Left ventricular remodeling after myocardial infarction: a corollary to infarct expansion

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ABSTRACT  Dilatation of infarcted segments (infarct expansion) may occur during recovery from myocardial infarction, but the fate of noninfarcted segments is uncertain. Accordingly, left ventricular geometric changes were assessed by left ventricular angiography and M mode echocardiography on admission and 2 weeks later in 30 patients with their first acute transmural myocardial infarction. All patients demonstrated chest pain, ST segment elevation with subsequent development of Q waves (15 anterior, 15 inferior), and elevation of cardiac enzymes. Sequential left ventricular angiographic and hemodynamic findings were available in these patients by virtue of their participation in a study of thrombolysis in acute myocardial infarction. By that study design, all patients treated successfully with thrombolytic therapy and demonstrating improvement of flow in an occluded coronary artery underwent repeat cardiac catheterization. At 2 weeks there was a significant decrease in left ventricular and pulmonary capillary wedge pressures (p < .01), whereas both left ventricular end-diastolic (LVEDV) and end-systolic (LVESV) volume indexes increased (p < .01). The increase in LVEDV correlated directly with the percentage of the ventriculographic silhouette that was akinetic or dyskinetic at the initial catheterization (r = .71, p < .001). To assess regional changes in both infarcted and noninfarcted segments, serial endocardial perimeter lengths of both the akinetic-dyskinetic segments (infarction zone) and of the remainder of the cardiac silhouette (noninfarction zone) were measured in all patients who demonstrated at least a 20% increase in their LVEDV at 2 weeks after myocardial infarction. Notably, there was a mean increase of 13% in the endocardial perimeter length of infarcted segments and a 19% increase in the endocardial perimeter length of noninfarcted segments. Serial M mode echocardiographic studies showed no significant change in the wall thickness of noninfarcted myocardial segments. Hemodynamic changes that occurred in this subgroup of patients included significant decreases in left ventricular end-diastolic and pulmonary capillary wedge pressures (p < .05) and significant increases in angiographic cardiac index (p < .01) and LVESV index (p < .01). We conclude that in patients who manifest cardiac dilatation in the early convalescent period after myocardial infarction, there is remodeling of the entire left ventricle including infarct expansion of akinetic-dyskinetic segments and volume-overload hypertrophy of noninfarcted segments. The magnitude of the remodeling process is directly proportional to infarct size as assessed by the extent of wall motion abnormality present during the acute phase of infarction. Moreover, the remodeling changes that occur are associated with hemodynamic improvement, including lower left ventricular filling pressures and increased cardiac output, but these hemodynamic changes appear to occur at the expense of a significant increase in left ventricular chamber volumes.

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Previous studies of ventricular structure after myocardial infarction have focused primarily on the fate of infarcted segments. In particular, Hutchins and Bulkley and Eaton et al. have described regional cardiac dilatation in the infarction zone and have defined the concept of "infarct expansion." According to their description, this process appears to be a form of intramural myocardial rupture in which the disruption of normal myocardial cells leads to thinning and dilatation of the necrotic zone. Such changes occur almost
exclusively in transmural infarcts and are most commonly seen with anterior and anteroseptal infarctions. The process has been observed to occur clinically as early as 3 days after infarction and may progress over days to weeks independent of additional myocardial necrosis or infarct extension. Most important, it is associated with increased mortality and may be important in the development of late aneurysm formation.

Although infarct expansion has been studied extensively, only limited information is available on the fate of noninfarcted segments during the infarction recovery period. A recent study by Weisman et al. reported that, in the rat, there may be global remodeling of the left ventricle immediately after infarction involving structural changes in both infarcted and noninfarcted segments. Similarly, a study by Anversa et al. found that myocardial infarction in rats results in myocyte hypertrophy of remaining viable myocardium. Studies on the fate of noninfarcted myocardium in man, however, have been limited; moreover, the determinants and hemodynamic effects of this remodeling process have not been defined. Wynne et al. found that regional ejection fraction in noninfarcted segments was abnormal in 69% of patients with anterior infarctions and in 30% with inferior infarctions. Although these limited studies suggest that regional function in noninfarcted segments may be abnormal, the etiology of this dysfunction and the possible role that left ventricular remodeling plays in producing these changes remains unclear.

This study was undertaken to assess the fate of noninfarcted myocardial segments after transmural infarction. Since patients admitted with acute transmural infarction who elected to undergo attempted thrombolysis were expected to undergo serial cardiac catheterizations with contrast ventriculography on admission and, if thrombolysis was successful, 2 weeks later, these patients were considered for enrollment and formed the study population.

Methods

Study group. Left ventricular hemodynamic and structural changes were assessed in a total of 30 patients. All patients presenting with their first acute transmural myocardial infarction were considered for enrollment in this study. Entry criteria included chest pain of at least 30 min duration, new ST segment elevation on the electrocardiogram with the subsequent development of Q waves in the involved leads, and elevation of cardiac enzymes (creatine kinase MB fraction, SGOT, LDH) during the first 24 to 72 hr of their hospitalization. Patients who manifested persistent ischemia or recurrent infarction during their in-hospital convalescent phase as evidenced by clinical, electrocardiographic, or cardiac enzyme criteria were excluded from the study. Patients with previous myocardial infarction, significant valvular disease, or cardiomyopathy were not considered. Informed consent was obtained from each patient after an appropriate explanation of risks and potential complications of the proposed study.

Cardiac catheterization

Protocol. Cardiac catheterization was performed at the time of admission and 2 weeks later, before discharge. For both catheterizations, right femoral venous and right femoral arterial sheaths were inserted after administration of local anesthesia. A No. 7F thermodilution flow-directed catheter was passed to the pulmonary artery–pulmonary capillary wedge position. Left ventriculography followed by coronary angiography were performed in the routine manner. Baseline hemodynamic measurements included pulmonary capillary wedge and left ventricular pressures. Recordings were inscribed with a Honeywell Electronics for Medicine (VR-16) recorder.

In each of the 30 patients, an occluded or subtotally occluded coronary artery whose distribution corresponded to the area of ST segment elevation by electrocardiographic criteria was noted. Each patient was treated subsequently with either 250,000 U of intracoronary streptokinase, 1.5 million U of intravenous streptokinase, or 80 mg of intravenous tissue-type plasminogen activator. Only patients in whom successful thrombolysis was achieved with dissolution of clot and improvement of flow in the involved coronary artery (and in whom this improvement persisted at 2 weeks) were included, since complete serial studies were available only in this group. After the initial catheterization, all patients were treated with intravenous heparin and intravenous lidocaine. Oral or topical nitrates, calcium-channel blockers, and or β-blockers were continued or added if clinically indicated. Lidocaine was discontinued 48 to 72 hr after admission and replaced with an oral antiarrhythmic only if significant ventricular ectopy was subsequently noted. All other medications were continued until the time of the second catheterization except for heparin, which was stopped 4 hr before that catheterization.

Data analysis. Ventricular volumes were measured by the area-length method with a regression equation developed for single-plane angiography based on left ventricular casts for measurement of true volume with calculation of end-diastolic and end-systolic volumes, angiographic cardiac index, and global ejection fraction.

Endocardial perimeters of akinetic-dyskinetic segments and of the remainder of the contrast ventriculogram silhouette were measured with a Tektronix 4956 digitizing computer. The percentage of the ventriculographic perimeter that was akinetic or dyskinetic was determined on admission and at 2 weeks. In addition, serial changes in the perimeters of akinetic-dyskinetic segments and of the remainder of the cardiac silhouette that occurred in the 2 week interval between the first and second catheterization were measured with appropriate corrections for differences in magnification.

M mode echocardiography. Echocardiography was performed on admission and at 2 weeks after infarction in 19 of the 30 patients by an ATL Mark VI machine. This machine is equipped with an M mode cursor that can be oriented perpendicular to the long axis of the left ventricle for optimal M mode recording of the septum and posterior wall. Changes in gain were used to define the endocardial and epicardial borders. Wall thicknesses were measured at the onset of the QRS complex on the electrocardiogram with the leading edge–to–leading edge technique.

Statistics. Means and standard deviations were calculated for all variables. Paired dimensional data were analyzed with either the paired t test or the Wilcoxon signed-rank test where appropriate, for parametric and nonparametric distributions. A p value of less than .05 was considered significant.
Results

Study group. A total of 30 patients with their initial acute myocardial infarction were included in this study. There were 28 men and two women, with a mean age of 55 years (range 33 to 69). Fifteen patients presented with electrocardiographic evidence of an anterior myocardial infarction, and each had a totally or subtotally occluded left anterior descending coronary artery. The remaining 15 patients demonstrated electrocardiographic changes in inferior leads with total occlusion of the right coronary artery. Fifteen patients had coronary disease limited to one coronary artery in the area of infarction; the remaining 15 had additional stenoses, with eight patients having two-vessel disease and seven patients having three-vessel disease. All patients were brought to the catheterization laboratory within 10 hr of the onset of their chest pain. Successful thrombolysis with opening of a totally occluded artery or improvement in coronary flow was achieved in all patients within 90 min with administration of either intracoronary or intravenous streptokinase or intravenous tissue-type plasminogen activator.

After the initial catheterization, patients were admitted to the coronary care unit for routine monitoring. All patients had an uncomplicated convalescent period without evidence of recurrent infarction, development of ventricular septal defect, or papillary muscle rupture. Repeat catheterization was performed in all patients at a mean of 14.1 days (range 9 to 18 days) after admission. All patients manifested persistent patency of their diseased coronary artery with a residual high-grade stenosis.

At the time of the first catheterization, medications included the following: nitrates, 30 patients; calcium-channel blockers, 12 patients; β-blockers, six patients; diuretics, two patients; digoxin, five patients; antiarrhythmics, 30 patients. At the time of the second catheterization, medications included the following: nitrates, 30 patients; calcium-channel blockers, 15 patients; β-blockers, six patients; diuretics, four patients; digoxin, five patients; antiarrhythmics, six patients. There were no significant differences in medications between the time of the first and second catheterization, except for the use of antiarrhythmics (all patients at the time of their first catheterization were treated with intravenous lidocaine; only six patients subsequently required long-term antiarrhythmic therapy).

Hemodynamic and ventricular volume changes. Hemodynamic changes that occurred over the 2 week study period in the 30 patients included decreases in heart rate (80 ± 17 to 72 ± 16 beats/min; p < .03), left ventricular systolic pressure (122 ± 19 to 113 ± 11 mm Hg; p < .01), left ventricular end-diastolic pressure (24 ± 8 to 18 ± 6 mm Hg; p < .01), and pulmonary capillary wedge pressure (18 ± 6 to 13 ± 6 mm Hg; p < .01). There was no significant change in either angiographic cardiac index (3.3 ± 1.2 to 3.5 ± 1.2 liters/min/m²; p = NS) or left ventricular ejection fraction (55 ± 11% to 54 ± 11%; p = NS). In addition, there were increases in left ventricular end-diastolic volume index (76 ± 22 to 93 ± 30 ml/m²; p < .01), end-systolic volume index (34 ± 10 to 47 ± 30 ml/m²; p < .02), and stroke volume index (42 ± 16 to 50 ± 13 ml/m²; p < .02). Table 1 summarizes hemodynamic and angiographic data at the time of admission and at 2 weeks for all patients.

Regional wall motion abnormalities. In 26 of the 30 patients, a discrete segment of akinesia and/or dyskinesia could be identified on the contrast left ventriculogram at the time of the first catheterization. This region of akinesia-dyskinesia was noted to persist or enlarge at the time of the second catheterization. The percentage of the left ventricular perimeter that was akinetic or dyskinetic was 20 ± 14% on admission and 25 ± 14% 2 weeks later (p = NS).

Determinants of the increase in end-diastolic volume index. The increase in the end-diastolic volume index that occurred over the 2 week period correlated significantly with the percentage of the initial contrast ventriculogram that was akinetic or dyskinetic (r = .71, p < .001) at the time of the first catheterization. Figure 1 summarizes the relationship between volume increases and the percentage of akinesia-dyskinesia. In addition, there was a modest inverse correlation between left ventricular ejection fraction on the first catheterization and volume increases from the initial study to the study at 2 weeks (r = -.51, p < .001).

Hemodynamic changes in patients with increased left ventricular volumes. Since left ventricular volume changes were related to the extent of initial infarction, a subgroup of 17 of the 30 patients who demonstrated at least a 20% increase in end-diastolic volume index was identified for further evaluation. This group consisted of 11 patients with anterior infarctions and six patients with inferior infarctions. Hemodynamic and volume changes that occurred in these patients included decreases in left ventricular end-diastolic pressure (23 ± 9 to 18 ± 6 mm Hg; p < .05) and pulmonary capillary wedge pressure (17 ± 6 to 12 ± 5 mm Hg; p < .03), with concomitant increases in angiographic cardiac index (2.9 ± 1.0 to 3.7 ± 1.1 liters/min/m²; p < .01), stroke volume index (36 ± 13 to 49 ± 12 ml/m²; p < .01), and end-systolic volume index (30 ±
TABLE 1
Serial hemodynamic data for patients with anterior myocardial infarction (Nos. 1 to 15) and inferior myocardial infarction (Nos. 16 to 30)

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CI = angiographic cardiac index (l/min/m²); EDVI = left ventricular end-diastolic volume index (ml/m²); EF = left ventricular ejection fraction (%); ESVI = left ventricular end-systolic volume index (ml/m²); HR = heart rate (bpm); LVEDP = left ventricular end-diastolic pressure (mm Hg); LVSP = left ventricular systolic pressure (mm Hg); PCW = pulmonary capillary wedge pressure (mm Hg); SVI = left ventricular stroke volume index (ml/m²).

*p < .03; **p < .02; ***p < .01; ^data not obtained because of technical reasons.

10 to 56 ± 37 ml/m²; p < .01). There were no significant changes in left ventricular systolic pressure (118 ± 17 to 112 ± 11 mm Hg; p = NS), heart rate (83 ± 16 to 76 ± 18 beats/min; p = NS), or ejection fraction (53 ± 12% to 50 ± 14%; p = NS). Hemodynamic and angiographic data for these patients are summarized in table 2.

Serial changes in endocardial perimeters in patients with increased volumes. To assess structural changes occurring in the 17 patients who demonstrated substantial (≥20%) increases in left ventricular end-diastolic volume, serial endocardial perimeter measurements were made of the akinetic-dyskinetic segments (representing infarcted zones) and of the remainder of the cardiac silhouette (representing noninfarcted segments) on the left ventricular angiograms obtained on admission and at 2 weeks. Table 3 summarizes changes in measurements of endocardial perimeter length of both akinetic-dyskinetic segments and of the remainder of the cardiac silhouette. Notably, there was a mean 13 ± 12% increase in endocardial perimeter length of infarcted segments and a 19 ± 13% increase in the endocardial perimeter length of noninfarcted segments. Figure 2 shows examples of end-diastolic and end-systolic cardiac silhouettes in four representative patients at the time of initial presentation with acute myocardial infarction and at follow-up study 2 weeks later.

M mode echocardiography. Table 4 summarizes M mode measurements of septal and posterior wall thickness in 19 of 30 patients who were studied, including 12 who manifested at least a 20% increase in left ventricular end-diastolic volume. Notably, patients with anterior myocardial infarction showed no significant change in posterior wall thickness and patients with inferior infarction showed no change in septal wall thickness.

Discussion
Our results demonstrate that global remodeling of the left ventricle occurs during the early convalescent period in certain patients with myocardial infarction. In particular, the findings indicate that those patients who exhibited cardiac dilatation with increased left ventricular end-diastolic and end-systolic volumes
during their in-hospital stay manifested changes in both infarcted and viable segments of their ventricles. Lengthening of endocardial perimeters of infarcted segments presumably represents infarct expansion.\(^3\) Equally important, lengthening of the endocardial perimeter of that part of the ventricle without regional wall motion abnormalities and with no evidence of wall thinning in these segments suggests that volume-overload hypertrophy with a net increase in the myocardial mass of these segments has occurred. These remodeling changes occurred as hemodynamics improved, including lower left ventricular filling pressures and increased cardiac output, perhaps at the expense of increased chamber volumes. Moreover, the magnitude of these remodeling changes were roughly related to infarct size as measured by the percentage of the ventricular silhouette exhibiting regional wall motion abnormality on admission and inversely related to initial left ventricular pump function as measured by ejection fraction.

Grossman and others\(^{15,16}\) have termed an increase in myocardial mass without relative wall thickening as “volume overload” hypertrophy when it occurs in the entire left ventricle. In volume-overload hypertrophy, as discussed below, mass increases primarily by series addition of new sarcomeres and fiber elongation, resulting in chamber enlargement. In pressure-overload hypertrophy, in contrast, a marked increase in wall thickness occurs as a consequence of the parallel addition of new myofibrils.\(^{16}\) Although usually associated

### TABLE 1

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<td>13 10 20 19 16 16 26 24 20 24 15 28 21 22 22 23 ± 7</td>
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</tr>
<tr>
<td>13 12 17 16 d 15 d d 14 23 5 20 21 15 14 18 ± 5</td>
<td></td>
</tr>
</tbody>
</table>

### FIGURE 1

Correlation between the percentage of the left ventricular silhouette that was akinetic-dyskinetic at the time of the first catheterization with the subsequent increase in left ventricular end-diastolic volume index (EDVI) at the second catheterization (r = .71, p < .001). The ordinate, “Change in EDVI,” was determined by dividing the EDVI at the 2 week catheterization by the EDVI obtained at the first catheterization.

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with some degree of wall thickening, chronic volume-overload hypertrophy produces far less thickening than does pressure-overload hypertrophy. Thus we believe that the absence of thinning in the noninfarcted segments, associated with concurrent elongation, is compatible with volume-overload hypertrophy of these segments.

**TABLE 3**
Left ventricular endocardial perimeter analysis in patients with greater than 20% increase in left ventricular end-diastolic volume index

<table>
<thead>
<tr>
<th>Catheterization</th>
<th>% Change in index</th>
<th>% Change noninfarcted index</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Akinesis-dyskinesis</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**TABLE 4**
Echocardiographic wall thickness measurements (mm)

<table>
<thead>
<tr>
<th>Catheterization 1</th>
<th>Catheterization 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Septum</td>
<td>Posterior wall</td>
</tr>
<tr>
<td>Septum</td>
<td>Posterior wall</td>
</tr>
</tbody>
</table>

Stimulus for volume-overload hypertrophy in the infarcted ventricle. Left ventricular hypertrophy is one of the principal adaptive mechanisms by which the heart compensates for an increased load. The pattern of hypertrophy that develops is dependent on the type of overload and the influence of this overload on systolic and diastolic wall stresses. According to this hypothesis, when the primary stimulus for hypertrophy is pressure overload, the resultant acute increase in systolic wall stress leads to parallel replication of sarcomeres, wall thickening, and concentric hypertrophy. The wall thickening that occurs tends to return systolic wall stress toward normal. In contrast, when the primary stimulus to hypertrophy is a volume overload, increased diastolic pressure causes an increase in diastolic wall stress and leads to sarcomere replication in series, fiber elongation, and chamber enlargement. Chamber enlargement accommodates the volume overload and returns diastolic pressure toward normal. However, the chamber enlargement also results in an increase in systolic wall stress, which subsequently leads to wall thickening. The combination of slight wall thickening and chamber enlargement return systolic and diastolic wall stress toward normal.

Given that hypertrophy will develop in response to increased wall stress, what evidence is there that wall...
Histories of myocardial infarction have been the subject of considerable interest. Two recent studies, however, are notable. Pfeffer et al. examined alterations in mass, volume, and end-diastolic wall stress in rats at 2, 21, and 100 days after coronary ligation and subsequent myocardial infarction and compared changes in these variables with findings in rats without coronary ligation.

PASSIVE PRESSURE-VOLUME CURVES WERE DETERMINED AND END-DIASTOLIC STRESS WAS CALCULATED FROM DATA ON LEFT VENTRICULAR MASS, END-DIASTOLIC PRESSURE, AND END-DIASTOLIC VOLUME. NO CHANGE IN MASS, VOLUME, OR WALL STRESS WAS NOTED IN ANY OF THE CONTROL RATS. IN RATS WITH MYOCARDIAL INFARCTION, HOWEVER, THERE WAS A PROGRESSIVE INCREASE IN BOTH VOLUME AND MASS, AND END-DIASTOLIC WALL STRESS WAS ELEVATED AT ALL TIMES. OF NOTE, THE RATIO OF MASS TO VOLUME DECREASED PROGRESSIVELY, INDICATING THAT LEFT VENTRICULAR VOLUME WAS INCREASING OUT OF PROPORTION TO MASS AND SUGGESTING THAT A VOLUME-OVERLOAD HYPERTROPHY WAS OCCURRING, PERHAPS IN RESPONSE TO THE INCREASED END-DIASTOLIC WALL STRESS.

Pouleur et al. also attempted to evaluate wall stresses in patients with previous myocardial infarction. Using a method for calculating regional wall stresses, they found that both systolic and diastolic regional wall stresses were abnormal in the infarcted and ischemic areas and that stresses in the noninfarcted segments were normal. Because serial studies were not available to them in each patient, they could not comment on changes in ventricular wall stress after infarction.

Thus, although available data are limited, there is evidence that wall stresses in healing left ventricles may be abnormal.

**A Model for Left Ventricular Remodeling After Infarction.** Based on the observations that wall stresses may be abnormal in the infarcted ventricle and the fact that increased diastolic wall stress may initiate a volume-overload type of hypertrophy, a model of left ventricular remodeling after myocardial infarction may be proposed. This model is summarized in figure 3. In this model, the immediate hemodynamic consequences of an acute myocardial infarction on ventricular function include both systolic and diastolic dysfunction. Systolic impairment secondary to loss of contractile function of the infarcted myocardium results in a decreased systolic ejection, increased end-systolic volume, an increase in cardiac size, and a secondary increase in diastolic filling pressure caused by the increase in ventricular volume. Diastolic function is characterized immediately by an increase in diastolic distensibility, which minimizes the rise in filling pressure. However, as necrotic tissue is replaced by fibrosis, a decrease in distensibility occurs. In addition, there may be upward shift in the diastolic pressure-volume curve secondary to ischemia in the border zone so that filling pressure may tend to be higher for any given volume. Thus diastolic volume increases and diastolic pressure also tends to increase, especially in patients with large infarctions.
In the presence of both systolic and diastolic dysfunction, there may be peripheral mechanisms mediated via the sympathetic nervous system and circulating catecholamines to help maintain a normal arterial blood pressure and cardiac output. These mechanisms may subsequently increase ventricular preload by augmenting venous return and increase ventricular afterload by causing arteriolar vasoconstriction. The resulting increases in ventricular radius and diastolic pressure will, in combination, lead to an increase in end-diastolic wall stress in all parts of the ventricle. Simultaneous with an increase in both end-diastolic wall stress and regional end-systolic wall stress in infarcted segments, there is weakening of the normal myocardial structure needed to resist wall stress. As a result, processes of dilatation and thinning progress in the infarct region. At some point, because of continued healing of the infarcted segments with increasing collagenization and the production of a firm scar, the ability of the infarction zone to resist wall stresses is increased and infarct expansion halts. However, one can imagine that before production of a mature scar, if wall stresses are elevated to a sufficient degree and if infarcted segment tensile strength has been sufficiently reduced, myocardial rupture may occur. Finally, in noninfarcted segments, elevation of end-diastolic wall stress may provide the stimulus for volume-overload hypertrophy, in which the combination of fiber elongation and wall thickening result in a return of systolic and diastolic wall stress toward normal.

**Possible determinants of left ventricular remodeling.**

One may predict from the preceding model that those factors leading to the greatest elevation of wall stresses would be expected to cause the greatest amount of left ventricular remodeling. Infarct size may be most important given that the larger infarcts would lead to greater systolic and diastolic impairment with larger increases in ventricular radius and filling pressure. In this regard, our results have shown a rough correlation between the magnitude of remodeling and the size of the infarction (figure 1) as assessed by the percentage of the cardiac silhouette exhibiting akinesis-dyskinesis at initial presentation.

Infarct location is a second factor which may be important in the production of left ventricular remodeling after infarction. Previous studies that have evaluated infarct expansion have noted that these changes occur predominantly in patients with anterior infarctions. In part this may be related to infarct size, since anterior infarctions are generally associated with more myocardial necrosis than occurs with inferior infarction. In addition, in the normal left ventricle there is a greater degree of shortening of the anterior than of the posterior wall, and thus similar degrees of depression of function might be expected to result in more severe derangements after anterior infarctions. It is notable that in this study a higher percentage of patients with anterior than with inferior infarctions demonstrated at least a 20% increase in end-diastolic volume index and that the magnitude of this remodeling, as measured by absolute changes in chamber volumes, was larger in patients with anterior infarctions.

A third factor or set of factors that may be important in the remodeling process after infarction are those
variables that affect ventricular loading conditions and thus affect ventricular wall stress. Hypertension, for example, increases afterload and therefore systolic wall stress and hastens the process of infarct expansion. In contrast, reduction of ventricular preload and afterload by vasodilators should lessen the tendency for ventricular remodeling. In this regard, Pfeffer et al. have shown recently that captopril may reduce the extent of topographic changes in a rat preparation of infarction. In Pfeffer’s studies, this blunting of remodeling with captopril was associated with improved survival at 1 year after infarction.

A final factor that may be important in the degree of remodeling is the success of thrombolysis. If in fact thrombolysis results in successful salvage of viable myocardium, then infarct size might be reduced and the degree of remodeling might be diminished. Since this study considered only patients with successful thrombolysis and since a comparable control group was not available for concurrent analysis, we cannot comment at present about the potential effects of thrombolysis on the remodeling process.

Hemodynamic consequences of left ventricular remodeling. The hemodynamic changes that occur in the 2 week period after myocardial infarction appear to be in part beneficial, with improvement in cardiac output despite lower left ventricular filling pressure. This may explain the common clinical observation that early in the course of an infarction, there may be mild clinical congestive heart failure followed by spontaneous improvement. It is notable, however, that these hemodynamic improvements occurred only while chamber volumes increased significantly. Although a portion of the increase in diastolic chamber volume may have been related to the concomitant small decreases in heart rate observed, similar decreases in heart rate occurred both in patients with a greater than 20% increase in end-diastolic volume in patients with a lesser increase in end-diastolic volume. Thus the degree of volume change was not proportional to fall in heart rate.

Although hemodynamic improvement may accompany ventricular remodeling early after infarction, the long-term hemodynamic consequences of remodeling are not known. Data from at least one study have suggested increased morbidity and mortality in postinfarction patients with increased ventricular size. In addition, a recent study from our institution has suggested that ventricular dilatation after myocardial infarction may be progressive, continuing for months after the original infarction. Perhaps a more important clinical consequence of infarct remodeling is that it may lead to late decreases in left ventricular performance with depression of both global and regional contractile function. This may be particularly important in the late and often “mysterious” appearance of congestive heart failure seen in patients with infarction, even in the absence of late ischemic events.

The etiology of this late ventricular dysfunction could be related to both infarct expansion of infarcted segments and volume-overload hypertrophy of noninfarcted segments. With respect to infarcted segments, the mechanical consequences of infarct expansion place an unusually high burden on the residual functioning myocardium. Moreover, the expanded infarct segment may act as a reservoir and receive blood during systole in competition with aortic outflow, a condition similar to mitral regurgitation. Perhaps more important than the hemodynamic consequences of infarct expansion are the possible late consequences of volume-overload hypertrophy. In most states of volume-overload hypertrophy (e.g., mitral regurgitation, aortic insufficiency) there is an early phase of adaptive hypertrophy in which contractile function of the hypertrophied myocardium remains normal. However, at some point in the hypertrophy process, there follows a transition when contractile function becomes abnormal. If ventricular remodeling involves volume-overload hypertrophy of noninfarcted segments, it is possible that these segments may show a similar pattern of initial “physiologic” hypertrophy followed by “pathologic” hypertrophy. Since these segments must compensate for the deleterious mechanical consequences of infarct expansion, a loss of function in these segments would be a major factor in the late appearance of clinical congestive heart failure.

If remodeling is associated with long-term deleterious hemodynamic changes, then attempts to limit this process should become important. The concept that elevated wall stresses are the primary stimuli for ventricular remodeling leads one to conclude that attempts to decrease wall stress may attenuate this process, limit progressive ventricular dilatation, and blunt any adverse hemodynamic consequences that result. Of note, some support for this notion comes from work by Pfeffer et al., who have shown that administration of captopril, an angiotensin-converting enzyme inhibitor that presumably reduces left ventricular systolic wall stress, resulted in less ventricular dilatation and prolonged survival in rats with experimentally induced myocardial infarction in comparison with untreated rats with infarcts of comparable size. If this concept were applicable to humans, then maneuvers to decrease ventricular wall stresses by decreasing both left
ventricular preload and afterload might favorably diminish topographic changes after infarction and might decrease the incidence of congestive heart failure in the late recovery period.

**Study limitations.** Several important limitations of this study should be emphasized. First, it is important to note that hemodynamic and geometric changes that are described in this study are in patients with acutely reperfused infarcts. Several recent investigations have noted that reperfusion into an infarcted region may alter the properties of the postinfarction tissue. Accordingly, one needs to ask whether the remodeling changes were caused by myocardial infarctions or by the early reperfusion of the infarct region. However, studies from our laboratory have shown that the success or failure of thrombolytic therapy (administered in the same period as in the present study) has no effect on ventricular volume changes after myocardial infarction.

A second important criticism that might be raised is the fact that no significant wall thinning was noted in the area of infarction as assessed by M mode echocardiography. In part, this may be related to lack of adequate sensitivity of the echocardiographic wall thickness measurements. Alternatively, the lack of infarct wall thinning may be related to the effect of reperfusion into the infarction zone.

Finally, although we have concluded that the hemodynamic changes observed in our study were consequences of the remodeling process, it is possible that other factors, such as recovery of ischemic myocardium, also had an effect on hemodynamic improvement. Only further, prospective, controlled, intervention trials will help answer this important question definitively.

**References**

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