Prognostic Implications and Predictors of Enhanced Regional Wall Motion of the Noninfarct Zone After Thrombolysis and Angioplasty Therapy of Acute Myocardial Infarction

Cindy L. Grines, MD, Eric J. Topol, MD, Robert M. Califf, MD, Richard S. Stack, MD, Barry S. George, MD, Dean Kereiakes, MD, Jane M. Boswick, MPH, Eva Kline, RN, William W. O’Neill, MD, and the TAMI Study Group*

Although impairment of left ventricular function in acute myocardial infarction is closely related to extent of necrosis, function in the noninfarct zone also contributes to global performance and thus may be of prognostic importance. We evaluated left ventricular regional wall motion by the centerline chord method in 332 patients treated with intravenous tissue-type plasminogen activator (t-PA) in the multicenter Thrombolysis and Angioplasty in Myocardial Infarction (TAMI) I trial. All patients had acute contrast ventriculograms of suitable quality for analysis, and 266 patients had paired acute and day 7 ventriculograms. Enhanced function of the noninfarct zone was present during acute catheterization (+0.3 SD/chord) and was associated with preservation of the acute ejection fraction (p=0.0001). Multiple linear regression analysis revealed the most powerful clinical factor associated with enhanced function of the noninfarct zone was the absence of multivessel disease (p=0.0001). Clinical factors that were related weakly to noninfarct zone function included female gender (p=0.08) and higher flow in the infarct artery (p=0.03). Neither the degree of infarct zone dysfunction nor infarct location was associated with hyperkinesis of the noninfarct zone. In hospital, mortality was closely related to function in the noninfarct zone (p=0.006), ejection fraction (p=0.025), and the number of diseased vessels (p=0.009) but was not related to infarct zone function (p=0.128). Improvement in regional wall motion of the noninfarct zone at day 7 was associated with worse function during acute catheterization (p=0.0001), enhanced perfusion in the infarct zone as assessed by Thrombolysis in Myocardial Infarction (TIMI) flow grade (p=0.004) and the use of emergency angioplasty (p=0.05), or complete revascularization with bypass grafting (p=0.006). These data suggest that early assessment of function within the noninfarct zone may provide useful information regarding the extent of coronary disease and subsequent prognosis. Identification of impaired noninfarct zone function may be useful to triage patients who may benefit from mechanical revascularization procedures. (Circulation 1989;80:245–253)

Improvement in regional function of the infarct zone has been uniform with early reperfusion therapy of acute myocardial infarction; conversely, improvement in global ventricular performance has been less impressive.1–3 During acute ischemia, many patients exhibit “compensatory” hyperkinesis of noninfarcted myocardium, which may normalize the global ejection fraction despite dysfunction within the infarct zone.4,5 This hyperkinesis of the noninfarct zone usually subsides by the time of hospital discharge and as a consequence, ejection fraction fails to improve or may

From the Division of Cardiology, Department of Internal Medicine, University of Michigan, and VA Medical Centers, Ann Arbor, Michigan.

Supported in part by the Veterans Administration, Washington, D.C. C.L.G. is an Associate Investigator of the Veterans Administration.

Address for reprints: Cindy L. Grines, MD, Division of Cardiology, MN670, University of Kentucky Medical Center, 800 Rose Street, Lexington, KY 40536-0084.

*A collaborating centers and coinvestigators are listed in Appendix 1.

Received October 3, 1988; revision accepted April 4, 1989.
worsen despite significant recovery of function in the infarct region.

In addition to understanding mechanisms responsible for evolution in global left ventricular function, knowledge of noninfarct zone function may aid in the evaluation of prognosis of patients with acute myocardial infarction. Although late prognosis after infarction is related to predischarge ejection fraction, few studies have focused on predictors of in-hospital mortality. Early assessment of regional function within the infarct zone appears to be of limited clinical value; however, function of the noninfarct zone may be predictive of hemodynamic status and survival. Likewise, the presence of multivessel coronary disease has been associated with a high mortality after acute myocardial infarction. Whether this increased mortality is due to large infarction size, suppression of compensatory hyperkinesis in the noninfarct zone, or a combination of these factors has not been investigated.

A better understanding of the pathophysiology of myocardial function remote from the infarct zone could lead to strategies enabling maximization of global ventricular function. Thus, the present study was undertaken to determine associated factors and clinical significance of noninfarct zone function.

Methods

Study Design

The study design has been previously described. Briefly, 386 consecutive patients with acute myocardial infarction presenting within 6 hours of symptom onset were enrolled in the multicenter Thrombolysis and Angioplasty in Myocardial Infarction (TAMI) trial. Each patient received intravenous tissue-type plasminogen activator (t-PA) (150 mg/6–8 hr).

Left ventriculography was performed as soon as arterial access was obtained. Coronary angiography was performed 90 minutes after initiation of t-PA infusion. Infarct vessel patency was made according to the Thrombolysis in Myocardial Infarction (TIMI) classification. Infarct vessels showing TIMI 2 or 3 flow patterns were considered to be patent. If a residual stenosis of more than 50% was present in a patent vessel amenable to angioplasty, patients were randomized at day 7 to either emergency percutaneous transluminal coronary angioplasty (PTCA) or deferred PTCA. Patients with an occluded infarct artery, defined as TIMI 0 or 1 flow, underwent emergency angioplasty to attempt reperfusion. Coronary angioplasty was performed in only the infarct artery, and success was defined as achievement of less than 50% residual stenosis and TIMI grade 2 or 3 flow. Stenoses in noninfarct vessels were not approached by angioplasty.

All patients received heparin infusion for 3–7 days, lidocaine infusion for 24 hours, aspirin 325 mg/day, dipyridamole 75 mg t.i.d., and diltiazem 30–60 mg q.i.d. β-Blocker therapy was withheld during hospitalization unless needed for control of hypertension, arrhythmias, or severe angina. If recurrent ischemia occurred, emergency catheterization was performed and revascularization with PTCA or coronary artery bypass grafting was considered. Repeat coronary arteriography and left ventriculography was obtained at day 7. Infarct vessel reocclusion was defined as angiographically documented occlusion of a vessel that was patent after the acute intervention. Multivessel coronary disease was defined as more than 50% stenosis in one or more vessels remote from the infarct artery. Left main coronary disease was considered to be at least two-vessel involvement.

Ventriculographic Analysis

All ventriculograms were analyzed at the University of Michigan core laboratory. The 30° right anterior oblique end-diastolic and end-systolic endocardial contours from a normal sinus beat were traced by a single observer blinded to patient identity, time of study, and therapy. Adequate ventriculograms were obtained in 332 patients during acute catheterization and were used for the analysis of acute ventricular function. Twenty-seven patients died before follow-up catheterization. An additional 93 subjects were excluded due to either patient refusal or technically inadequate ventriculograms (ventricular tachycardia or substandard opacification) during acute or follow-up studies. Thus, paired acute and follow-up ventriculograms of adequate quality were obtained on 266 surviving patients and were the basis for analyses of changes in noninfarct zone function.

Global ejection fraction was determined by the area-length method. Regional wall motion for the infarct and noninfarct zones was determined by the centerline chord method. Within each territory, regional wall motion was calculated as the mean motion of one half of the most abnormally contracting contiguous chords and is expressed in standard deviations per chord. Hypokinesis is indicated by negative values, and hyperkinesis by positive values.

Statistical Analysis

Multiple linear regression analysis was used to determine factors that were associated with enhanced function of the noninfarct zone in the 332 patients with adequate ventriculograms during acute catheterization. Nineteen variables that may affect ventricular function were prospectively collected (Table 1). To place these findings in the most useful clinical context, a sequential analysis strategy was used. First, clinical variables obtained from the initial history and physical examination were placed in a multiple linear regression model with acute regional wall motion of the noninfarct zone as the independent variable. Significant clinical variables were then entered into a linear regression model with characteristics from the acute catheterization. Finally, a third model was constructed, again using
TABLE 1. Regression Analysis Variables

Baseline clinical characteristics
- Age
- Sex
- Home β-blocker use
- Heart rate
- Infarct location
- Duration of chest pain before entry into the study
- Presence of chest pain at onset of t-PA infusion
- Chest pain status on arrival in the catheterization laboratory

Catheterization variables
- Use of nitroglycerin during catheterization
- Infarct artery location
- TIMI flow grade 90 minutes after initiating t-PA
- Infarct vessel percentage stenosis
- Number of diseased vessels
- Baseline regional wall motion of noninfarct zone

Treatment variables
- Use of PTCA during acute catheterization
- Need for urgent PTCA before day 7 follow-up
- Emergency coronary artery bypass grafting
- Coronary bypass, nonemergency but occurring before follow-up studies
- Coronary artery reocclusion

Multiple linear regression and combining significant variables from the baseline clinical examination and cardiac catheterization with information regarding interim events that occurred during the hospitalization, mostly reflecting treatment received. These same steps were then repeated using the change in noninfarct zone function from acute to day 7 studies in 266 patients with paired ventriculograms. The change in noninfarct zone was calculated by subtracting the acute value from the day 7 value; thus, a positive number indicates improvement from acute to day 7 studies, and a negative number indicates deterioration in noninfarct zone wall motion. The Wilcoxon signed rank test was used to evaluate changes in regional or global left ventricular function. Univariate logistic regression analysis was used to determine the relation between in-hospital mortality and acute angiographic variables. Data are presented as mean±1 SD unless otherwise stipulated.

Results

Patient Characteristics

Characteristics of the 332 patients with acute ventriculograms and the 266 patients with paired ventriculograms of suitable quality for analysis are listed in Table 2. Eighty percent of the population were men; 15% were previously taking β-blockers; location of the infarct was anterior in 40%; and multivessel coronary disease was present in 47%. Emergency PTCA of the infarct artery was performed in 50% and was considered successful in 79%. Five percent of patients underwent emergency coronary bypass grafting for either failed PTCA, left main disease, or left main-equivalent disease. Elective bypass grafting was performed in 14%. Patient characteristics were similar except the group with acute ventriculograms contained 14 patients who died before follow-up catheterization.

TABLE 2. Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Acute study (n=332) (%)</th>
<th>Paired studies (n=266) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>262 (79)</td>
<td>218 (82)</td>
</tr>
<tr>
<td>Home β-blocker use</td>
<td>51/330 (15)</td>
<td>41/265 (15)</td>
</tr>
<tr>
<td>Anterior myocardial infarction</td>
<td>130/328 (40)</td>
<td>105/264 (40)</td>
</tr>
<tr>
<td>Diseased vessels</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>19 (6)</td>
<td>16 (6)</td>
</tr>
<tr>
<td>1</td>
<td>165 (50)</td>
<td>141 (53)</td>
</tr>
<tr>
<td>2</td>
<td>97 (29)</td>
<td>70 (26)</td>
</tr>
<tr>
<td>3</td>
<td>58 (17)</td>
<td>38 (14)</td>
</tr>
<tr>
<td>TIMI flow grade*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–1</td>
<td>101 (30)</td>
<td>74 (28)</td>
</tr>
<tr>
<td>2–3</td>
<td>231 (70)</td>
<td>192 (72)</td>
</tr>
<tr>
<td>Emergency PTCA</td>
<td>166 (50)</td>
<td>140 (52)</td>
</tr>
<tr>
<td>Successful PTCA</td>
<td>131/166 (79)</td>
<td>114/140 (81)</td>
</tr>
<tr>
<td>Pain in laboratory</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improved</td>
<td>265/329 (81)</td>
<td>216/265 (82)</td>
</tr>
<tr>
<td>Unchanged or worse</td>
<td>64/329 (19)</td>
<td>49/265 (18)</td>
</tr>
<tr>
<td>Emergency CABG</td>
<td>18 (5)</td>
<td>14 (5)</td>
</tr>
<tr>
<td>Elective CABG</td>
<td>48 (14)</td>
<td>34 (13)</td>
</tr>
<tr>
<td>Death</td>
<td>14 (4)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Reocclusion</td>
<td>51/300 (17)</td>
<td>42 (16)</td>
</tr>
</tbody>
</table>

* Ninety minutes after initiation of t-PA infusion.
PTCA, percutaneous transluminal coronary angiography; CABG, coronary artery bypass grafting.
Acute Function of the Noninfarct Zone

Ventricular function within the noninfarct zone was heterogenous and ranged from -4.8 to +4.8 SD/chord. Enhanced regional wall motion of the noninfarct zone (defined as any positive value) was present in 197 of 332 (59%) patients, and the median noninfarct zone regional wall motion was +0.4 SD/chord. As expected, augmented function in both the noninfarct ($r=0.48$, $p<0.001$) and the infarct zone ($r=0.58$, $p<0.001$) contributed to a higher acute ejection fraction (Figure 1). Multiple linear regression analysis revealed that the absence of multivessel coronary disease was the most potent predictor of enhanced function of the noninfarct zone ($p=0.0001$). Female gender ($p=0.08$) and higher TIMI flow grade of the infarct vessel ($p=0.03$) were also associated with enhanced regional wall motion of acute noninfarct zone function (Table 3). Of note, the degree of hyperkinesis of the noninfarct zone was not associated with severity of infarct zone dysfunction. Thus, the presence of remote hyperkinesis was associated with an augmented ejection fraction in groups with severe infarct zone dysfunction (53% with hyperkinesis vs. 44% without hyperkinesis, $p<0.001$) and mild infarct zone dysfunction (63% with hyperkinesis vs. 55% without hyperkinesis, $p<0.001$) (Figure 2).

The relation of the number of diseased vessels to regional left ventricular function is demonstrated in Figure 3. One-, two-, and three-vessel coronary disease were associated with a similar degree of dysfunction of the infarct zone ($-2.6$, $-2.4$, and $-2.8$ SD/chord, respectively). Conversely, the noninfarct zone functioned quite differently as the number of diseased vessels increased, with regional wall motion measurements of $+0.6$, $-0.2$, and $-0.8$ SD/chord in one-, two-, and three-vessel disease, respectively. Impaired function within the noninfarct zone resulted in a reduced global ejection fraction (49.6 ± 11.7%) in three-vessel coronary disease compared with one- and two-vessel disease (52.1 ± 10.6% and 53.1 ± 11.3%, respectively).

**Improvement in Noninfarct Zone Function at Day 7**

In the 266 patients with paired left ventriculographic studies, the acute ejection fraction was 52.4 ± 11% and infarct zone regional wall motion

---

**Table 3. Relation Between Patient Characteristics and Acute Function in the Noninfarct Zone**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Regression coefficients</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical variables only</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female gender</td>
<td>0.413</td>
<td>0.07</td>
</tr>
<tr>
<td>Symptom duration before t-PA</td>
<td>-0.003</td>
<td>0.07</td>
</tr>
<tr>
<td>Clinical and catheterization variables</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female gender</td>
<td>0.364</td>
<td>0.08</td>
</tr>
<tr>
<td>TIMI grade</td>
<td>0.157</td>
<td>0.03</td>
</tr>
<tr>
<td>Number of diseased vessels</td>
<td>-0.640</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

---

**Figure 1. Scatterplots demonstrating relative contributions of the noninfarct zone (top) and infarct zone (bottom) on acute ejection fraction. Augmented function in both the noninfarct ($r=0.48$, $p<0.001$) and the infarct zone ($r=0.58$, $p<0.001$) contributed to a higher acute ejection fraction.**

**Figure 2. Bar graphs of hyperkinesis of the noninfarct zone was not associated with infarct zone dysfunction and thus resulted in a higher median ejection fraction in both severe (≥2 SD/chord) and mild (≤−2 SD/chord) infarct zone dysfunction.**
was $-2.6 \pm 1.1$ SD/chord. At the time of hospital discharge, global ejection fraction was unchanged (53.2% ± 11%, $p=0.267$), despite significant improvement in regional wall motion of the infarct zone to $-2.2 \pm 1.2$ SD/chord ($p<0.001$). Regional wall motion of the noninfarct zone was $0.3 \pm 1.6$ SD/chord acutely and did not significantly change at follow-up ($0.3 \pm 1.5$ SD/chord, $p=0.29$). Thus, the lack of improvement in ejection fraction could not be fully accounted for by regression of hyperkinesis.

When logistic regression modeling was used to evaluate improvement in noninfarct zone function during the hospitalization, the factor most closely associated with improvement during the hospitalization was the degree of dysfunction at baseline ($p=0.0001$) (Figure 4). As demonstrated in Table 4, older age ($p=0.006$) and TIMI flow grade of the infarct-related artery after thrombolytic therapy ($p=0.004$) were significantly associated with improvement in function of the noninfarct zone during the course of the hospitalization. Complete revascularization with emergency coronary artery bypass grafting resulted in substantial improvement ($p=0.006$) while revascularization of the infarct-related artery with angioplasty was marginally associated with improvement in the noninfarct zone ($p=0.05$).

**Prognosis**

Twenty-seven patients died before hospital discharge. Although this study contained too few deaths to make major statements with regard to prognosis, the clinical significance of function within infarct and noninfarct zones and the presence of multivessel coronary artery disease was evaluated in the 332 patients with adequate acute ventriculography. As demonstrated in Table 5, in-hospital mortality was not predicted by the extent of dysfunction within the infarct zone. Although mortality was associated with a lower ejection fraction ($p=0.025$), the difference in median ejection fraction among patients who died and those who survived was not striking (50% vs. 53%, respectively). The most potent univariate predictor of in-hospital mortality was the degree of dysfunction within the noninfarct zone ($p=0.006$). A marked difference in median noninfarct zone function was observed between nonsurvivors and survivors ($-1.3$ vs. $+0.4$ SD/chord, respectively). The number of diseased vessels was also predictive ($p=0.009$) with mortality rates of 4%, 8%, and 14% in patients with one-, two-, and three-vessel disease, respectively. These analyses are complicated.

**FIGURE 3.** Plot of regional left ventricular function in 332 patients with acute ventriculograms. Function within the infarct zone was not affected by the extent of coronary artery disease. Conversely, regional wall motion of the noninfarct zone deteriorated with measurements of $+0.6$, $-0.2$, and $-0.8$ SD/chord in one-, two-, and three-vessel disease, respectively. (Negative values denote hypokinesis; positive values denote hyperkinesis.)

**FIGURE 4.** Plot of improvement in noninfarct zone function at day 7 compared with baseline function. Acute function of the noninfarct zone is displayed in quartiles based on the percentile distribution. Improvement in noninfarct zone function occurred when initial function was impaired, conversely deterioration or "regression" occurred when noninfarct zone function was initially hypercontractile.

**TABLE 4.** Relation Between Patient Characteristics and Improvement in Noninfarct Zone Function at Day 7

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Regression coefficients</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical variables only</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.013</td>
<td>0.05</td>
</tr>
<tr>
<td>Sex</td>
<td>$-0.363$</td>
<td>0.04</td>
</tr>
<tr>
<td>Angina at time of treatment</td>
<td>$-0.165$</td>
<td>0.07</td>
</tr>
<tr>
<td>Use of $\beta$-blockers before study</td>
<td>0.416</td>
<td>0.03</td>
</tr>
<tr>
<td>Clinical and catheterization variables</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.016</td>
<td>0.006</td>
</tr>
<tr>
<td>TIMI grade</td>
<td>0.129</td>
<td>0.01</td>
</tr>
<tr>
<td>Number of diseased vessels</td>
<td>$-0.134$</td>
<td>0.09</td>
</tr>
<tr>
<td>Acute noninfarct zone function</td>
<td>$-0.342$</td>
<td>0.001</td>
</tr>
<tr>
<td>Clinical, catheterization, and treatment variables</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.016</td>
<td>0.006</td>
</tr>
<tr>
<td>TIMI grade</td>
<td>0.159</td>
<td>0.004</td>
</tr>
<tr>
<td>Number of diseased vessels</td>
<td>$-0.143$</td>
<td>0.065</td>
</tr>
<tr>
<td>Acute noninfarct zone function</td>
<td>$-0.343$</td>
<td>0.0001</td>
</tr>
<tr>
<td>Emergency angioplasty</td>
<td>0.236</td>
<td>0.07</td>
</tr>
<tr>
<td>Urgent angioplasty</td>
<td>0.319</td>
<td>0.05</td>
</tr>
<tr>
<td>Emergency bypass surgery</td>
<td>0.739</td>
<td>0.006</td>
</tr>
</tbody>
</table>
by the fact that adequate ventriculography was available in only 14 of 27 (52%) patients who died compared with 318 of 359 (89%) patients who survived. If the population with adequate coronary arteriograms is considered (n=380), the \( \chi^2 \) value for multivessel disease is higher (\( \chi^2, 9.4; p=0.002 \)), reflecting inclusion of more patients with endpoints.

**Discussion**

During the early hours of acute myocardial infarction, enhanced function of the noninfarct zone resulted in greater preservation of ejection fraction and improved prognosis and was predictive of the extent of coronary artery disease. Improvement in noninfarct zone function at day 7 occurred in patients with worse function acutely and was further enhanced by greater perfusion of the infarct zone (as assessed by TIMI flow grade or the use of emergency angioplasty) or complete revascularization with bypass surgery. These data suggest that acute assessment of noninfarct zone ventricular function may enable risk stratification and triage of patients who may benefit from more aggressive revascularization strategies.

**Acute Hyperkinesis of Noninfarct Zone**

In the present study, noninfarct zone function was heterogenous and hyperkinesis of more than 1 SD/chord from normal was present in only 13% of patients. This finding is in contrast to animal studies where significant hyperkinesis of myocardium remote from the area of infarction occurs frequently.\(^{18-20}\) Many factors may contribute to the high incidence of compensatory hyperkinesis in the experimental setting. An open-chest preparation may alter regional left ventricular shape, loading conditions, and contraction patterns, thereby influencing the interaction between ischemic and non-ischemic areas. Furthermore, in the clinical setting, factors such as medication use and multivessel coronary disease may affect ventricular function.

As expected, function within both infarct and noninfarct zones contributed to left ventricular ejection fraction. Because function of the noninfarct zone was not related to the degree of infarct zone dysfunction, remote hyperkinesis may not occur as a compensatory mechanism. Indeed, other studies have not demonstrated a relation between infarct size and noninfarct zone function.\(^{21,22}\) Augmented contractile performance of remote myocardium may relate to increased sympathoadrenergic stimulation,\(^{23}\) neurovascular reflex,\(^{24}\) or regional left ventricular unloading\(^{25}\) independent of infarct size.

The presence of a stenosis of more than 50% in a noninfarct vessel was associated with lack of hyperkinesis of the noninfarct zone. Recent studies have shown that interactions between vascular beds can be quite complex, with occlusion in one bed leading to ischemia in the other.\(^{26-30}\) After occlusion of a coronary vessel in the dog, flow normally increases in the remaining coronary arteries due to an increase in metabolic demand. However, an acute coronary occlusion may impair recruitment of collateral blood flow, thus increasing the relative hemodynamic significance of a stenosis in the noninfarct vessel. This phenomenon may result in "ischemia at a distance" and prevent augmented contraction of remote myocardium. Remote ischemia and lack of compensatory hyperkinesis of the noninfarct zone may be responsible for severe hemodynamic collapse associated with acute myocardial infarction in multivessel coronary artery disease.\(^{12,13,31}\) Indeed, the global impact of acute coronary occlusion may be determined by the extent of coronary disease and its effect on contraction of the noninfarct zone. Thus, early assessment of function in the noninfarct zone may provide useful information regarding the extent of coronary artery disease.

Interestingly, enhanced perfusion of the infarct zone (as assessed by TIMI flow grade) was associated with augmented contraction of remote myocardium. Restoration of flow in the infarct-related artery may allow recruitment of collateral blood flow from the infarct zone to remote myocardium perfused by a stenotic vessel.

Previous studies focusing on late prognosis after myocardial infarction found a relation with predischarge ejection fraction.\(^{6-10}\) We have shown that after an aggressive reperfusion strategy consisting of thrombolysis, angioplasty, and bypass grafting when necessary, survival after hospital discharge is excellent.\(^{32}\) Because the majority of deaths occur within the first few days, we believe it is important to define risk factors during the acute phase of infarction. Our data demonstrated that acute global ejection fraction was associated with in-hospital mortality. However, differences in median ejection fraction between survivors and nonsurvivors was not striking, perhaps limiting one's clinical ability to predict survival. The discrepancy between our study and others may be due to aggressive revascularization (50% underwent coronary angioplasty and 19%
received bypass grafting before follow-up catheterization) or the small sample size of patients who died in our study. Likewise, the analysis of in-hospital rather than long-term survival using acute rather than predischarge ventriculography may alter the relative significance of predictive variables. Although both infarct and noninfarct zones contribute to global ventricular function, only noninfarct zone function significantly predicted in-hospital mortality. Despite successful reperfusion of the infarct-related artery, "stunned" myocardium may result in late recovery of function in the infarct zone. During this period of posts ischemic dysfunction, global ventricular performance appears to be predominately dependent on function in the noninfarct zone. Thus, it is not surprising that mortality and hemodynamic collapse are closely related to noninfarct zone performance. Furthermore, our data suggest that the poor prognosis associated with multivessel coronary artery disease may be due to ischemia within the noninfarct zone (Figure 3). Thus, early assessment of wall motion within the noninfarct zone may provide additional useful information regarding the extent of coronary artery disease and prognosis.

**Improvement in Noninfarct Zone Function at Day 7**

Because function of the noninfarct zone was heterogenous during acute catheterization, it is not surprising that on the average "regression of hyperkinesis" at day 7 was minimal (−0.05 SD/chord). As demonstrated in Figure 4, deterioration or "regression" occurred when the noninfarct zone was initially hypercontractile, conversely improvement occurred when the noninfarct zone was acutely depressed. Serial evaluation of ventricular function after acute myocardial infarction has demonstrated the phenomenon of "regression to the mean," whereby initially high ejection fractions may fall and initially low ejection fractions tend to improve. This phenomenon may in part relate to the changes in noninfarct zone function described in our study.

Recovery in function of the noninfarct zone at day 7 occurred with enhanced perfusion of the infarct zone as evidenced by TIMI flow grade or the use of emergency angioplasty in the infarct artery. The mechanism again may relate to improved collateral perfusion from the infarct artery to the noninfarct zone. Alternatively, limitation of infarct size after recanalization of an occluded coronary artery may allow augmented function of bordering and remote myocardium.21,22 Certainly, complete revascularization with bypass surgery results in enhanced perfusion of both infarct and noninfarct zones. Thus, improved regional or global perfusion may result in greater function in myocardium remote from the area of infarct.

**Limitations**

Use of a single-plane, right anterior oblique ventriculogram may underestimate hyperkinesis of the noninfarct zone. Nevertheless, because ejection fraction was calculated from a right anterior oblique projection, compensatory hyperkinesis of a magnitude sufficient to maintain the ejection fraction should be apparent in the same view. Many of the postulated interactions between infarct and noninfarct perfusion beds may relate to collateral blood flow. Because angiographically visible collaterals may quickly disappear after reperfusion, the status of collateral flow could not be accurately assessed in post-treatment angiograms. Although acute infarct zone function appeared to be of little prognostic importance, measurement of the length of the abnormally contracting segment was not performed. While ejection fraction and noninfarct zone function appeared to be predictive of in-hospital mortality, acute ventriculograms could not be obtained in 13 of 27 (48%) patients who died, limiting the power of assessing the prognostic importance of these findings. Although this problem is frustrating, it is consistent with other clinical trials. Patients who ultimately die are frequently too ill to undergo the careful ventriculography required for research-quality studies. Finally, information regarding a history of previous infarction was not prospectively collected; thus, its effect on noninfarct zone function and ejection fraction could not be assessed.

**Conclusions and Clinical Implications**

Enhanced function of the noninfarct zone during acute ventriculography resulted in preservation of acute ejection fraction and improved prognosis. This phenomenon occurred in the setting of successful reperfusion of the infarct artery and the absence of multivessel coronary disease. Improvement in noninfarct zone function at day 7 is chiefly influenced by the initial level of impairment and is further enhanced by perfusion of the infarct zone (as evidenced by TIMI flow grade and the use of emergency angioplasty) or complete myocardial revascularization by bypass grafting. Early identification of impairment in noninfarct zone function may predict the extent of coronary artery disease and may identify patients at high risk for hemodynamic collapse or death. Because noninfarct zone function and ejection fraction may improve with the use of emergency angioplasty or bypass surgery, development of noninvasive methods to identify high-risk patients who may benefit from emergency angiography and subsequent revascularization would be desirable.

**Acknowledgments**

The authors extend appreciation to Jo Ann Neal and Lynne Cornish for manuscript preparation and to Lynn Harrelson for statistical assistance.
Appendix 1

The TAMI Study Group

University of Michigan: Eric J. Topol, MD (Principal Investigator), William W. O’Neill, MD, Joseph A. Walton, MD, Eric R. Bates, MD, Stephen G. Ellis, MD, M. Anthony Schork, PhD, Eva Kline, RN, BSN, Laura Gorman, RN, BSN, Raymond Worden, BS, Bertram Pitt, MD. Satellite Centers: Foote Hospital, Jackson, Michigan: Gregory Baumman, MD, John Maino, MD, Mary Ann Mengersdon, MD, Constance Doyle, MD, Patricia Lamb, MD, South Macomb Hospital, Warren, Michigan: Stanley Wolfe, MD, Leonard Bayer, DO, Armando Madrazo, MD, Robert Moore, MD.

Duke University: Robert M. Califf, MD (Co-Principal Investigator), Richard S. Stack, MD, Harry R. Phillips III, MD, Tomaoki Hinohara, MD, Robert H. Peter, MD, Ken Morris, MD, Victor Behar, MD, Y. Kong, MD, Charles Simonton, MD, Thomas Bashore, MD, Eric Carlson, MD, Susan Mantell, RN, BS, Jane M. Boswick, MPH.

Riverside Methodist Hospital: Barry S. George, MD, Richard J. Candela, MD, Joanne Dillon, RN, BS, Ramona Masek, RN, BS.

Christ Hospital: Dean J. Kereiakes, MD, Charles W. Abbottsmith, MD, Linda Anderson, RN, BSN, Linda Martin, RN, BSN.

William Beaumont Hospital: Gerald C. Timmis, MD, Renato Ramos, MD, V. Gangadharan, MD, Cindy Tollis, RN, BSN.

Duke University Biostatistical Core Laboratory: Jane M. Boswick, MPH, Lynne Aronson, BS, Kerry L. Lee, PhD, Robert M. Califf, MD.

University of Michigan Core Angiographic Laboratory: Raymond Worden, BS, Cindy L. Grines, MD, Mark Sanz, MD, Eric J. Topol, MD.

Data Monitoring Committee: Mark Hlatky, MD, Daniel B. Mark, MD, MPH, Kerry L. Lee, PhD.

University of Vermont Core Hematology Laboratory: David Stump, MD, Desire Collen, MD, PhD, Dainija Thornton, BS.

References

11. Alexopoulos D, Horwitz SF, Macari M, Slater W, Schleifer S, O’Hara M, Gorlin R: Is regional or global dysfunction the most important prognostic indicator following anterior myocardial infarction (abstract)? J Am Coll Cardiol 1988;11:188A


KEY WORDS * myocardial infarction • ventricular function • tissue-type plasminogen activator • reperfusion
Prognostic implications and predictors of enhanced regional wall motion of the noninfarct zone after thrombolysis and angioplasty therapy of acute myocardial infarction. The TAMI Study Groups.
C L Grines, E J Topol, R M Califf, R S Stack, B S George, D Keretakes, J M Boswick, E Kline and W W O’Neill

_Circulation._ 1989;80:245-253
doi: 10.1161/01.CIR.80.2.245

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1989 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/80/2/245

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the _Permissions and Rights Question and Answer_ document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org/subscriptions/