Remote Ischemia in the Setting of Acute Myocardial Infarction: Echocardiographic Assessment of Left Ventricular Wall Thickening Using the Modified Centerline Method

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Abstract

Severe stenosis of a non-infarct-related artery may cause regional remote ventricular asynergy during the acute phase of myocardial infarction (MI). Such lesions may contribute to left ventricular dysfunction and poor prognosis following MI. We performed two-dimensional echocardiography in 140 patients with their first acute anterior MI on admission and 1 month after MI. Using the modified centerline method, the left ventricular short axis image was used to determine % wall thickening (%WT) of the left anterior descending artery (LAD) area, the right coronary artery (RCA) area, and the left circumflex artery (LCX) area. The study compared the accuracy of %WT and visual assessment of wall motion for the diagnosis of remote coronary stenosis. Of the 140 patients, 100 had single-vessel disease occurring in the LAD (group S) and 40 had multivessel disease (group M). In group M, remote asynergy in the non-infarcted area was identified in 33 patients (83%) by abnormal %WT and in 16 (40%) by abnormal wall motion (p<0.001). The %WT of the RCA area was lower in group M than in group S (p<0.0001). The %WT of the LCX area was also lower in group M than in group S (p<0.0001). The %WT in the non-infarcted area improved 1 month after the onset of MI (p<0.0001). %WT determined by two-dimensional echocardiography and the modified centerline method is more sensitive than visual assessment of wall motion for the identification of multivessel disease in patients with acute anterior wall MI.

Introduction

During the acute phase of myocardial infarction (MI), oxygen demand in the non-infarcted area increases because of increases in preload and afterload and increased contraction in the non-infarcted area compensates for diminished contractility in the infarcted area.

Key words: acute myocardial infarction, remote ischemia, wall thickening.
area. Critical stenosis in the coronary artery supplying a non-infarcted area may induce ischemia in the non-infarcted area\(^{[6]}\) (i.e., remote ischemia). Coronary lesions inducing remote ischemia may cause deterioration of left ventricular function during the acute phase of MI and adversely affect prognosis\(^{[1,7,8]}\).

Identifying remote ischemia during the acute phase of MI would help in determining therapy and in predicting prognosis. Dobutamine or dipyridamole stress two-dimensional echocardiography and radionuclide perfusion imaging are widely used to assess remote ischemia in non-infarcted areas\(^{[9,10]}\). However, these examinations can not be performed in patients in the setting of acute MI. Furthermore, detection of remote ischemia in the non-infarcted area during the acute phase of MI is difficult using conventional echocardiographic evaluation of left ventricular wall motion, especially in patients with small infarcts or mild stenosis in the culprit coronary artery\(^{[11]}\). Therefore, we used quantitative echocardiographic evaluation of left ventricular wall thickening to identify the presence or absence of multivessel lesions in the patients with acute MI.

**Materials and Methods**

**Patient population**

The study group included 186 consecutive patients with acute anteroseptal MI who underwent two-dimensional echocardiography within 24 hours after the onset of symptoms. Patients were admitted to the coronary care unit of our hospital between December 1991 and July 1997. Eligible criteria included [1] no prior myocardial infarction and [2] adequate echocardiographic image quality. One hundred forty patients (114 men and 26 women, mean age 62 years, range 29–84 years) with technically adequate echocardiographic studies were included in the present investigation. The diagnosis of acute myocardial infarction was made based on three specific findings: (1) typical chest pain lasting for more than 30 minutes, (2) an increase in the serum creatine kinase activity to more than twice the normal value, and (3) 1 mm ST-segment elevation in two or more leads on the 12-lead electrocardiogram. The control group consisted of 30 healthy individuals who had no history of heart disease (22 men and 8 women, 40 to 70 years of age, mean age 61) who underwent two-dimensional echocardiography.

**Echocardiography**

Two-dimensional echocardiography was performed with the patient in the left decubitus position within 24 hours after the onset of acute myocardial infarction. A Toshiba SSH160A (Toshiba, Tokyo, Japan) or a Hewlett-Packard SONOS 1500 (Andover, MA) echocardiographic system was used with a 2.5-MHz transducer. Short-axis views at the mitral valve level and the midpapillary muscle level and the apical long-axis view were recorded on a 1/2-inch videotape with a VHS recorder (model BR-6000, Victor, Yokohama, Japan). An off-line image analysis system (TomTec Imaging, Boulder, Co.) was used to measure left ventricular end-diastolic wall thickness and end-systolic wall thickness in the short-axis view at the midpapillary muscle level.

Echocardiographic images at end-diastole

Abbreviations: %WT, % wall thickening (%WT); LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery.
were analyzed in a random sequence by an experienced echocardiographer. The endocardial and epicardial borders excluding the papillary muscles were manually digitized by a leading-edge method. One hundred chords were constructed perpendicular to a center line drawn midway between the endocardial and epicardial borders. The chords were numbered counterclockwise from 0 to 99, starting at the anterior papillary muscle. The length of each end-systolic chord was subtracted from each end-diastolic chord and divided by the length of the end-diastolic chord. To adjust for differences in heart size, the wall thickening of each chord was calculated as:

$$\text{% wall thickening (}\%\text{WT}) = \frac{\text{end-systolic perimeter}}{\text{end-diastolic perimeter}} - 1$$
end-diastolic perimeter) \times 100\%$. The contours of the left ventricle were divided in anteroseptal [chords 0-50, region of the left anterior descending artery (LAD)], inferior [chords 51-75, region of the right coronary artery (RCA)], and lateral [chords 76-100, region of the left circumflex artery (LCX)] regions.

The mean±SD of the %WT for the 100 left ventricular chords was determined for 30 healthy individuals. Wall thickening was considered to be within normal limits when it was within the range of mean±SD. The RCA and LCX areas, which were non-infarcted, were both divided into 10 chords. The mean %WT for each chord was determined, and remote asynergy was considered to be present when the highest mean %WT was less than 1SD below the mean control value.

Two-dimensional M-mode measurements were obtained at end-diastole and end-systole using criteria recommended by the American Society of Echocardiography\textsuperscript{30}. Left ventricular end-diastolic and left ventricular end-systolic dimensions were calculated from the long-axis images obtained by two-dimensional echocardiography. The left ventricular wall was divided into 11 segments, and segmental wall motion was graded on a 4-point scale: 0=normal; 1=hypokinetic; 2=akinetie; 3=dyskinetic. Total wall motion index was calculated as the sum of all 11 segments\textsuperscript{30}. Each two-dimensional echo was analyzed by two independent blinded observers. If wall motion in the non-infarcted segment was depressed beyond hypokinesia, remote asynergy was considered to be present.

Coronary angiography

All of the patients in this study underwent routine coronary angiography in multiple projections within 24 hours after symptom onset. Coronary anatomy was reviewed by two experienced angiographers, and the locations of stenoses were recorded according to the 23-segment model established by the Coronary Artery Surgery Study\textsuperscript{31}. The maximal luminal narrowing was determined by caliper reading, and significant angiographic stenosis was defined by a diameter narrowing ≥75%. Patients were further classified as having 1-, 2-, or 3-vessel disease. Non-infarcted areas with coronary artery stenosis ≥75% were defined as remote ischemic areas, and non-infarcted areas without significant coronary stenosis were defined as remote non-ischemic areas.

Statistical analysis

Values are expressed as means±standard deviation. Significant differences between two groups were determined by Student’s $t$ test. Significant differences three or more groups were identified by analysis of variance. Analysis of variance and Scheffe’s $F$ for repeated measures were used to compare values during the acute and chronic stages. Differences were considered statistically significant if $p<0.05$.

Results

1. Clinical characteristics (Tables 1 and 2)

Of 140 the patients with acute anteroseptal myocardial infarctions, 100 had single-vessel disease affecting the LAD (group S) and 40 had multivessel disease (group M). There were no significant differences between the two groups with respect to history of hypertension (systolic pressure $>140$ mm Hg, diastolic pressure $>90$ mm Hg), hyperlipidemia (serum cholesterol concentration $>240$ mg/dl or fasting serum triglyceride concentration $>200$ mg/dl), or hyperuricemia (serum uric acid concentration $>8.0$ mg/dl), or history of
Table 1 Clinical characteristics of the study groups

<table>
<thead>
<tr>
<th></th>
<th>Group S (n=100)</th>
<th>Group M (n=40)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (Male/Female)</td>
<td>82/18</td>
<td>32/8</td>
<td>NS</td>
</tr>
<tr>
<td>Age (years)</td>
<td>62±11</td>
<td>62±8</td>
<td>0.71</td>
</tr>
<tr>
<td>Hypertension</td>
<td>39 (39%)</td>
<td>22 (56%)</td>
<td>0.42</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>18 (18%)</td>
<td>14 (35%)</td>
<td>0.0493</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>25 (25%)</td>
<td>12 (30%)</td>
<td>0.82</td>
</tr>
<tr>
<td>Hyperuricemia</td>
<td>10 (10%)</td>
<td>6 (15%)</td>
<td>0.99</td>
</tr>
<tr>
<td>Smoking</td>
<td>73 (73%)</td>
<td>32 (80%)</td>
<td>0.26</td>
</tr>
<tr>
<td>Peak creatine kinase activity (IU/I)</td>
<td>5748±3827</td>
<td>3188±2516</td>
<td>0.0002</td>
</tr>
<tr>
<td>Left ventricular end-diastolic dimension (mm)</td>
<td>46.9±5.2</td>
<td>45.5±5.1</td>
<td>0.21</td>
</tr>
<tr>
<td>Total wall motion index</td>
<td>11±3</td>
<td>10±4</td>
<td>0.16</td>
</tr>
<tr>
<td>% wall thickening (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infarction area (%)</td>
<td>93±10</td>
<td>100±12</td>
<td>0.75</td>
</tr>
<tr>
<td>Non-infarction area (%)</td>
<td>155±39</td>
<td>133±25</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>% stenosis of the LAD (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute phase (%)</td>
<td>96±9</td>
<td>98±5</td>
<td>0.71</td>
</tr>
<tr>
<td>Chronic phase (%)</td>
<td>59±33</td>
<td>69±31</td>
<td>0.78</td>
</tr>
<tr>
<td>% stenosis of the RCA (%)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>% stenosis of the LCX (%)</td>
<td></td>
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</table>

LAD, left anterior descending artery; RCA, right coronary artery; LCX, left circumflex artery.

Table 2 Treatment during the acute phase

<table>
<thead>
<tr>
<th></th>
<th>Group S</th>
<th>Group M</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>LAD &amp; RCA</td>
</tr>
<tr>
<td>No.</td>
<td>100</td>
<td>40</td>
</tr>
<tr>
<td>PTCA (%)</td>
<td>63 (63)</td>
<td>18 (45)*</td>
</tr>
<tr>
<td>Thrombolysis (%)</td>
<td>29 (29)</td>
<td>17 (18)</td>
</tr>
<tr>
<td>Conservative therapy (%)</td>
<td>8 (8)</td>
<td>10 (25)*</td>
</tr>
<tr>
<td>CABG (%)</td>
<td>0 (0)</td>
<td>5 (12)*</td>
</tr>
</tbody>
</table>

*, P<0.01 vs Group S; *, P<0.05 vs Group S. No, number of patients.
PTCA, percutaneous transluminal coronary angioplasty; CABG, coronary artery bypass graft; LAD, left anterior descending artery; RCA, right coronary artery; LCX, left circumflex artery.

Of the 40 patients in group M, 15 had 2-vessel disease with significant stenoses in the LAD and RCA (LAD & RCA group), 19 had 2-vessel disease with significant stenoses in the LAD and LCX (LAD & LCX group), and 6 had 3-vessel disease (3VD group). There were no significant differences between smoking (>10 cigarettes/day). The prevalence of diabetes (blood sugar concentration >120 mg/dl, HbA1c activity >7.0) was significantly higher in group M than in group S (p<0.05). The peak creatine kinase activity was significantly higher in group S than in group M (p=0.0002).
groups S and M with respect to the severity of stenosis in the infarct-related coronary artery (LAD) during the acute phase or in the degree of residual stenosis 1 month after MI. Of 40 the patients in group M, a significant stenosis was present in the RCA (86±11%) in 21 patients and in the LCX (88±11%) in 25 patients.

The number of patients undergoing percutaneous transluminal coronary angioplasty was significantly higher in group S than in group M (63% vs. 45%; p=0.0106). None of the patients with 3-vessel disease in group M underwent percutaneous transluminal coronary angioplasty. No significant difference was noted between groups S and M in the number of patients undergoing thrombolytic therapy. The number of patients undergoing conservative therapy was significantly lower in group S than in group M (8% vs. 25%, p=0.0095). In addition, coronary artery bypass graft was performed only in patients in group M.

2. Echocardiographic data and diagnosis of remote ischemia (Tables 3 and 4)

There were no significant differences between groups S and M with respect to the left ventricular end-diastolic dimension and total wall motion index (Table 1). Based on visual assessment of left ventricular wall motion, remote asynergy was present in 16 of the 40 patients in group M (40%), in 12 of the 34 with 2-vessel disease (35%), and 4 of the 6 with 3-vessel disease (67%). Of the remaining 24 patients in whom remote asynergy was not present in the non-infarct areas with a significant stenosis, 16 (67%) had small anterior infarcts with a left ventricular wall motion index <3, and 8 (33%) had significant stenoses in the distal portion of the non-infarct related coronary artery. Reduced wall motion was noted in the non-infarcted area in 3 of the group S patients (3%) in whom the LAD had a proximal lesion.

Based on the %WT findings, remote asynergy was noted in 33 of the 40 patients (83%) in group M. Asynergy was present in 28 of the 34 patients with 2-vessel disease (82%) and 5 of the 6 patients with 3-vessel disease (83%). Seven patients (17%) in group M had no remote asynergy in areas supplied by coronary arteries with significant stenoses. Visual assessment of LV wall
Detection of Remote Ischemia

Fig. 2  Upper panel: A representative case of significant stenosis of the left ventricular descending artery and right coronary artery in group M. The % wall thickening is markedly decreased in the septum and slightly decreased in the inferior area. The % wall thickening is increased in the lateral area. Middle panel: A representative case of significant stenosis of the left anterior descending artery and left circumflex artery. The % wall thickening is markedly decreased in the anterior wall and septum and increased in the inferior wall. The % wall thickening is decreased in the lateral area. Lower panel: A representative case of three-vessel disease in group M. The % wall thickening is markedly decreased in the anterior and septum to inferior area and is slightly decreased in the lateral area.
motion did not detect asynergy in these 7 patients. In 2 of the 100 patients with 1-vessel disease in the LAD (2%, group S), the %WT in the non-infarcted area was decreased. These patients had cardiogenic shock at the time of admission, and their infarct-related lesions were in the proximal LAD.

The sensitivity, specificity, positive predictive value, and negative predictive value of %WT criteria for diagnosing remote asynergy were 83%, 98%, 94%, and 93%, respectively. Lower values for sensitivity and negative predictive accuracy, and similar values for specificity and positive predictive accuracy were obtained based on the visual assessment of LV wall motion to detect remote asynergy (40%, 97%, 84%, and 80%, respectively). Diagnosis of remote asynergy based on %WT had significantly higher selectivity (p<0.001).

3. %WT of the infarcted and non-infarcted areas during the acute phase (Table 5)

During the acute phase, there was no significant difference between groups S and M in the mean %WT in the infarcted (LAD-perfusion) area. The mean %WT in the non-infarcted area in group M was significantly lower than in group S (133±25% vs. 155±39%, p<0.0001); (Table 1). In group

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**Fig. 3** The % wall thickness in the infarct area, remote ischemic area, and remote non-ischemic area in group M during the acute and chronic phases. The % wall thickness during the acute phase is significantly higher in the remote ischemic area than in the infarcted area, but is significantly lower than in the remote non-ischemic area. During the chronic phase, the % wall thickness is higher in the remote ischemic area, but does not change in the remote non-ischemic area.
Detection of Remote Ischemia

4. Changes in the %WT for the infarcted and non-infarcted areas during the acute and chronic phases (Table 5)

The mean %WT for the infarcted area in group S increased significantly from the acute phase to 1 month after myocardial infarction (93±10% vs. 105±17%; p<0.001). The three subgroups of group M (LAD & RCA, LAD & LCX, 3VD) showed no significant difference with respect to %WT in the infarcted area between the acute and chronic phases.

In group M, the mean %WT in the remote ischemic area significantly increased during the chronic phase (116±12% vs. 145±11%; p<0.0001); (Fig. 3). In the remote ischemic areas in the LAD & RCA and LAD & LCX groups, the mean %WT increased significantly from the acute to the chronic phase (p<0.0001). The mean %WT in the remote ischemic areas in the 3VD group did not change significantly from the acute to the chronic phases. The %WT of the remote nonischemic area in group S and group M did not change significantly from the acute to the chronic phase (Fig. 3). In the chronic phase, the mean %WT in the remote ischemic area did not differ significantly from that of the remote nonischemic area. Although the %WT in the remote ischemic area decreased during the acute phase, it improved to the same extent as the remote nonischemic area during the chronic phase.

Discussion

Regional hypokinesia

Jaarsma et al.\(^1\) reported that remote asynergy during the acute phase of myocardial infarction was diagnosed by 2-dimensional echocardiography in none of 39 patients with 1-vessel disease (0%), 5 of 34 patients (15%) with 2-vessel disease, and 12 of 25 patients (48%) with 3-vessel disease. We also found that remote asynergy in the non-infarcted area was detected in only 16 of 40 patients (40%) with multivessel disease (35% in patients with 2-vessel disease and 67% in patients with 3-vessel disease) based on the wall motion index. Consequently, we conclude that conventional wall motion analysis is not satisfactory for detecting remote asynergy in non-infarcted areas supplied by significantly stenotic coronary arteries. Therefore, we used %WT, determined by the modified centerline method, to assess remote asynergy. The %WT enabled us to detect remote asynergy in 33 of 40 patients with multivessel disease (83%); (28 of 34 patients with 2-vessel disease (82%), and 5 of 6 patients (83%) with 3-vessel disease). The %WT assessment was more sensitive in detecting remote asynergy than the wall motion index (p<0.0001). In 7 patients with a significant stenosis in the distal LCX, remote asynergy could not be detected by either %WT assessment or the wall motion index. Based on our findings %WT assessment is
more useful than the conventional wall motion index in detecting remote asynergy during acute myocardial infarction.

In group S, remote asynergy was present in 2 of the 100 (2%) patients in whom no significant stenosis was present in the non-infarct-related coronary artery. Previous reports, including studies from our laboratory, indicate that a reduction in LV wall motion in the non-infarcted area occurs in patients with antero-septal myocardial infarction in whom a significant stenosis was detected only in the LAD. It is believed that asynergy in the non-infarcted area represents left ventricular remodeling caused by extensive anterior myocardial infarction. The 2 patients mentioned above also had a large area of infarction with coronary occlusion in the proximal portion of the LAD and suffered cardiogenic shock during the acute phase. Based on these findings, the remote asynergy might be due to LV remodeling.

Remote ischemia during the acute phase of myocardial infarction

Because the mean %WT was decreased only in the non-infarcted area fed by a stenotic coronary artery, a non-infarct-related coronary artery lesion could be detected by the modified centerline method of assessing wall thickening.

Changes in the %WT from the acute to chronic phase

The mean %WT for group S improved significantly from the acute to the chronic phase, while the %WT for group M did not improve. This may be because 92 of the 100 patients (92%) in group S underwent percutaneous transluminal coronary angioplasty (63%) or thrombolytic therapy (29%) within 24 hours after myocardial infarction. In group M, only 25 of the 40 patients (63%) underwent percutaneous transluminal coronary angioplasty (45%) or thrombolytic therapy (18%). The percentage undergoing revascularization therapy in group M was significantly lower than in group S (p < 0.0001). This may explain why the mean %WT for the infarcted area did not significantly improve in group M during the chronic phase.

The mean %WT in the remote ischemic area of patients with 2-vessel disease (LAD & RCA and LAD & RCA groups) improved markedly during the chronic phase, regardless of the treatment. Remote asynergy during the acute phase of MI may be due to increased oxygen demands induced by catecholamine stimulation or alterations in the preload and afterload when the perfusion capacity of the obstructed vessel in the non-infarcted area is exceeded. In the chronic phase, oxygen demand in the myocardium may improve because the preload and afterload and the compensatory increase in contraction in the non-infarcted area decrease with improvement in the remote ischemia. In contrast to the findings in 2-vessel disease, the mean %WT in the remote ischemic area in patients with 3-vessel disease did not improve during the chronic phase. This difference may be due to the fact that patients with 3-vessel disease did not undergo percutaneous transluminal coronary angioplasty.

Study limitations

Several potential methodologic limitations exist in this study. Our study largely depended on image quality. Exact tracing of the endocardial and epicardial borders is essential to determine wall thickness accurately. Because poor echocardiographic images prevented us from identifying the endocardial and epicardial borders, we tried
to obtain clear echocardiographic images. In addition, the exact duplication of short-axis images may be difficult. However, we made every effort to use the same planes at the midpapillary level for measurements.

Conclusions

Determination of the %WT from two-dimensional echocardiographic images using the modified centerline method is more useful than visual assessment of wall motion for the diagnosis of multivessel disease in the setting of acute anterior wall MI. We conclude that the %WT is useful when estimating the extent of coronary artery disease and the prognosis in the early stage of MI.

References


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