Return of left ventricular function after reperfusion in patients with myocardial infarction: importance of subtotal stenoses or intact collaterals

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ABSTRACT To determine whether subsequent improvement in left ventricular ejection fraction can be predicted from preintervention coronary arteriograms, we divided 63 patients with acute myocardial infarction into two groups based on findings at emergency coronary arteriography at a mean of 7 hr after onset of symptoms: (1) a “no-flow” group with an occluded infarct-related artery and no easily visible collaterals (n = 36) and (2) a “limited-flow” group with either subtotal stenosis or total occlusion of the infarct-related vessel with intact collaterals (n = 27). Of the 63 patients, 61 underwent emergency procedures to establish reperfusion. At follow-up arteriography (contrast or radionuclide) performed 12 ± 7 days after infarction, global ejection fraction had increased significantly in patients with limited flow to the infarct zone and “successful” early reperfusion intervention due primarily to a significant increase in the regional ejection fraction in the infarct zone. Global ejection fraction fell significantly between baseline and follow-up in patients with no flow to the infarct zone and “unsuccessful” early reperfusion intervention due primarily to a fall in the regional ejection fraction of the noninfarct zone. Global and regional ejection fractions did not change significantly in patients with no flow to the infarct zone and successful early reperfusion or in patients with limited flow to the infarct zone and unsuccessful early reperfusion intervention. The elapsed time before reperfusion did not correlate significantly to the change in either regional or global ejection fraction. However, the magnitude of improvement in both global and regional ejection fraction at follow-up was greater among patients with anterior infarcts than among those with inferior infarcts, possibly because baseline ejection fraction was lower in patients with anterior infarcts. These data indicate that among patients with acute myocardial infarction undergoing emergency coronary arteriography at a mean of 7 hr after onset of symptoms, improvement in global ejection fraction is unlikely to occur even after a successful early reperfusion intervention in the absence of preserved flow to the infarct area. However, among patients with subtotally occluded infarct-related arteries or significant collateral blood flow to the infarct zone, subsequent improvement in global and regional ejection fraction in the zone of myocardial infarction frequently occurs. Improvement in both global and regional ejection fraction may be more readily demonstrated in patients initially having more severe depression of these parameters.


INVASIVE METHODS are being used with increasing frequency to reperfuse the coronary arteries of patients with acute myocardial infarction. Despite the widespread enthusiasm for these invasive techniques, limited data are available for predicting which patients with acute myocardial infarction will derive maximal benefit from reperfusion. The primary goals of reperfusion therapy are twofold: (1) to reestablish flow in a totally or subtotally occluded coronary arterial vessel and (2) to limit the evolution of the acute infarction process and reverse left ventricular functional impairment in ischemic but viable zones. The first goal can often be accomplished through a variety of means such as intracoronary or intravenous thrombolytic therapy, emergency coronary angioplasty and emergency coronary revascularization surgery. Unfor-
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Unfortunately, achieving the first goal — reperfusion — does not always guarantee achievement of the second goal — functional improvement.

There is currently no general agreement regarding the effectiveness of reperfusion therapy in restoring left ventricular function in patients with evolving acute myocardial infarction. Initial reports4, 15 documented significant improvement in left ventricular ejection fraction in patients with successful thrombolysis after intracoronary infusion of streptokinase. Huhmann et al.16 cautioned that significant improvement in ventricular function can be expected only when thrombolytic therapy is administered within 3 hr of symptoms; however, Smalling et al.17 found improvement in left ventricular function in patients who received intracoronary streptokinase up to 18 hr after onset of symptoms. Two recent randomized prospective studies comparing intracoronary streptokinase with conventional treatment reached different conclusions regarding the likelihood of return of left ventricular function after thrombolytic therapy.18, 19 Furthermore, significant improvement in left ventricular ejection fraction has been found in patients showing either enzymatic or angiographic evidence of spontaneous reperfusion.20, 21

The purpose of this study was to determine whether subsequent improvement in left ventricular ejection fraction could be predicted from baseline clinical data and preintervention coronary arteriogram in patients undergoing emergency invasive procedures to establish reperfusion during evolving acute myocardial infarction.

Methods

Patients. We studied 63 consecutive patients admitted for suspected acute evolving myocardial infarction between October 1981 and December 1982, who underwent immediate coronary and left ventricular angiography on admission and follow-up left ventricular angiography (either contrast or radionuclide) before discharge. Included in this study were patients who, after the emergency coronary and left ventricular angiographic procedures, underwent streptokinase treatment, percutaneous transluminal coronary angioplasty (PTCA), emergency coronary revascularization surgery, some combination of these, or no intervention. However, patients who failed to demonstrate a typical rise and fall of creatine kinase (CK)-MB isoenzyme were judged to have no evidence for acute myocardial infarction and were excluded from the study. All patients gave informed consent.

Angiographic studies and reperfusion therapy. After providing a brief medical history and undergoing a physical examination, patients underwent emergency cardiac catheterization, including left ventriculography and coronary angiography. They were premedicated with diphenhydramine hydrochloride (50 mg iv). A No. 7F or 8F side-arm valved sheath22, 23 was inserted into the right or left femoral artery and sutured in place. Heparin (5000 IU) was administered intravenously. A pigtail ventriculographic catheter was inserted, baseline left ventricular pressure was recorded, and left ventriculography was performed with patients in the 20 degree cranial–60 degree left anterior oblique (LAO)/45 degree right anterior oblique (RAO) projections, with 45 ml of sodium and meglumine diatrizoates (Renografin-76) power-injected over 3 sec.

Coronary arteriography of the suspected non–infarct-related artery was then performed, followed by injections of the infarct-related artery. The following radiographic views of the coronary arteries were routinely obtained: right coronary artery (1) left lateral, (2) 60 degree LAO/15 degree cranial, and (3) 30 degree RAO; left coronary artery (1) 60 degree LAO/15 degree cranial, (2) left lateral, (3) 30 degree RAO, (4) 30 degree RAO/15 degree caudal, and (5) 30 degree RAO/15 degree cranial.

The decision for the mode of reperfusion therapy to be used, if any, was left to the discretion of the angiographer, but in general, patients with totally occluded infarct-related arteries initially received a trial of streptokinase, delivered as described below. Patients with subtotally occluded vessels received different treatment modalities depending on the severity, location, and anatomic appearance of the stenotic lesion and whether thrombus was suspected angiographically.

Patients receiving streptokinase were premedicated with methylprednisolone (1.0 g iv) and then were given either 4000 IU/min streptokinase for 1 hr via the intracoronary route or 0.5 to 1.0 million units of streptokinase over 15 to 45 min by the peripheral intravenous route. Contrast injections of the infarct-related artery were repeated at 15, 30, 45, and 60 min after beginning the streptokinase infusion to document the effects of therapy.

PTCA, when performed, was done according to the technique of Gruentes et al.23 Patients receiving emergency coronary revascularization surgery were taken immediately from the catheterization laboratory to the operating room, where coronary revascularization surgery was performed according to previously described techniques.26

Of the 63 patients, 46 (73%) were treated with streptokinase alone (29 with intracoronary streptokinase, two with intravenous streptokinase, and 15 with a combination of intravenous [0.5 to 1.0 million IU over 15 to 45 min] and intracoronary streptokinase [120,000 IU over 30 min]). Among the remaining patients, PTCA was performed in three, coronary revascularization surgery in 11, and a combination of PTCA and coronary artery bypass grafting in one. PTCA followed thrombolytic therapy in two patients, and bypass grafting followed thrombolytic therapy in four patients. There was no intervention after emergency coronary angiography in two patients. Five patients who were initially treated with streptokinase alone as the emergency intervention subsequently underwent urgent coronary revascularization surgery at a mean of 3.4 ± 2.4 days (range 1 to 6) after streptokinase administration. In these five patients, streptokinase treatment had failed to produce thrombolysis in three, and in the remaining two patients recurrent chest pain had occurred in one and severe three-vessel disease had remained after successful thrombolytic therapy in the second.

Cardiac enzyme determinations. CK-MB isoenzyme was determined on admission and at 6 hr intervals for 72 hr after catheterization by means of a cellulose acetate electrophoretic assay (Helena Laboratories, Beaumont, TX). Serial CK-MB data were considered diagnostic for acute myocardial infarction if there was a typical rise and fall of CK-MB after admission and if peak CK-MB exceeded 10 IU/l.

Evaluation of baseline coronary arteriograms. The coronary arteriograms from the initial study were examined in conjunction with the patient’s electrocardiogram and contrast left ventriculogram to identify the infarct-related coronary arterial lesion. The extent of angiographically visualized collateral connections to the infarct-related coronary artery was determined
by the consensus of two experienced observers reviewing the baseline coronary arteriogram independently without knowledge of the follow-up left ventricular angiogram. The patients were divided into two groups according to the visibility of collaterals to the infarct-related coronary artery: (1) a “no-flow” group with either absent or “faintly visualized” collaterals and (2) a “limited-flow” group with either “readily visualized” collaterals or a subtotally occluded infarct-related coronary artery. The distinction between faintly visualized and readily visualized collaterals was made as follows: Faintly visualized collaterals were rarely seen in more than one angiographic projection and failed to clearly fill a segment of the major trunk of the infarct-related artery distal to the lesion. Readily visualized collaterals were defined as those usually visible in two or more angiographic projections, reliably filling one or more segments of the major trunk of the distal infarct-related vessel.

The result of the emergency procedure was classified as either successful or unsuccessful in reperfusing the infarct-related artery. Streptokinase therapy was designated as successful if during the initial angiographic observation in the catheterization laboratory there was an increase of the vessel diameter from total (100%) to subtotal (<100%) stenosis or an increase in the diameter of an initially subtotally occluded vessel, the latter determined by measurement of the diameter of the vessel in at least two projections. PTCA was successful if it resulted in any measurable increase in the diameter of the initially subtotally stenotic vessel. Coronary artery bypass graft surgery was assumed to be successful in reperfusing the infarct-related vessel whenever it was performed. All other outcomes were designated unsuccessful, including the decision not to perform emergency intervention in some patients with acute myocardial infarction after emergency coronary arteriography.

**Global and segmental ejection fraction.** From the baseline preintervention contrast left ventriculogram and from the follow-up contrast or radionuclide ventriculogram obtained at a mean of 12 days after infarction, we calculated (1) global left ventricular ejection fraction and (2) segmental ejection fractions in both the zone of myocardial infarction and in the noninfarct zone. Angiographic and radionuclide global and regional ejection fractions were derived according to techniques previously described from our laboratory. 24-29

In the analysis of global ejection fraction the baseline ejection fraction was computed from the baseline contrast left ventricular angiogram in all 63 patients, and the follow-up ejection fraction was obtained from a follow-up contrast angiogram in 37 patients and from a follow-up radionuclide angiogram in 26 patients. Direct comparison of the baseline contrast ventriculogram with a follow-up scintigraphic radionuclide ventriculogram was believed to be justified because previous studies from our laboratory 29 and elsewhere 30 have shown comparability of these techniques for assessment of ejection fraction.

In the serial analysis of regional ejection fraction, comparison between scintigraphic and angiographic segmental ejection fractions was not believed to be reliable because the regions subtended by the segments are not precisely identical. Furthermore, the contrast segmental ejection fraction represents an area ejection fraction, whereas the scintigraphic segmental ejection fraction represents more of a volumetric ejection fraction. 29 Thus we restricted comparison of segmental ejection fractions to the 51 patients with either serial contrast angiographic studies (37 patients) or serial radionuclide angigraphic studies (14 patients), the latter consisting of a baseline scintigraphic ejection fraction study immediately after intervention followed by another scintigraphic ejection fraction study before hospital discharge.

The zone of myocardial infarction was determined from a combined analysis of the initial coronary arteriogram and contrast left ventriculogram. Left ventricular end-diastolic and end-systolic silhouettes in the biplane projections were superimposed by means of a stationary external reference system. The left ventricular circumference was divided into 10 regions, each region having perfusion by predetermined, designated coronary arterial segments (figure 1). 31 Occlusion of one of these coronary segments was assumed to jeopardize each of its corresponding ventriculographic regions, and these regions were

**FIGURE 1.** Determination of infarct zone. Left ventricular end-systolic (dashed lines) and end-diastolic (solid lines) silhouettes in biplane projections were superimposed by means of two stationary external radiographic markers (large dots) as references. With a computerized technique, 28, 29 the left ventricular circumference was divided into 10 regions. Each region was assumed to be perfused by the coronary segments indicated. In a left-dominant coronary arterial distribution, segments 4, 5, and 8 were assumed to be supplied by the circumflex coronary artery. Occlusion of the coronary segment was assumed to jeopardize each of its corresponding ventriculographic regions, and these regions were designated the infarct zone. The remainder of the ventricle was designated the noninfarct zone. LMCA = left main coronary artery; PROX = proximal; DIAG = diagonal; RCA = right coronary artery; PDA = posterior descending artery; Cx = circumflex coronary artery; RPLS = right posterior lateral segment artery.
designated as the infarct zone. The remaining portion of the ventricle was designated the noninfarct zone (figure 2). This system therefore obligated certain left ventricular segments to be considered within the infarct or noninfarct zones simply by the location of the infarct-producing lesion, irrespective of the contractile pattern of the left ventricle. However, to compensate for the variable length of the left anterior descending coronary artery (LAD) (which could not be ascertained when the vessel was occluded and lacked collateral filling), the posterolateral segment (segment 8, figure 1) was assumed to be supplied by the LAD when it was akinetic on the baseline ventriculogram and not to be supplied by the LAD when it showed normal or near-normal motion.

Statistical methods. Data are reported as mean ± standard deviation. A paired or unpaired t test was used to assess the significance of difference between continuous variables. The chi-square test with Yates’ continuity correction was used to assess the significance of difference between dichotomous variables.

Results

Patients. Of the 63 patients satisfying the study criteria, 36 were classified on the basis of their baseline coronary arteriogram as having no flow distal to the infarct-related lesion and 27 were classified as having limited flow distal to the lesion. In the latter group, nine patients had subtotally occluded infarct-related vessels and 18 had totally occluded infarct-related vessels with readily visualized collaterals to the distal infarct-related artery.

Although the groups with no flow and limited flow had generally similar clinical and angiographic baseline characteristics (table 1), the group with limited flow was slightly older, had a greater prevalence of women, had a slightly longer interval between onset of myocardial infarction and coronary arteriography, had a greater preponderance of right coronary lesions, and had somewhat fewer infarct segments. Although baseline ejection fractions, both global and segmental, were similar in the two patient groups, the baseline left ventricular end-diastolic pressure was significantly lower in the group with limited flow than in the group with no flow. Similar methods of reperfusion were attempted in the two groups, and the rate of success of the interventions, as defined previously, was similar between the two groups.

There were two patients in whom no intervention was attempted after the initial angiographic examination, one in each group. One of these patients had an occlusion of a right posterolateral branch artery, and the area of myocardium at risk from this lesion was believed to be too small to justify the potential danger of further intervention. The second patient without intervention had only a subtotal right coronary artery occlusion and is described in more detail below. The interval between baseline and follow-up angiography was 12 ± 8 days (range 3 to 47) in the group with no flow and 12 ± 7 days (range 4 to 31) in the group with limited flow (p = NS).

Enzymatic data. In 57 patients for whom complete CK-MB data were available, maximal CK-MB was significantly lower (p < .005) in patients with limited flow than in those with no flow (table 2). This difference was especially notable among the successfully reperfused patients, although the trend was also present, but not statistically significant, among unsuccessfully reperfused patients. The interval from onset of symptoms of myocardial infarction until peak CK-MB did not differ between the two groups, irrespective of the success of reperfusion. However, the interval from
TABLE 1
Clinical and angiographic data (mean ± SD)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>&quot;No flow&quot; group</th>
<th>&quot;Limited flow&quot; group</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>52 ± 10</td>
<td>56 ± 10</td>
<td>&lt;.10</td>
</tr>
<tr>
<td>Sex</td>
<td>32 M, 4 F</td>
<td>19 M, 8 F</td>
<td>&lt;.10</td>
</tr>
<tr>
<td>Prior MI</td>
<td>7 (19%)</td>
<td>4 (15%)</td>
<td>NS</td>
</tr>
<tr>
<td>Interval between onset of MI and cath (hr)</td>
<td>6.3 ± 1.9</td>
<td>7.6 ± 3.3</td>
<td>&lt;.10</td>
</tr>
<tr>
<td>Infarct-related artery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAD</td>
<td>24 (67%)</td>
<td>10 (37%)</td>
<td></td>
</tr>
<tr>
<td>LCx</td>
<td>3 (8%)</td>
<td>3 (11%)</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>RCA</td>
<td>9 (25%)</td>
<td>14 (52%)</td>
<td></td>
</tr>
<tr>
<td>Single-vessel disease</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Baseline LV pressure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>132 ± 24</td>
<td>130 ± 18</td>
<td>NS</td>
</tr>
<tr>
<td>Diastolic</td>
<td>24 ± 8</td>
<td>20 ± 8</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>No. of infarct-related segments</td>
<td>4.2 ± 1.5</td>
<td>3.5 ± 1.5</td>
<td>&lt;.10</td>
</tr>
<tr>
<td>Baseline EF</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Global</td>
<td>45 ± 13</td>
<td>47 ± 10</td>
<td>NS</td>
</tr>
<tr>
<td>Infarct zone&lt;sup&gt;a&lt;/sup&gt;</td>
<td>20 ± 20</td>
<td>26 ± 18</td>
<td>NS</td>
</tr>
<tr>
<td>Noninfarct zone&lt;sup&gt;a&lt;/sup&gt;</td>
<td>51 ± 12</td>
<td>50 ± 12</td>
<td>NS</td>
</tr>
<tr>
<td>Method(s) of reperfusion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Streptokinase</td>
<td>30 (83%)</td>
<td>22 (81%)</td>
<td></td>
</tr>
<tr>
<td>PTCA</td>
<td>2 (6%)</td>
<td>2 (7%)</td>
<td></td>
</tr>
<tr>
<td>CABG</td>
<td>8 (22%)</td>
<td>4 (15%)</td>
<td>NS</td>
</tr>
<tr>
<td>None</td>
<td>1 (3%)</td>
<td>1 (4%)</td>
<td></td>
</tr>
<tr>
<td>Successful intervention(s)</td>
<td>25 (61%)</td>
<td>15 (68%)</td>
<td>NS</td>
</tr>
<tr>
<td>Interval between onset of MI and reperfusion (hr)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>7.2 ± 2.2</td>
<td>8.4 ± 3.8</td>
<td>NS</td>
</tr>
<tr>
<td>Interval between baseline and follow-up ventriculography (days)</td>
<td>12 ± 8</td>
<td>12 ± 7</td>
<td>NS</td>
</tr>
</tbody>
</table>

MI = myocardial infarction; LCx = left circumflex coronary artery; RCA = right coronary artery; LV = left ventricular; cath = emergency cardiac catheterization with coronary angiography and left ventriculography; EF = ejection fraction; CABG = coronary artery bypass graft surgery.

<sup>a</sup>Includes data from 28 patients in "no-flow" group and 23 patients in "limited-flow" group on whom serial measurements of segmental ejection fraction were available.

<sup>b</sup>Includes data from 40 patients with successful reperfusion.

onset of symptoms until peak CK-MB was significantly shorter among successfully reperfused patients than among unsuccessfully reperfused patients (17.3 ± 6.7 vs 24.9 ± 7.1 hr; p = .0002).

Changes in global ejection fraction. Among patients with unsuccessful early reperfusion intervention, global ejection fraction fell in 10 of the 11 patients in the group with no flow (figure 3). Overall, the mean global ejection fraction in the group with no flow was significantly lower (p < .02) at follow-up than at baseline. In the patients with limited flow having unsuccessful early reperfusion intervention there was no consistent direction in the change in global ejection fraction between the baseline and follow-up studies (figure 3). Three patients of the 12 in the group with limited flow actually showed a striking improvement in global ejection fraction between the baseline and follow-up studies.

One of these patients had a totally occluded but well collateralized LAD that did not reperfuse with streptokinase infusion. After emergency coronary revascularization surgery performed on the third hospital day

Consistent with sequential data, reperfusion of the infarct-related artery was associated with an improvement in global ejection fraction from baseline to follow-up (figure 3). The change in global ejection fraction at follow-up was not significantly different among patients with successful reperfusion and those with unsuccessful reperfusion.

![chart](chart.png)

FIGURE 3. Change in global ejection fraction (EF) after unsuccessful early reperfusion. On the follow-up left ventriculogram performed 12 ± 7 days after infarction, global ejection fraction was significantly lower in patients without flow to the infarct zone ("NO FLOW" GP), but no consistent trend was noted in patients with preserved flow to the infarct zone ("LIMITED FLOW" GP). BSL = baseline; F/U = follow-up. Bars indicate mean ± SD.
because of recurrent severe chest pain, the patient’s global left ventricular ejection fraction rose from 34% to 52%. A second patient had an inferior myocardial infarction with a 90% thrombotic stenosis of the right coronary artery, which showed no apparent change during streptokinase administration. However, on follow-up coronary arteriography 12 days later, the right coronary artery was virtually normal and the left ventricular ejection fraction had risen from 46% to 66%.

The third patient in this group had an acute inferior myocardial infarction and an 80% stenosis of the right coronary artery on his baseline study. No intervention was attempted. At follow-up the global ejection fraction had risen from 50% to 70% and the severity of the right coronary artery stenosis had fallen from 80% to 70%. Thus improvement in left ventricular ejection fraction was noted in selected patients with subtotally occluded vessels or intact collaterals, even when the attempt at early reperfusion was unsuccessful.

Among patients with successful early reperfusion intervention, global ejection fraction did not change in a consistent manner in the 25 patients in the group with no flow (figure 4). However, 11 of the 15 (73%) patients with limited flow and successful early reperfusion intervention showed an increase in global ejection fraction between the baseline and follow-up studies. Follow-up coronary arteriography was performed in three of the four patients in whom follow-up global ejection fraction was not improved, and in each instance the infarct-related artery had reoccluded since the baseline study. Overall, the mean global ejection fraction at follow-up was significantly greater than at baseline in the group with limited flow and successful reperfusion (p < .025) (figure 4).

In the 63 patients, follow-up coronary arteriography was performed at a mean of 15 ± 7 days after infarction in 37 patients (59%) — 22 (61%) of the group with no flow and 15 (56%) of the group with limited flow. Reocclusion of the infarct-related artery was found in three (19%) of the 16 successful cases in the group with no flow and in three (30%) of the 10 successful cases in the group with limited flow. Among the group with no flow, open infarct-related vessels on follow-up angiography were found in 88% (7/8) of those with improvement in global ejection fraction and in 43% (6/14) of those without improvement in global ejection fraction (p < .05). Among patients in the group with limited flow who underwent follow-up angiography, patent infarct-related vessels were found in 89% (8/9) of those with improvement in global ejection fraction at follow-up and in 17% (1/6) of those without improvement in ejection fraction (p < .01).

Changes in segmental ejection fraction. Among the patients with unsuccessful attempts at early reperfusion in whom serial segmental ejection fraction data were available, no statistically significant changes were noted in ejection fraction of the infarct zone in either group (figure 5). Of the three patients discussed above who had striking improvement in global ejection fraction despite unsuccessful early reperfusion, serial segmental ejection fraction data were available in two. In both of these patients the ejection fraction of the infarct zone increased strikingly, from 14% and 16% at baseline to 55% and 55% at follow-up (figure 5).

In the patients having successful early reperfusion and serial segmental ejection fraction data, ejection fraction of the infarct zone at follow-up was not significantly different from that at baseline among 17 patients in the group with no flow. However, among the 12 patients in the group with limited flow, ejection fraction of the infarct zone was significantly greater at follow-up than at baseline (p < .01) (figure 6). Indeed, only two patients in the group with limited flow had an ejection fraction of the infarct zone that failed to increase at follow-up, and one of these two patients had reocclusion of the infarct-related artery.

Changes in segmental ejection fractions of the infarct and noninfarct zones are contrasted in figure 7. In patients with successful early reperfusion the improvement in global ejection fraction observed in the group with limited flow is explained by a substantial improvement in ejection fraction of the infarct zone and

![FIGURE 4. Change in global ejection fraction (EF) after successful early reperfusion intervention. In patients without preserved flow to the infarct zone ("NO FLOW" GP), there was no significant overall change in global ejection fraction at follow-up, whereas in patients with preserved flow to the infarct zone ("LIMITED FLOW" GP) there was a significant increase in global ejection fraction at follow-up. BSL = baseline; F/U = follow-up. Bars indicate mean ± SD.](image-url)
perhaps by a smaller, but not statistically significant, increase in ejection fraction of the noninfarct zone. In contrast, in the group with no flow neither global nor regional ejection fraction changes significantly from baseline. However, in the patients with unsuccessful early reperfusion the significant fall in global ejection fraction in the group with no flow is primarily explained by a significant fall in ejection fraction of the noninfarct zone in that group, since ejection fraction of the infarct zone does not change substantially. Comparison of the segmental ejection fractions of the noninfarct zones in the unsuccessfully reperfused patients with no flow with normal standards for our laboratory reveals that 38% (23/61) of the noninfarct segments at baseline were hyperkinetic (greater than 1 SD above normal). Among patients with limited flow and unsuccessful early reperfusion intervention mean ejection fractions, both global and regional, do not change significantly.

**Location of myocardial infarct.** Baseline global and infarct-zone ejection fractions were uniformly higher among inferior infarcts (table 3). Moreover, the change (in ejection fraction units) between follow-up and baseline global and infarct-zone ejection fractions was uniformly lower among inferior infarcts. The largest improvement in ejection fraction at follow-up thus tended to occur in anterior infarcts, the group with greater baseline depression of ejection fraction and the larger potential for improvement.

**Elapsed time before reperfusion.** No significant relationship was observed between either global ejection fraction (figure 8) or ejection fraction of the infarct zone (figure 9) and the interval between the onset of symptoms of acute myocardial infarction and reperfu-

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**FIGURE 5.** Change in ejection fraction (EF) of the myocardial infarction (MI) zone after unsuccessful early reperfusion intervention. Ejection fraction of the infarct zone showed no consistent change after unsuccessful early reperfusion intervention in either the patients without ("NO FLOW" GP) or with ("LIMITED FLOW" GP) preserved flow to the infarct zone. BSL = baseline; F/U = follow-up. Bars indicate mean ± SD.

**FIGURE 6.** Change in ejection fraction (EF) of the myocardial infarction (MI) zone after successful early reperfusion intervention. At follow-up, ejection fraction of the infarct zone was not significantly changed in patients without preserved flow to the infarct zone ("NO FLOW" GP) but was significantly increased among patients with preserved flow to the infarct zone ("LIMITED FLOW" GP). BSL = baseline; F/U = follow-up; R = known reocclusion of infarct-related vessel after initially successful streptokinase treatment. Bars indicate mean ± SD.
Discussion

Reperfusion therapy and return of left-ventricular function. It now seems likely that subgroups of patients may exist that have the potential for improvement of left ventricular function after myocardial infarction. Other subgroups may also exist whose damage is irreversible and in whom reperfusion therapy will prove futile and perhaps even counterproductive. The ability to prospectively identify those patients most likely to benefit from reperfusion therapy is clearly needed to properly select patients for these costly and potentially dangerous emergency procedures.

Our study examined three potentially important baseline variables: (1) the extent of perfusion of the infarct zone on the baseline (preintervention) coronary arteriogram, (2) the interval between onset of symptoms of myocardial infarction and intervention, and (3) the location of the infarct. We found that a successful reperfusion intervention did not guarantee subsequent improvement in left ventricular ejection fraction. Indeed, patients with totally occluded infarct-related vessels and poor or absent collaterals to the distal infarct-related vessel showed no overall improvement in either global or regional ejection fraction of the infarct zone, regardless of the success of the intervention (figures 3 to 6). However, the group with subtotally occluded infarct-related vessels or extensive collaterals to the distal infarct-related vessel predictably showed improvement in both global and infarct-zone regional ejection fraction with successful early reperfusion interventions and occasionally even with unsuccessful interventions. These observations are in agreement with the experimental animal studies of Schaper and Pasyk and with recent clinical studies showing greater improvement in ejection fraction and reduction in thallium perfusion defect among subjects with adequate collateral blood supply to the infarct area before recanalization therapy.

In our study, patients with some preserved perfusion of the infarct zone, either antegrade through subtotally occlusive stenoses or retrograde through adequate collaterals, had a lower peak CK-MB than did patients with preserved flow. The interval from onset of symptoms until peak CK-MB was not significantly different between the two groups, implying that early spontaneous reperfusion was not an important factor. These enzymatic data lend further support to the angiographic data, suggesting that patients with preserved flow to the infarct zone may have smaller infarct size and better preservation of left ventricular function than patients without preserved flow.

Our study showed no significant correlation be-
Reimer et al. and also contrary to recent clinical studies showing duration of ischemia to be a major determinant of return of left ventricular function after recanalization therapy, especially among patients receiving therapy within 4 hr of onset of symptoms. It is possible that the duration of ischemia might have been a more important factor in predicting the recovery of left ventricular function in the present study had there been more patients with symptom duration of less than 4 hr before intervention.

**Contribution of regional ejection fraction.** Although many studies have considered changes in global ejection fraction after reperfusion, relatively few have related changes in global ejection fraction quantitatively to changes in regional ejection fraction. Our study demonstrates that among patients with a successful early reperfusion intervention, an increase in global ejection fraction, when observed, is primarily related to an increase in ejection fraction of the infarct zone, as might be expected. Among patients with acute myocardial infarction and with unsuccessful early reperfusion intervention, a fall in global ejection fraction was often noted and was found to be due, in many cases, to a fall in the ejection fraction in the noninfarct zone rather than to a further decrease in ejection fraction of the infarct zone. This finding is consistent with the data of others demonstrating that in many patients with acute myocardial infarction studied early, there is initially relative hyperkinesis in the noninfarct zone that is no longer apparent at the time of the follow-up study. Other explanations for the decline at follow-up of the segmental ejection fraction in the noninfarct zones might be extension of the in-

### TABLE 3

**Influence of infarct location on change in ejection fraction**

<table>
<thead>
<tr>
<th></th>
<th>Anterior MI&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Inferior MI&lt;sup&gt;a&lt;/sup&gt;</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Global EF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline EF</td>
<td>38 ± 14 (34)</td>
<td>53 ± 9 (29)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>ΔEF</td>
<td>2 ± 13 (34)</td>
<td>−4 ± 11 (29)</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Infarct zone EF&lt;sup&gt;b&lt;/sup&gt;</td>
<td>12 ± 19 (25)</td>
<td>31 ± 15 (26)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>ΔEF</td>
<td>10 ± 12 (25)</td>
<td>4 ± 12 (26)</td>
<td>&lt;.10</td>
</tr>
<tr>
<td>&quot;No-flow&quot; group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Global EF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline EF</td>
<td>38 ± 15 (24)</td>
<td>56 ± 9 (12)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>ΔEF</td>
<td>−1 ± 10 (24)</td>
<td>−8 ± 7 (12)</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Infarct zone EF&lt;sup&gt;b&lt;/sup&gt;</td>
<td>8 ± 13 (17)</td>
<td>36 ± 17 (11)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>ΔEF</td>
<td>6 ± 7 (17)</td>
<td>2 ± 8 (11)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>&quot;Limited-flow&quot; group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Global EF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline EF</td>
<td>40 ± 8 (10)</td>
<td>51 ± 9 (17)</td>
<td>&lt;.005</td>
</tr>
<tr>
<td>ΔEF</td>
<td>11 ± 16 (10)</td>
<td>−1 ± 13 (17)</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Infarct zone EF&lt;sup&gt;b&lt;/sup&gt;</td>
<td>22 ± 26 (8)</td>
<td>28 ± 13 (15)</td>
<td>NS</td>
</tr>
<tr>
<td>ΔEF</td>
<td>17 ± 18 (8)</td>
<td>7 ± 14 (15)</td>
<td>NS</td>
</tr>
</tbody>
</table>

<sup>a</sup> Data expressed as percent (mean ± SD), with number of patients in parentheses.

<sup>b</sup> Includes data from 51 patients on whom serial measurements of segmental ejection fraction were available.

between the return in left ventricular function and the interval between onset of symptoms of infarction and reperfusion in patients with successful reperfusion (figures 8 and 9). This lack of correlation is contrary to the data from experimental animals described by
Infarct into these zones or a change in left ventricular loading conditions.

Analysis of changes in ejection fraction of the infarct zone relative to the changes in ejection fraction of the noninfarct zone in our four patient groups suggests that there might indeed be some interrelationship between the two categories of segmental ejection fraction (figure 7). Ejection fraction of the noninfarct zone tends to fall when ejection fraction of the infarct zone fails to improve significantly, but ejection fraction of the noninfarct zone shows a trend toward improvement when that of the infarct zone increases significantly. This observation might relate to some imprecision in our technique for discriminating between the infarct and noninfarct zones, producing an "overlap" between the various zones in certain patients. Alternatively, since both the infarct and noninfarct zones are intimately related within the same ventricle, it may be that the contractile pattern of the noninfarct zone is to some extent determined by the contractile pattern of the infarct zone, since the former must "strut" against the latter.

**Location of myocardial infarct.** Because inferior myocardial infarction characteristically involves less myocardium than anterior infarction, less left ventricular dysfunction is expected. We observed high baseline global and segmental ejections fractions among inferior or infarcts but less improvement in these parameters between follow-up and baseline in inferior compared with anterior infarcts (table 3). Our observations are consistent with the postulate of DeFeyer et al. that greater potential for improvement in ejection fraction exists among patients having the largest initial depression of left ventricular function.

**Limitations of the study.** This study examines the serial changes in ventricular function in patients undergoing a variety of different procedures, each of which might conceivably have produced somewhat different effects on left ventricular function. Our patient population was not large enough to separate the effects of individual procedures, but it seems likely that because all of these procedures were designed to produce coronary arterial reperfusion, their effects on restoring left ventricular function would be similar, allowing them to be considered together.

As acknowledged above, our population included very few patients in whom reperfusion was accomplished within 4 hr of onset of symptoms, making the application of our conclusions less certain in that subset, an important group clinically.

Improvement in left ventricular function was defined in this study by a repeat, resting ventriculogram obtained approximately 12 days after infarction. Experimental animal studies have demonstrated that an even longer time may be necessary to appreciate the ultimate effects of reperfusion therapy on return of myocardial function. Thus, had our follow-up studies been performed later, different conclusions might have been reached. On the other hand, Smalling, et al. have shown that global ejection fraction in patients receiving thrombolytic therapy does not change significantly between hospital discharge and 6 month follow-up.

Finally, and most importantly, the present study is a retrospective, observational study. It is not possible in this study to relate changes in ventricular function directly to the reperfusion therapy itself because there is no adequate control group in whom reperfusion interventions were not performed. Spontaneous changes in left ventricular function cannot be ruled out, and indeed recent studies have confirmed that improvement in ventricular function in certain patients not undergoing reperfusion intervention is possible, probably related to spontaneous reperfusion of the infarct-related vessel.

In our study, patients with subtotally occluded infarct-related vessels might have represented those who had undergone spontaneous reperfusion before emergency catheterization and in whom improvement in ventricular function was destined to occur irrespective of whether an emergency intervention was performed. Large-scale prospective randomized studies will be required to evaluate definitively the comparative benefits of reperfusion therapy vs spontaneous recanalization of coronary arteries in patients with acute myocardial infarction.

**Clinical implications.** This study demonstrates that in patients with evolving acute myocardial infarction undergoing emergency coronary arteriography at a mean of approximately 7 hr after infarction, subsequent improvement in left ventricular function with, and perhaps sometimes without, reperfusion intervention seems most likely to occur in those patients with either subtotally occluded infarct-related vessels or intact collaterals to the distal infarct-related artery. In the remaining patients, even successful reperfusion does not guarantee subsequent improvement in left ventricular ejection fraction. Thus some discretion should be used in deciding whether such patients should be subjected to the potential risks of emergency interventions.

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References


manns H, Mehmel HC, Kubler W: Intracoronary thrombolysis in acute myocardial infarction: duration of ischemia as a major determinant of late results after recanalization. Am J Cardiol 50: 933, 1982
Return of left ventricular function after reperfusion in patients with myocardial infarction: importance of subtotal stenoses or intact collaterals.

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