Natural History of Left Ventricular Size and Function After Acute Myocardial Infarction
Assessment and Prediction by Echocardiographic Endocardial Surface Mapping

Michael H. Picard, MD, Gerard T. Wilkins, MB, ChB,
Patricia A. Ray, BS, and Arthur E. Weyman, MD

To investigate the natural history of regional dyssynergy and left ventricular size after myocardial infarction, 57 patients with a first Q wave myocardial infarction (18 anterior, 35 inferior, and four apical by echocardiography) were studied by two-dimensional echocardiography and compared with 30 control patients. Measurements from the echocardiograms were used to construct maps of the left ventricular endocardial surface from which the endocardial surface area index (ESAi) and the percent of the endocardial surface area involved by abnormal wall motion (%AWM) were calculated. The maps from entry and 3-month echocardiograms were used to classify patients based on changes in ESAi and abnormal wall motion. Two subgroups of patients were identified at entry—those with a normal ESAi (group 1, n = 50) and those with an increased ESAi (group 2, n = 7). Group 1 patients was subdivided at 3 months by changes occurring in ESAi (1A, 5% increase [n = 19]; 1B, no change [n = 23]; 1C, 5% decrease [n = 8]). The increase in ESAi (64.9 ± 5.2 to 75.4 ± 7.5 cm²/m², p < 0.0001) in group 1A was associated with global ventricular dilatation (n = 11) and clinically silent infarct extension (n = 8). Groups 1B and 1C were composed predominantly of patients with inferior infarctions, and all exhibited either no change or a significant decrease in infarct size (infarct regression). Group 2 patients demonstrated a continued increase in ESAi by 3 months (88.2 ± 10.0 to 101.4 ± 15.5 cm²/m², p < 0.007). This group comprised only patients with anterior infarctions, and all exhibited infarct expansion at the left ventricular apex. The changes in left ventricular size and functional infarct size are heterogeneous after acute myocardial infarction and relate to the initial endocardial surface area, infarct location, and functional infarct size. (Circulation 1990;82:484–494)

Two-dimensional echocardiography is an ideal noninvasive method for visualizing the changes in left ventricular structure and function that occur during myocardial ischemia and after infarction. Clinical studies with this technique have demonstrated a clear relation between the location and extent of echocardiographically defined regional dysfunction and electrocardiographic infarct location, pathological size of infarction, clinical status of the patient, occurrence of complications, and survival.

Despite the number of studies relating echocardiographically defined abnormal wall motion (AWM) to other correlates of infarction, little is known about the natural history of these structural and functional abnormalities, and the data available are contradictory. For example, some investigators have reported infarct expansion associated with a high mortality in as many as 28% of patients, whereas others have reported extension of infarct, no significant change in infarct size, or improvement in extent of asynergy during the first weeks after myocardial infarction. Although the differences in these observations may relate to methods of analysis and the populations studied, it has not been established which patients demonstrate infarct expansion, which maintain a stable infarct and ventricular size, and which demonstrate infarct extension or spontaneous infarct regression. Identification of these subgroups and determination of the point in the evolution of infarction at which these changes occur have important

From the Cardiac Unit, Massachusetts General Hospital, Harvard Medical School, Boston, Mass.
Supported by National Institutes of Health grant HL-07535 and Ischemic Heart Disease Specialized Center of Research grant HL-26215, Bethesda, Md.
Address for correspondence: Michael H. Picard, MD, Cardiac Noninvasive Laboratory, Phillips 8, Massachusetts General Hospital, Fruit Street, Boston, MA 02114.
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therapeutic implications because the approach to patients at risk for infarct expansion would clearly be different from those in whom spontaneous regression is likely.

The purpose of this study was to use two-dimensional echocardiography to further delineate the natural history of left ventricular size, shape, and area of dysfunction during the 3 months after myocardial infarction.

Methods

Study Group

Patients admitted to the coronary care units of the Massachusetts General Hospital from December 1984 through September 1987 with a first transmural myocardial infarction were prospectively screened for inclusion into the study as part of the Massachusetts General Hospital Ischemic Heart Disease Specialized Center of Research Project. Transmural infarction was defined by the combination of a compatible clinical course including chest pain lasting at least 30 minutes, new ST segment elevation and appearance of new Q waves on serial electrocardiograms, and a significant rise in creatine kinase and cardiac isozyme fraction during the first 36 hours of hospitalization. Cross-sectional echocardiograms were performed on eligible patients on admission to the hospital and at 3 months. Patients excluded from the study included those with previous myocardial infarction, primary valvular heart disease, cardiomyopathy, the onset of symptoms more than 24 hours before screening, and those treated with interventions such as thrombolytic therapy, coronary angioplasty, intra-aortic balloon pump insertion, or coronary surgery. Patients with echocardiograms of inadequate quality for quantitative analysis were also excluded from the study. In addition, patients exhibiting evidence of recurrent infarction represented by a second episode of chest pain accompanied by a separate rise in cardiac enzymes or the appearance of new Q waves on the electrocardiogram at any time during the 3-month follow-up period were excluded from further study.

Of the 204 patients screened because of an initial suspicion of myocardial infarction, 123 did not meet eligibility requirements (49 did not have a myocardial infarction, 18 had presence of valve disease or previous myocardial infarction, 22 received interventions, one had a recurrent myocardial infarction, five had symptoms for more than 24 hours, five were eligible but died before follow-up, and 23 had images that were inadequate for quantitative analysis). Eighty-one patients met the eligibility criteria, and 57 completed the study (Table 1). Of the 24 eligible patients not completing the required follow-up, seven refused follow-up and 17 lived outside the geographical area and were unavailable for the 3-month follow-up study. Age, peak creatine kinase, body surface area, and baseline echocardiographic characteristics of these patients did not differ from those of the patients completing the study.

Cross-Sectional Echocardiography

Data acquisition. All patients underwent cross-sectional echocardiographic studies with either an Advanced Technologies Laboratory (ATL) Mk 300 mechanical sector scanner, an ATL Mk 600 mechanical sector scanner, or a Hewlett-Packard 77020A phase-array scanner, and images were recorded on ½-in. VHS videotape. All studies were performed by the same sonographer (P.A.R.). Echocardiographic images of the left ventricle were obtained from five standard imaging planes—parasternal short-axis views at the mitral valve level, the midportion of the papillary muscles, and the apex as well as the apical four-chamber and two-chamber views.

Data analysis. Suitable images from the five recorded planes were used to derive cardiac dimensional and wall motion measurements for an endocardial mapping technique previously reported and validated. By this method, the left ventricular surface is represented graphically by a planar map comprising four sections (Figure 1). Dimensional data necessary to construct the maps were obtained with off-line analysis systems (Microsonics Easy View II, Nova-Microsonics, and Sony Cardiologic Analysis System, Sony Medical Electronics), and measurements were made from end-diastolic frames with optimum image quality. The measurements obtained have been described in detail previously. A computer-assisted algorithm reconstructed the endocardial surface of the left ventricle using the left ventricular long-axis length, the mean length of endocardial segments from the apical four- and two-chamber views, and the left ventricular circumferences at mitral valve, midventricular, and apical levels. Once the maps were completed, the endocardial surface area of the left ventricular (ESA), a measure of left ventricular size, was calculated as the sum of the surface area of the four map quadrants.

Assessment of wall motion was performed by two experienced observers (G.T.W. and M.H.P.) blinded to patients’ identification or electrocardiography results. In each view, the region of dysynchrony was identified by repeated viewing to define the margins of normal and abnormal segments; dysynchrony was defined as any reduction in systolic endocardial excursion and thickening. The endocardial length of the abnormal segment was then measured along with its distance from predetermined internal landmarks. The area and location of this AWM was then transferred to the planar map of the total endocardial surface and represented the area of infarct-related dysfunction (Figure 1). The area of AWM was calculated as the sum of the surface area of AWM in the four quadrants. The percentage of the endocardial surface that moved abnormally (%AWM) was expressed as the ratio (AWM/ESA)×100.

Because body surface area has been identified as a primary determinant of normal left ventricular
dimensions,15,16 the ESA was corrected for variations in patient size by dividing by the body surface area. This corrected ESA, or ESA index (ESAi), was used in analyses for between-patient comparisons.

All patients in the study had a region of AWM demonstrable on the initial study. The sites of AWM were classified based on the predominant wall involved. When only the true apex of the left ventricle was involved (without a predominance of anterior, inferior, or lateral wall involvement), the location of infarction was classified as apical.17

**Control Group**

The endocardial surface maps from a group of 30 normal subjects matched for body size and without evidence of coronary artery disease or ventricular dysfunction were used as controls. This group consisted of 18 men and 12 women ranging in age from 23 to 65 years (mean age, 35±14 years). The mean body surface area for this group was 1.84±0.15 m². Echocardiographic studies were performed with the same standard imaging planes described above to record the required left ventricular dimensions. The mapping technique was then applied to generate a normal range for ESA. The range of normal for ESAi was from 53 to 78.9 cm²/m² (mean ESAi, 64.9 cm²/m²).

To define the normal temporal variation in ESA, endocardial surface maps were constructed in six control subjects without heart disease and 11 patients with stable coronary artery disease in whom serial echocardiography had been performed. The serial studies were separated by a mean of 129 days (range, 3-600 days). In this group, a mean change in ESA of 0.18±2.01% (range, −4.4−3.4%) was observed between the two studies.

**Infarct Groups**

The computer-generated planar maps of the entry and 3-month echocardiograms were used to classify patient groups based on the changes in ESA and extent of AWM. Because the temporal variability in ESA in subjects without acute ischemia was less than 5% and, as previously shown, the interobserver and intraobserver variability in the measurements of ESA

<table>
<thead>
<tr>
<th>Table 1. Patient Demographics</th>
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<th>Control (n=30)</th>
<th>Nonsurvivors (n=5)</th>
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<td>Gender (male/female)</td>
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<td>%MB</td>
<td>13±5%</td>
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<td>Onset of chest before entry (hr)</td>
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<td>Hematocrit (%)</td>
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<td>ESAi (cm²/m²)</td>
<td>Entry 67.4±9.9</td>
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<td>3 months</td>
<td>71.7±14.7</td>
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<td>%AWM</td>
<td>Entry 28.5±16.0</td>
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<td>3 months</td>
<td>29.4±18.0</td>
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AWM, abnormal wall motion; ESAi, endocardial surface area index.
*p=NS, study population versus control.
†p=NS, entry versus 3 months.
‡p<0.00008, entry versus 3 months.
and AWM are less than 5%, an increase or decrease of more than 5% was defined as a significant change.

Ventricular size. Patients with an ESAi within 2 SDs of the control group mean were defined as having a normal ESAi. An initial ESAi of more than 2 SDs above the control mean (77.9 cm²/m²) was defined as ventricular enlargement. No patient had an ESAi of less than 2 SDs below the control mean.

Infarct size. “No significant change” in functional infarct size was defined as a change in the absolute size of the wall motion abnormality of less than 5% (Figure 2a). “Ventricular dilatation” was defined as a symmetrical enlargement of both normal and abnormal endocardial segments. The criteria for this subgroup were a more than 5% enlargement of the total ESA and no significant change in the calculated %AWM area since the relation between normal and abnormal segment areas remained unchanged (Figure 2b). “Infarct expansion” was defined as a more than 5% enlargement of the total ESA accompanied by a more than 5% increase in the %AWM area (Figure 2c). “Infarct regression” was represented by a more than 5% decrease in the absolute area of AWM (Figure 2d). “Infarct extension” occurred with a more than 5% increase in the area of AWM and extension into a previously uninvolved echocardiographic wall segment (Figure 2e).

Electrocardiography

Twelve-lead electrocardiograms were performed serially during the first 3 hospital days. The electrocardiogram performed between 24 and 72 hours after admission with the largest Q wave distribution was used to assess the presence and location of pathological Q waves. New York Heart Association criteria were used to assign the anatomical sites of Q waves.¹⁸

Creatine Kinase

The serial total creatine kinase was determined by a standard enzymatic reaction with the upper limit of normal being 148 for men and 79 for women.

Statistics

Values are given as mean±1 SD. Between-group comparisons were performed with Student’s t test. Comparisons of frequency of events were performed with either Fisher’s test or χ² analysis depending on event frequency. The differences and interactions between multiple subgroups were examined by multivariate repeated-measures analysis of variance (ANOVA).

Results

Study Group

Table 1 displays patient demographics, electrocardiographic data, and echocardiographic data for the entire study population. In all patients, the initial echocardiogram was performed between 2 and 24 hours after the onset of chest pain (mean time, 17 hours).

The initial mean ESAi for the study population was 67.4 cm²/m², which did not differ significantly from the control value of 64.9 cm²/m² (p=NS). At 3 months after myocardial infarction, there was a significant increase in the mean ESAi to 71.7 cm²/m² compared with the entry ESAi (p=0.00008). The mean functional infarct size or mean %AWM was 28.5% on entry and 29.4% at 3 months (p=NS).

Although the mean ESAi of the total study population at entry did not differ from that of the controls, there were seven patients with a significantly enlarged ESA at the initial study. Separation of patients based on the initial ESAi is shown in Table 2. No patient had an initial ESAi that was less than the normal range.

The data for the five patients who were initially entered into the study and died before the second echocardiogram are also given in Table 1. Compared with the study population, the nonsurvivors demonstrated a larger mean entry ESAi (86.7±17.5 versus 67.4±9.9 cm²/m², p=0.029) as well as a larger mean %AWM (55.6±17.3% versus 28.5±16.0%, p=0.00034).

Comparison of Patients Based on Ventricular Size at Entry

Patients with normal ventricular size (group 1) and those with ventricular enlargement at entry (group 2) did not differ in age or peak creatine kinase (Table 2). The groups differed significantly in echocardiographic sites of Q waves and echocardiographic
FIGURE 2. Serial computer-generated maps (at entry and at 3 months) showing (a) no significant change, (b) ventricular dilatation, (c) infarct expansion, (d) infarct regression, and (e) infarct extension. ESA, endocardial surface area (cm²); ESAl, ESA index (cm²/m²); AWM area, area of abnormal wall motion (cm²); %AWM, percent of total ESA involved by AWM.
locations of wall motion abnormalities. Group 2
primarily comprised patients with anterior Q wave
infarctions by electrocardiography. All of the group 2
patients had echocardiographic abnormalities of wall
motion localized to the anterior region.

The mean initial ESAi was 64.5 cm²/m² for group 1
patients (p=NS versus controls) and 88.7 cm²/m² for
group 2 patients (p<0.00005 versus controls and
group 1) (Figure 3). The percent of the left ventricle
involved by AWM differed significantly between the
two groups. The initial mean %AWM for group 1 was
25.5%, whereas the mean %AWM for group 2 was
52.5% (p=0.00005).

Natural History of Patients With Normal Ventricular
Size of Entry (Group 1)

The 3-month trend in ventricular size was hetero-
genous in the patients who had a normal ESAi on
entry (group 1). As a whole, this group did not have
a statistically significant change in ESAi (64.5±5.5
versus 67.5±8.7 cm²/m²), and there was no change in
the mean size of AWM area (25.5±12.9% versus
25.5±14.7%). However, 19 of these patients (38%)
demonstrated a more than 5% increase in ESAi
(group 1A), 23 (46%) had no change in ESAi (group
1B), and 8 (16%) had a more than 5% decrease in
ESAi at 3 months (group 1C) (Figure 4). The data
for these subgroups are displayed in Table 3.

Group 1A comprised 10 patients with echocardi-
ographic anterior infarctions and nine patients with
echocardiographic inferior infarctions. The increase in
ESA was associated with both ventricular dilatation
(n=11) and infarct extension (n=8). Eight of the 11
patients with ventricular dilatation had echocardiog-
graphic anterior myocardial infarctions, whereas six of
the eight patients with extension had inferior infarctions.
The increase in %AWM observed for this subgroup
was accounted for by increases in the extension
subgroup. While the %AWM for the dilatation
group did not significantly change (34.4±12.4% at entry
versus 31.5±14.2% at 3 months), the %AWM for the
extension group increased from 24.6±9.3% to
41.5±5.7% (p=0.001).

Group 1B comprised one patient with an anterior
infarction, 19 with inferior infarctions, and three with
apical infarctions. During the 3 months, 16 patients
had no significant change in %AWM, whereas seven
patients exhibited infarct regression as defined by a
more than 5% decrease in %AWM.

Group 1C comprised seven patients with inferior
infarctions and one with an apical infarction. No
patients with an anterior infarction exhibited a
decrease in ESAi. The decrease in ESA was asso-
ciated with a significant decrease in AWM area in
five patients.

Natural History of Patients With Enlarged Ventricular
Size on Entry (Group 2)

As displayed in Table 2, all patients with an
abnormally large ESAi on entry (group 2) had ante-
rior sites of AWM by echocardiography. All of these
patients demonstrated infarct expansion during the 3
months of observation. The 15% increase in the total
ESAi observed in these patients was accounted for by
a 25% increase of the ESA of the echocardiograph-
determined area of dysfunction and a 3% increase in the ESA of the normal region.

Relation of Morphological and Functional Change to
Site of Infarction

Table 4 shows the echocardiographic data stratified
by location of wall motion abnormality. Multivariate
repeated-measures ANOVA demonstrated a signifi-
cant interaction of time and location of infarction when
ESA and area of AWM were examined. The entry
ESAi for the anterior group of 73.7 cm²/m² was
significantly larger than the entry ESAi of either the inferior
or apical groups (p<0.0001 and p=0.0077, respec-
tively). In addition, the functional infarct size for the
anterior group of 41.7% was significantly larger than
either the 23.8% of the inferior group or the 10.5% of
the apical infarct group (p<0.0001).

Ninety-four percent of the infarctions (17 of 18)
associated with echocardiographic anterior sites of
AWM demonstrated an increase in ESA by 3 months,
due to either infarct expansion (n=7), global ventricu-
dilatation (n=8), or infarct extension (n=2). These
types of change could be separated on the basis
of entry ESAi. An abnormal initial ESAi correctly
identified all patients with infarct expansion. A normal
entry ESAi associated with an anterior location of
dysfunction identified 73% of all patients (eight of 11)
with global ventricular dilatation.

Infarctions associated with inferior sites of AWM
were a more heterogeneous group. Fifty-one percent
of patients with inferior infarctions demonstrated no
significant change, 23% exhibited infarct regression,
17% developed infarct extension, and 9% exhibited
ventricular dilatation. There were no patients who
had wall motion abnormalities confined to inferior
regions who exhibited infarct expansion.

Apical infarctions were associated with the small-
est area of AWM as a consequence of the definition of
this subgroup. There were only four patients with
discrete apical sites of AWM—three of these
patients demonstrated infarct regression, and one
showed no change during the 3 months.

Discussion

The present study demonstrates that specific pat-
terns of change in left ventricular morphology and
extent of dysfunction can be detected by echocardi-
ography during the 3 months after acute myocardial
infarction. More important, it suggests that these
changes relate to initial left ventricular size and site
of infarction and thus can be identified at the time of
the initial postinfarct study (i.e., within 24 hours).

These relations have not previously been well
characterized because earlier echocardiographic nat-
ural history studies examined only specific subgroups
of patients (e.g., those with anterior infarction19),
followed patients for short periods of time,8,11 or used
TABLE 2. Entry Endocardial Surface Area Index

<table>
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<tr>
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<th>Group 1 (normal ESAi)</th>
<th>Group 2 (enlarged ESAi)</th>
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<td>Age (yr)</td>
<td>57±13</td>
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<td>ESAi (cm²/m²)</td>
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<td>Entry</td>
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<td>3 months</td>
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AWM, abnormal wall motion; ESAi, endocardial surface area index.
*p<0.007.

single-plane or segmental methods of analysis that could not accurately relate left ventricular size and infarct size at all levels of the ventricle.

In contrast, the echocardiographic methods used in this study enabled simultaneous quantification of infarct size and ventricular size and thus provided a more precise characterization of the interaction of dysfunction and morphology. For example, an increase in the percent of left ventricle involved by a wall motion abnormality could be due to extension into a new territory, expansion or stretching of infarcted myocardium, or decrease in the total ESA without any change in the absolute infarct area. On the other hand, a decrease in percent infarct size may be due to an actual decrease in the amount of ventricle

FIGURE 3. Mean endocardial surface area index (ESAi) (at entry and at 3 months) and echocardiographic location of abnormal wall motion for groups 1 and 2 (see text for definition of groups). Range of ESAi for control group is displayed in stippled region.

FIGURE 4. Mean endocardial surface area index (ESAi) (at entry and at 3 months) and echocardiographic location of abnormal wall motion of groups 1A, 1B, and 1C (see text for definition of groups).
involved by AWM or enlargement of the total left ventricular surface area. Thus, to fully understand the natural history of these variables, it is necessary to quantitate their absolute and relative changes with a three-dimensional model of the ventricle.

In the present study, we observed a highly significant increase in the ESA during the 3 months after acute myocardial infarction for the total population. This increase in the mean ESAi was accounted for by 3 distinct processes: infarct expansion, global ventricular dilatation, and infarct extension.

Infarct expansion was observed in 12% of this population with first Q wave infarction and 39% of patients with anterior wall motion abnormalities. All cases of infarct expansion were identified within the first 24 hours of clinical symptoms of myocardial infarction by enlargement of ESA outside of the normal range. Although the initial echocardiogram for the entire population was performed a mean of 17 hours after the onset of chest pain, the enlargement of the ESA was observed as early as 2 hours after the onset of chest pain. The initial increase in ESA was accounted for by enlargement of myocardial segments within the infarct zone only and occurred predominantly at the left ventricular apex. No patients with a normal ESAi developed subsequent echocardiographic evidence of infarct expansion. Location rather than size of infarct alone was the most important predictor of expansion. The anterior location with apical involvement was most often associated with infarct expansion.

These findings regarding infarct expansion are similar to those initially reported by Eaton et al using echocardiography and by Meizlish et al using radionuclide angiography in that they all involve anterior myocardial infarction; however, they differ in the timing and characterization of the maximal area of the expansion process. The difference in timing of infarct expansion relates to the difference in timing of the initial study. In previous studies, infarct expansion was observed 3–10 days after acute myocardial infarction in patients studied within 3 days of hospital admission. Our findings of infarct expansion within 24 hours of acute myocardial infarction and as early as 2 hours after symptom onset are analogous to those reported in experimental models where immediate expansion of the left ventricular apex is observed with occlusion of the left anterior descending coronary artery. These differences in timing of identification of infarct expansion, although small, are critical when considering acute interventions.

The difference in localization of the expansion process is due to differences in the methods used to

### Table 3. Group 1—Normal Endocardial Surface Area Index on Entry

<table>
<thead>
<tr>
<th></th>
<th>Group 1A (5% increase)</th>
<th>Group 1B (no change)</th>
<th>Group 1C (5% decrease)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>59±12</td>
<td>57±13</td>
<td>55±17</td>
<td></td>
</tr>
<tr>
<td>Creatine kinase (IU)</td>
<td>1,057±737</td>
<td>974±1,060</td>
<td>703±664</td>
<td></td>
</tr>
<tr>
<td>Electrocardiographic Q wave location (n)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>11</td>
<td>4</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Anterolateral</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Inferior</td>
<td>7</td>
<td>14</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Inferolateral</td>
<td>1</td>
<td>0</td>
<td>9</td>
<td>&lt;0.008</td>
</tr>
<tr>
<td>Posterior</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Lateral</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Echocardiographic AWM location (n)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>10</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Inferior</td>
<td>9</td>
<td>19</td>
<td>7</td>
<td>&lt;0.0006</td>
</tr>
<tr>
<td>Apical</td>
<td>0</td>
<td>3</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>ESAi (cm²/m²)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Entry</td>
<td>64.9±5.2</td>
<td>63.8±5.0</td>
<td>65.8±7.3</td>
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</tr>
<tr>
<td>3 months</td>
<td>75.4±7.5</td>
<td>63.7±5.0</td>
<td>60.2±5.1</td>
<td></td>
</tr>
<tr>
<td>%AWM</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Entry</td>
<td>30.3±12.0</td>
<td>23±13.0</td>
<td>19±10.3</td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>35.7±12.3</td>
<td>21.7±13.0</td>
<td>12.3±8.2</td>
<td></td>
</tr>
<tr>
<td>No change (n)</td>
<td>0</td>
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<td>3</td>
<td></td>
</tr>
<tr>
<td>Regression (n)</td>
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<td>7</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Extension (n)</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>Dilatation (n)</td>
<td>11</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Expansion (n)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

AWM, abnormal wall motion; ESAi, endocardial surface area index.

*p<0.0001; †p=NS; ‡p<0.05.
measure infarct size and left ventricle. Previous echocardiographic studies used measurements of the left ventricular short axis at only the midventricular level, whereas our technique of endocardial surface mapping involves measurements of the ventricular short axis at the base, midportion, and apex. With this technique, the degree of infarct expansion observed at the papillary muscle level is similar to that previously reported; however, the findings of infarct expansion at the left ventricular apex are new and represent the more severe change.

In contrast to the 50% mortality reported by Eaton et al., we observed no deaths in patients with infarct expansion. This difference is due to the fact that survival for at least 3 months was a requirement for inclusion into this study. An enlarged entry ESAi, however, was observed in two of the five eligible patients who did not survive to 3 months. If these patients are included in the groups based on their entry ESA, then an enlarged entry ESA (group 2) would have been associated with a 3-month mortality of 22% compared with a group 1 (normal ESA) mortality of 6%.

The predominance of expansion at the left ventricular apex may be explained by the fact that circumferential wall stress will be greatest in this region where the wall is least thick.23,24 The increases in wall stress in the infarcted segments at the left ventricular apex that occur as the apical myocardium thins further could account for the rearrangement of myocytes ("myocyte slippage") and sarcomere stretching associated with the expansion process.21,25,26

The other two groups of patients who had increases in ventricular size due to ventricular dilatation and infarct extension had normal ventricular sizes on entry (group 1A). Like infarct expansion, global dilatation of the left ventricle was observed primarily in patients with anterior myocardial infarction. Dilatation was rarely observed in patients with inferior infarction; however, when present, it was observed in patients with large regions of inferior wall motion abnormalities extending from the base to the apex of the left ventricle. In contrast to the infarct expansion group in whom the enlargement occurs only within infarcted segments, dilatation was due to symmetrical enlargement of the left ventricular circumference in both infarcted and noninfarcted segments. This global enlargement has been observed in both clinical and experimental studies of infarction27-31 and has been hypothesized to represent a compensatory remodeling of the left ventricle in response to alterations in systolic function.28

Clinically silent infarct extension was observed in 14% of this population with acute Q wave myocardial infarction. This is similar to previous reports in which the prevalence of silent extension of infarction ranged from 13% to 25%.32,33 The significant increase in ESA in association with infarct extension has not been previously described. Infarct extension was more commonly observed in patients with inferior infarctions. The exact mechanism of the extension process was not delineated by this data. As observed in the dilatation group, the increase in ESA may represent a remodeling of the left ventricular end-diastolic volume in an attempt to compensate for decreases in stroke volume due to significant loss of regional myocardial systolic function. This observation of an alteration in left ventricular morphology supports aggressive efforts to limit infarct extension in inferior myocardial infarctions in an attempt to limit left ventricular dilatation.

Although the mean ESAi for the study population demonstrated a significant increase in size during the 3 months, 54% of the study population and 74% of patients with inferior infarctions demonstrated either a stable ESAi or a decrease in ESAi. No change in ESA (group 1B) was observed predominantly with inferior infarctions, and most of these patients demonstrated no change in infarct size. A stable ESA would be expected to occur in patients with infarcts

<table>
<thead>
<tr>
<th>TABLE 4. Patient Characteristics Stratified by Infarct Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location</td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>ESAi (cm²/m²)</td>
</tr>
<tr>
<td>Entry</td>
</tr>
<tr>
<td>3 months</td>
</tr>
<tr>
<td>%AWM</td>
</tr>
<tr>
<td>Entry</td>
</tr>
<tr>
<td>3 months</td>
</tr>
<tr>
<td>No change (n)</td>
</tr>
<tr>
<td>Regression (n)</td>
</tr>
<tr>
<td>Extension (n)</td>
</tr>
<tr>
<td>Dilatation (n)</td>
</tr>
<tr>
<td>Expansion (n)</td>
</tr>
</tbody>
</table>

ESAi, endocardial surface area index; AWM, abnormal wall motion.

*p<0.0001 versus inferior; †p<0.0077 versus apical; ‡p=NS versus apical; §p<0.0001 versus apical; ¶p<0.017 versus apical.
that are small and do not significantly compromise overall left ventricular function.

This observation of stable left ventricular size and infarct size is complementary to the findings with serial radionuclide angiograms by Jeremy et al.29 and the echocardiographic study of Eaton et al.,3 who found no infarct expansion in all patients with infero-posterior infarctions.

A decrease in total ESAi (group 1C) was present in 14% of the study population. The ESAi of all but one patient remained within the normal range. A significant proportion of this group demonstrated a spontaneous regression in the size of the echocardiographic region of AWM. Infarct regression has previously been observed echocardiographically in studies using segmental scoring systems8,11 and angiographically in studies recording serial improvement of left ventricular function.34 These findings might be explained by overestimation of infarct size on the entry echocardiogram due to the inability to differentiate ischemic from infarcted myocardium at the border zone or the identification of normal functioning myocardium as abnormal due to mechanical tethering of normally perfused tissue by bordering akinetic myocardium.35-37 However, the decrease in ESA associated with the decrease in the extent of AWM suggests that the change in the area of dysfunction is due to a dynamic process such as scar contraction38 or reperfusion of ischemic zones by recruitment of collateral vessels or spontaneous thrombolysis of the infarct-related artery.34

Because the hospital at which this study was performed serves as both a primary-care base for a local population and a tertiary-care center for a large geographic region, the population initially screened for this study might not reflect a representative sample of patients with acute myocardial infarction. However, the eligibility requirements disqualified many of the complicated patients referred for tertiary care. A follow-up period of 3 months was also required; thus, patients undergoing coronary revascularization procedures such as percutaneous transluminal coronary angioplasty or coronary artery bypass graft surgery were excluded from analysis.

Measurement of the ESA is dependent on both accurate echocardiographic views of the left ventricle from the parasternal and apical imaging planes and accurate measurement of the endocardium of each of these images. Although 22% of potentially eligible patients were excluded due to echocardiograms of inadequate quality to completely visualize all endocardial borders, a majority of these echocardiograms provided clinically useful information. In these cases, a qualitative assessment of location and extent of AWM was possible.

The method used to identify AWM integrated 1) quantitative measures of ventricular dimensions, 2) qualitative assessment of the extent of regional myocardial dysfunction, and 3) quantitation of the spatial extent of dyssynergy. The accuracy of echocardiographic measurement of the ESA has been demonstrated in computer models, casts of the left ven-

tricular endocardial surface, canine ventricles, and human autopsy specimens.9,13 Visual determination of the extent of ventricular dyssynergy has been validated for individual echocardiographic imaging planes and for the three-dimensional area of dysfunction.9,14 Although quantitative measures of dyssynergy offer the potential advantage of being more objective, the accuracy of such measurements depends on the center of reference, method of measurement, criteria for separating normal from abnormal, and echocardiographic planes examined.39 While appropriate for experimental studies, none has been demonstrated to provide increased accuracy in humans. Given that such methods require extensive digitization and computer processing with no documented increase in accuracy, we have chosen an approach that allows us to address the questions posed by this study with methods that are generally applicable.

Factors that might affect ventricular size, such as ventricular filling, blood pressure, and systemic vascular resistance, were not controlled in this study. However, there was no difference in the incidence of hypertension or in the proportion of patients prescribed nitrates, β-blockers, and calcium channel antagonists in the expansion, dilatation, extension, regression, and no change subgroups.

A potential application of this technique includes the identification on entry to the hospital of patients who might benefit from immediate therapy to limit infarct expansion. This identification can be based on ESA and echocardiographic location of AWM (i.e., abnormal ESA and anterior AWM involving the apex). In addition, the measurement of ESA by echocardiography is a reproducible, noninvasive method that can be used to display the potential changes in left ventricular morphology occurring due to interventions aimed at recanalizing infarct-related coronary arteries.40

Echocardiographic endocardial surface mapping enables the assessment of changes in left ventricular morphology and infarct size after acute myocardial infarction. Normal ventricular size that increased during 3 months was observed in patients with anterior infarctions exhibiting global dilatation and inferior infarctions exhibiting infarct extension. Normal ventricular size that remained constant or decreased in size was predominantly observed in patients with inferior infarctions and was associated with no change in infarct size as well as with infarct regression. An enlarged ESA on entry was observed only in patients with anterior infarctions with apical involvement and identified all patients with infarct expansion. The early prospective identification of these subgroups may enable optimal management and prevention of infarct expansion and global ventricular dilatation, while identifying those patients at low risk for change in ventricular morphology and increases in infarct size.

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M H Picard, G T Wilkins, P A Ray and A E Weyman

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