraobserver variability in SR measurements that might be
affected by longitudinal lengthening, so we cannot address radial and circumferential components. Moreover, wall motion was evaluated as the degree of radial motion, while SR measurements at the apical views reflected longitudinal shortening in the present study. However, because the myocardium is incompressible, radial lengthening and longitudinal shortening might be closely related.

Mitral flow velocities are influenced by many physio-
logic factors, particularly by alterations in filling pressures. Diastolic filling is categorized as normal, impaired relaxation, pseudonormal, or restrictive filling. In the present study, because diastolic filling in all patients was an impaired relaxation pattern, the relationship between regional myocardial relaxation and global left ventricular early diastolic function in patients with pseudonormal or restrictive filling was not evaluated.

All 18 segments could be assessed in only 6 patients, and 39 patients had unassessable segments. Because the number of assessable segments varied in each patient, this might affect the assessment of Srs and Esr indexes.

Clinical Implications

Patients with CAD presenting with global diastolic dys-
function have a worse prognosis than those without diastol-
ic impairment, and the prognostic information provided by the diastolic assessment is independent from that derived from the systolic evaluation alone. Wang et al showed that early diastolic function provides incremental predictive power for cardiac mortality compared with clinical data and standard echocardiographic measurements, and adds a significant value to the clinical management of cardiac pa-
tients.\textsuperscript{34} Thus, to assess the degree of diastolic dysfunction in patients with CAD early diastolic function might be important for the prediction of diastolic dysfunction prognosis and mortality. SR imaging is a new echocardiographic method that can be used to assess regional diastolic function. Some authors have reported that SR imaging parameters were sensitive methods for detecting the subtle left ventricular dysfunction that was unable to be detected by using conventional global functional assessment, and they also suggested that these SR imaging parameters might be useful methods for predicting early phases of myocardial dysfunction.\textsuperscript{35,36} Accordingly, regional myocardial functional assessment might be useful to provide additional important diagnostic and prognostic clinical information over that provided by conventional global functional assessment alone.

Conclusions

Regional myocardial contraction and relaxation, as assessed by SR imaging, were closely related in patients with CAD. Furthermore, regional myocardial contraction and relaxation were important factors affecting global left ventricular systolic and early diastolic function. Echocardiographic evaluation using SR imaging is a useful noninvasive method for quantifying regional myocardial con-
traction and relaxation.

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