Quantification of regional left ventricular systolic dysfunction in patients with coronary artery disease by pulsed Doppler tissue imaging

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Abstract. – Objectives: To analyze and compare quantitatively regional myocardial functional abnormalities of the left ventricle by pulsed Doppler tissue imaging (DTI) in patients with unstable angina (UA) and prior myocardial infarction (MI), and to explore the value of systolic velocity and time intervals in evaluating regional left ventricular systolic dysfunction.

Methods: Patients with coronary artery disease (CAD) were divided into UA (16 cases) and anterior wall MI (ant-MI, 21 cases) groups. Sixteen age-matched normal subjects served as the control group. The septal and lateral, anterior and inferior walls of the left ventricle were displayed, and basal and middle segments of each wall were selected for myocardial motion spectrum sampling. DTI parameters were: peak systolic myocardial velocity (s), regional pre-ejection period (PEP), time to peak of the systolic wave (Ts), regional ejection time (ET) and PEP/ET ratio.

Results: Compared with the control group, s was significantly lower in all segments in the ant-MI group, and in lateral and anterior segments in the UA group. It was even lower in the ant-MI than in the UA group, and in infarct compared with corresponding non-infarct segments in the ant-MI group. PEP and Ts were significantly longer in both the UA and the ant-MI groups.

Conclusion: Not only s, but also PEP and Ts as measured by pulsed DTI are sensitive markers of regional left ventricular systolic dysfunction in patients with CAD; s and PEP may even indicate the severity of myocardial ischemia and aid in estimating the site of MI.

Key Words: Doppler tissue imaging, Echocardiography, Coronary artery disease, Ventricular function.

Material and Methods

Subjects
The study population included 37 patients with clinically established CAD, among which 16 with UA (UA group) and 21 with anterior wall MI (ant-MI group). The UA group patients had at least one major coronary artery stenosis (≥ 50% reduction in the luminal diameter) in recent coronary angiography, among which there were 10 with single-vessel disease, 3 with double- and 3 with triple-vessel disease, respectively. Left ante-
rior descending coronary artery was involved in all of them. The ant-MI group consisted of patients with isolated anterior wall MI. Medications taken by the patients included mainly nitrates, beta-blockers, angiotensin-converting enzyme inhibitors (ACEI), oral anti-aggregants, statins, aspirin, and diuretics. Patients with myocardial hypertrophy, valvular heart disease, complex arrhythmias, severe heart failure, or chronic obstructive pulmonary disease were excluded. The control group consisted of 16 healthy individuals, who had no evidence of clinically significant cardiovascular disease on the basis of history, physical examination, chest radiography, electrocardiography (ECG), treadmill stress ECG and routine echocardiographic results. All subjects were in the sinus rhythm, without moderate to severe mitral or aortic regurgitation. Written informed consent was obtained from all participants.

**Instrument and Methods**

A commercially available ultrasound system equipped with DTI capabilities (Sonos 5500, Agilent Technologies, Andover, Massachusetts, USA) with an S4 transducer was used in this study. Patients were imaged in the left lateral decubitus position, and ECG was recorded simultaneously. Initially, a conventional echocardiographic examination was performed, and LVEF was determined using the modified Simpson et al method. Then, the system was switched to DTI velocity mode. Apical four- and two-chamber views were obtained, respectively, to display the movement of the septal and lateral, anterior and inferior walls of the left ventricle, and the basal and middle segments of each wall were selected for myocardial motion spectrum sampling. The direction of the beam was adjusted to be in alignment with the direction of the longitudinal myocardial motion. All images were stored digitally on MO disk for subsequent offline analysis. The DTI data were analyzed by an independent investigator who was unaware of the patients’ clinical data, including conventional echocardiographic findings. DTI parameters were: peak systolic myocardial velocity ($v$), regional pre-ejection period (PEP), time to peak of the systolic wave (Ts), regional ejection time (ET) and PEP/ET ratio. Three beats were averaged for each parameter. For the measurement of PEP and Ts, the beginning of the QRS complex was used as the reference point.

**Statistical Analysis**

All data were analyzed using a standard statistical software program (SPSS for Windows, Version 10.0; SPSS Inc., Chicago, Illinois, USA). Continuous data were expressed as mean ± standard deviation (SD). The differences in values among the three groups were compared by one-way analysis of variance (ANOVA) followed by post hoc multiple comparisons. The comparison of values between the anterior and corresponding inferior walls in the same group was made by Student’s paired $t$-test. Differences in categoric data were compared using the chi-square test. A $P$ value of less than 0.05 was considered statistically significant.

**Results**

**Clinical Characteristics**

As shown in Table I, there were no significant differences among the three groups regarding baseline characteristics, except for a slower heart rate in the UA group than in the control group.

**Table I.** Baseline characteristics of CAD and control groups.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control group (n = 16)</th>
<th>UA group (n = 16)</th>
<th>Ant-MI group (n = 21)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>58.38 ± 5.85</td>
<td>63.68 ± 5.98</td>
<td>61.24 ± 11.60</td>
<td>0.230</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>10/6</td>
<td>10/6</td>
<td>18/3</td>
<td>0.103</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>74.99 ± 11.94</td>
<td>63.50 ± 9.92*</td>
<td>68.93 ± 10.92</td>
<td>0.018</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>118.80 ± 13.05</td>
<td>125.73 ± 24.00</td>
<td>121.33 ± 12.52</td>
<td>0.524</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>73.33 ± 5.23</td>
<td>73.20 ± 7.93</td>
<td>70.95 ± 7.48</td>
<td>0.518</td>
</tr>
</tbody>
</table>

CAD = coronary artery disease; UA = unstable angina; Ant-MI = anterior wall myocardial infarction; BP = blood pressure.

*Significant difference was found between the UA and the control groups.
No significant difference was found between the UA and the ant-MI groups with respect to revascularization (i.e., percutaneous coronary intervention, PCI) underwent and medications used \((P > 0.05)\), except that ACEI and diuretics were taken more often in the ant-MI group than in the UA group \((both \ P < 0.05)\).

**LVEF by Conventional Echocardiography**

LVEF was not significantly different between the UA and the control groups \([(66.57 \pm 5.10)\% \; vs \; (67.73 \pm 5.05)\%, \; P > 0.05]\). But it was significantly lower in the ant-MI group than in the control and the UA groups \([(49.95 \pm 9.70)\% \; vs \; (67.73 \pm 5.05)\% \; and \; (49.95 \pm 9.70)\% \; vs \; (66.57 \pm 5.10)\%, \; respectively; \; both \; P < 0.01]\).

**Systolic Velocity by Pulsed DTI**

Compared with the control group, \(s\) was significantly lower in all segments in the ant-MI group, and in lateral and anterior wall segments in the UA group. Compared with the UA group, \(s\) was also significantly lower in all segments, with exception of the middle lateral segment, in the ant-MI group (Table II).

In the control group, \(s\) was not significantly different between anterior and corresponding inferior walls. In the ant-MI group, \(s\) of the anterior infarct segments was compared with that of the corresponding inferior non-infarct segments, and it turned out that \(s\) of the basal and middle anterior segments was significantly lower than that of the corresponding inferior segments \((8.06 \pm 1.14 \; \text{cm/s} \; vs \; 9.85 \pm 1.26 \; \text{cm/s}, \; and \; 6.79 \pm 1.19 \; \text{cm/s} \; vs \; 8.20 \pm 1.20 \; \text{cm/s}, \; respectively; \; both \; P < 0.01)\).

**Systolic Time Intervals by Pulsed DTI**

The systolic time intervals in the basal segment of the lateral and anterior walls of the left ventricle were compared among the three groups, and significant differences were found with respect to PEP, Ts and PEP/ET. But ET was not significantly different among the three groups. Compared with the control group, PEP and Ts were significantly longer in both the UA and the ant-MI groups, and PEP/ET was significantly larger, except in the basal anterior wall in the UA group. Compared with the UA group, only PEP in the basal anterior wall was significantly longer in the ant-MI group (Table III).

**Discussion**

Derumeaux et al.\(^4\) first reported that pulsed DTI could identify and quantify regional myocardial velocities during ischemia and reperfusion. During reduction of coronary blood flow, the decrease in peak systolic myocardial velocity determined by pulsed DTI correlated well with systolic segment shortening measured by sonomicrometry and regional myocardial blood flow assessed by radioactive microsphere technique, suggesting that pulsed DTI could sensitively detect and accurately quantify ischemia-induced regional myocardial dysfunction. In the present study, \(s\) decreased significantly in the lateral and anterior walls in the UA group, while LVEF did not change significantly. Moreover, \(s\) in the ant-MI group was significantly lower not only than that in the control group, but also than that in the UA group. These results indicate that \(s\) can re-

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**Table II.** Comparison of systolic myocardial velocity among three groups.

<table>
<thead>
<tr>
<th>Segment (s, cm/s)</th>
<th>Control group (n = 16)</th>
<th>UA group (n = 16)</th>
<th>Ant-MI group (n = 21)</th>
<th>ANOVA</th>
<th>Post Hoc Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal lateral</td>
<td>12.48 ± 2.13</td>
<td>10.94 ± 1.83</td>
<td>9.60 ± 1.65</td>
<td>0.000</td>
<td>0.022 0.000 0.035</td>
</tr>
<tr>
<td>Middle lateral</td>
<td>10.99 ± 2.27</td>
<td>9.21 ± 1.55</td>
<td>8.28 ± 1.36</td>
<td>0.000</td>
<td>0.006 0.000 0.111</td>
</tr>
<tr>
<td>Basal septal</td>
<td>11.07 ± 1.16</td>
<td>10.24 ± 1.23</td>
<td>9.21 ± 1.32</td>
<td>0.000</td>
<td>0.067 0.000 0.016</td>
</tr>
<tr>
<td>Middle septal</td>
<td>9.24 ± 1.08</td>
<td>9.01 ± 1.48</td>
<td>7.76 ± 1.18</td>
<td>0.001</td>
<td>0.604 0.001 0.004</td>
</tr>
<tr>
<td>Basal anterior</td>
<td>11.47 ± 1.83</td>
<td>9.36 ± 1.35</td>
<td>8.06 ± 1.14</td>
<td>0.000</td>
<td>0.000 0.000 0.009</td>
</tr>
<tr>
<td>Middle anterior</td>
<td>10.05 ± 1.37</td>
<td>7.90 ± 1.64</td>
<td>6.79 ± 1.19</td>
<td>0.000</td>
<td>0.000 0.000 0.019</td>
</tr>
<tr>
<td>Basal inferior</td>
<td>11.65 ± 1.57</td>
<td>10.87 ± 1.60</td>
<td>9.85 ± 1.26</td>
<td>0.002</td>
<td>0.142 0.001 0.040</td>
</tr>
<tr>
<td>Middle inferior</td>
<td>10.33 ± 1.54</td>
<td>9.46 ± 1.21</td>
<td>8.20 ± 1.20</td>
<td>0.000</td>
<td>0.068 0.000 0.006</td>
</tr>
</tbody>
</table>

ANOVA = analysis of variance; \(s\) = systolic myocardial velocity; C = control group; U = UA group; M = Ant-MI group.
flect ischemia-induced regional systolic dysfunction earlier, and the severity of ischemic damage as well. In the ant-MI group, $s$ in the infarct segments was significantly lower than that in the corresponding non-infarct segments, suggesting that it can also aid in estimating the site of MI. The systolic myocardial velocity measured by pulsed DTI is more sensitive than conventional LVEF, partly because the latter represent global left ventricular systolic function, while regional abnormalities occur earlier than global dysfunction. Another reason might be that the longitudinal myocardial fibers are more sensitive to early ischemia. Therefore, longitudinal myocardial systolic velocity measured from the apical window may be a more sensitive marker of impaired left ventricular systolic function.

As myocardial ischemia and/or necrosis occurred, regional myocardial function would be severely damaged because of impaired intrinsic myocardial contractility. The contraction of the diseased myocardium became markedly weakened or disappeared, or only passive motion caused by contraction of the neighboring myocardium existed, resulting in significantly reduced myocardial systolic velocity. In addition, in consistent with other observations, our study demonstrated that $s$ also reduced significantly in the non-infarct segments in patients with MI, which might be the tethering effect of the infarct myocardium, together with myocardial stunning. Furthermore, in the absence of visible myocardial motion abnormalities, the parameters from pulsed DTI have revealed reduced systolic function, which have been confirmed by coronary angiography. Thus, it can be speculated that the mechanical dysfunction of the stunning myocardium can be determined more sensitively by pulsed DTI than by conventional methods. On the other hand, there might be stenosis of the nutrient artery. Myocardial stunning could also develop in the presence of partial occlusion of the arterial lumen while tissue oxygen requirement was increased temporarily. When infarct area was larger, the non-infarct tissue would be subject to additional working load and, in the presence of a non-significant lesion in the artery supplying to these regions, myocardial stunning at the DTI sensitivity level might be produced.

One of the major advantages of pulsed DTI is its excellent temporal resolution, thereby the capability to record myocardial velocities during different phases of the cardiac cycle, and to determine the time intervals of myocardial motion. Exact timing of myocardial velocities in relation to different phases of the cardiac cycle is possible by simultaneous recording of ECG and myocardial velocities. In the present study, time to the onset, to the peak and duration of myocardial systolic wave were measured. In contrast to earlier study by Bach et al, ET in patients with CAD was not significantly different from that in the controls, suggesting that it cannot reflect systolic functional changes caused by ischemia. Ts was significantly longer in CAD patients, which is similar to the observations by Iyisoy et al, confirming that Ts is also a useful index for the early detection of myocardial ischemia.
Pulsed Doppler in coronary artery disease

Some investigators\(^\text{12}\) used pulsed DTI to study patients with old MI, and compared the results with that from myocardial single photon emission computed tomography (SPECT) with \(^{99}\text{Tc}\)-MIBI. They found that regional PET/ET as measured by pulsed DTI at rest had significantly negative correlation with regional \(^{99}\text{Tc}\)-MIBI uptake calculated by SPECT. PET/ET in viable segments was significantly lower than that in nonviable segments. PET/ET demonstrated comparable diagnostic accuracy for the detection of viable myocardium compared with myocardial perfusion imaging, which suggested that the measurements of regional time intervals by pulsed DTI at rest might also be used for quantitatively assessment of myocardial viability. In our study, PEP/ET was significantly larger, with exception of the basal anterior wall in the UA group, but PEP was significantly longer in all segments in CAD patients, which may suggest that the latter is more sensitive to ischemia. PEP in the infarct segment was even longer, indicating that PEP may also reflect the severity of ischemic myocardial damage.

Although heart rate in the UA group was slower than that in the control group, no significant difference was found between the ant-MI and the control as well as the UA group. Moreover, earlier study had shown that systolic time intervals were not affected by heart rate\(^\text{13}\). Therefore, the difference in heart rate between the UA and the control groups negligibly influenced the results of this study.

It is not clear whether the medications taken by the patients affected DTI parameters. Shan et al\(^\text{14}\) observed a significant relationship between myocardial adrenergic receptor density and myocardial velocities, which might suggest that systolic DTI data may be influenced by cardiac drugs with negative inotropic properties, such as beta-blockers. However, no significant difference was found between the two patient groups with respect to this kind of drugs taken. Although there were significantly more patients in the ant-MI group who took ACEI and diuretics, which might change the loading condition, earlier studies had shown that DTI parameters were relatively independent of the loading condition of the heart\(^\text{15,16}\).

As a Doppler based technique, angle dependency remains a crucial issue, leading to the potential for error when trying to quantify tissue velocities accurately. Nevertheless, time intervals should be angle independent, and the problems with cardiac translation and rotation are less important. And, from the cardiac apex, the impact of translational motion of the heart within the thorax becomes much less significant\(^2\), longitudinal shortening velocity may be reliably measured.

In summary, not only s, but also PEP and Ts as measured by pulsed DTI are sensitive markers of regional left ventricular systolic dysfunction in patients with CAD; s and PEP may even indicate the severity of myocardial ischemia and aid in estimating the site of MI.

References


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