Postinfarction ventricular septal rupture: the importance of location of infarction and right ventricular function in determining survival

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ABSTRACT Over a 5.5 year period, 1264 consecutive patients with acute myocardial infarction as confirmed by enzyme levels were prospectively identified. Of these, 25 (2%) suffered ventricular septal rupture (pulmonary/systemic flow range 1.5 to 6) 7 ± 7 days after onset of myocardial infarction. Death occurred in 14 patients (56%) and was more common after inferior than anterior myocardial infarction (11 of 15 [73%] vs three of 10 [30%), p < .05). Among 133 variables analyzed, survivors and nonsurvivors were similar with respect to all premorbid clinical characteristics. Infract size as assessed by peak creatine kinase values, shunt size, two-dimensional echocardiographic and hemodynamic indexes of left ventricular function, and extent of coronary disease. Compared with survivors, the nonsurvivors had greater impairment of right ventricular function as determined by a higher two-dimensional echocardiographically derived right ventricular wall motion index (RVWMI) (0.55 ± 0.87 vs 1.70 ± 0.45, p < .001), greater elevation of right ventricular end-diastolic pressure (11 ± 6 vs 17 ± 6, p < .02), and greater mean right atrial pressure (10 ± 6 vs 16 ± 3, p < .01). Of interest, two of the three patients who presented with anterior myocardial infarction and who died had inferiorly extended infarcts and all had abnormal RVWMIs (≥ 1.0). As expected, cardiogenic shock shortly after onset of ventricular septal rupture was associated with a 91% mortality, but was more common after inferior than anterior myocardial infarction (60% vs 20%, p < .05). The mean effective cardiac index was also higher in survivors than nonsurvivors (2.1 ± 0.5 vs 1.2 ± 0.5, p < .001). Finally, multivariate analysis indicated that all nonsurvivors could be identified based on: (1) an effective cardiac index of 1.75 liters/min/m² or less, (2) the presence of extensive right ventricular and septal dysfunction on the two-dimensional echocardiogram, (3) a mean right atrial pressure of 12 mm Hg or more, and (4) early onset of ventricular septal rupture. Thus, our data demonstrate that: (1) mortality is higher when ventricular septal rupture complicates inferior than when it complicates anterior myocardial infarction, (2) survivors can be distinguished from nonsurvivors and the prediction of outcome is highly accurate, and (3) combined right ventricular and septal dysfunction has a substantial impact on prognosis.


VENTRICULAR SEPTAL RUPTURE is a well-recognized but often fatal complication of acute myocardial infarction. Interestingly, many reports have suggested that mortality may be higher when the index myocardial infarction involves the inferior than when it involves the anterior wall.1-7 Others have observed that parameters of left ventricular dysfunction are simi-

lar in survivors and nonsurvivors,8-9 leading some to postulate that right ventricular function is perhaps the major determinant of outcome.8-11 Accordingly, the present study focused on three objectives: (1) to determine if mortality is indeed higher after inferior myocardial infarction, (2) to identify, among 133 clinical, echocardiographic, hemodynamic, and angiographic variables that were recorded, those that distinguish survivors from nonsurvivors, and (3) to investigate the importance of right ventricular function and the role of the interventricular septum on outcome.

Methods

Patient selection. Between February 1979 and June 1984, 5033 consecutive patients who were admitted to the coronary intensive care unit at the University of Virginia Hospital were
prospectively screened. Of these, 1264 patients were identified as having acute myocardial infarction as confirmed by MB-creatine kinase (CK) or lactate-dehydrogenase (LD-1) levels; LD-1 was used only when the time interval between onset of symptoms and admission was sufficiently long to result in the disappearance of MB-CK from the serum. In 25 patients (2%), myocardial infarction was complicated by ventricular septal rupture. In all cases, the diagnosis of postinfarction ventricular septal rupture was documented by oximetry step-up during right heart catheterization, which was performed at the bedside.12

**Clinical and electrocardiographic evaluation.** On admission, a detailed history and physical examination were obtained. Serum CK levels were measured on admission and at 4 hr intervals until peak concentration was established, then daily until a normal level was found. Each patient was assigned by clinical criteria to Killip class I, II, III, or IV.13 For further characterization, the Norris coronary prognostic index14 was calculated for each patient.

During hospitalization, each patient was evaluated daily by at least one staff cardiologist and a research nurse. Complications that were recorded included: recurrent angina pectoris, infarct extension confirmed by a secondary rise in MB-CK, ventricular tachycardia or fibrillation, heart block requiring pacemaker insertion, congestive heart failure, hypotension, mitral regurgitation, right ventricular infarction before onset of ventricular septal rupture,15 and cardiogenic shock, which was diagnosed if the systolic and mean blood pressures were less than 90 and 70 mm Hg, respectively, and there was evidence of end-organ hypoperfusion (i.e., obtundation, oliguria, or peripheral vasoconstriction). All clinical data were recorded with respect to the day after onset of myocardial infarction, the day ventricular septal rupture was suspected and the day its presence was confirmed by oximetry, and, when appropriate, the day left heart catheterization and surgical repair were performed. For patients undergoing surgery, the details of the operation were reviewed with regard to the location and size of ventricular septal rupture, distribution and extent of infarcted myocardium, techniques used for repair, and the number and location of aortocoronary bypass grafts. Each patient was followed until death or hospital discharge. If death occurred, the primary cause was determined.

**Hemodynamic and angiographic evaluation.** All 25 patients underwent right heart catheterization at the bedside as soon as the diagnosis was suspected or on admission if the patient was transferred from another hospital. The diagnosis of ventricular septal rupture was confirmed in each patient by the presence of a step-up in oxygen content from the right atrium to the pulmonary artery. The magnitude of the left-to-right shunt was derived by calculating pulmonary/systemic flow ratios (Qp/Qs) by a standard method.16 A Qp/Qs flow ratio of 1.5 : 1 or greater was considered significant for the purpose of the study. Measurements of cardiac output were obtained by the icd saline thermodilution method in 12 patients and by the assumed Fick method in 13 patients. In the 12 patients in whom thermodilution measurements were obtained, effective forward cardiac index (an estimate of systemic cardiac perfusion) was obtained by dividing the thermodilution cardiac index (pulmonary flow) by the Qp/Qs.

Additionally, all hemodynamic parameters in the 21 patients undergoing left heart catheterization were recorded. In 13 patients requiring intra-aortic balloon counterpulsation, baseline hemodynamic parameters were recorded before insertion of the balloon. Among the 21 patients who underwent left heart catheterization, biplane cine left ventriculograms were obtained in 17. Localization of the site of rupture was possible in 15 patients and corresponded to the electrocardiographic infarct region in all cases. The left ventricular ejection fraction was obtained from the single-plane right anterior oblique projection by calculating systolic and diastolic volumes from digitized perimeters with use of a computer-integrated digitizing pad and the area-length method of Kennedy et al.17 and a grid correction factor for magnification. Left ventricular perimeters were constructed based on the methods of Radford et al.8 The extent, location, and severity of left ventricular segmental wall motion abnormalities were recorded. Finally, adequate simultaneous opacification of the right ventricle via the septal defect during left ventriculography allowed analysis of right ventricular segmental wall motion in 13 patients; this was based on a modification of the method of Fananapazir et al.9 with the use of the left anterior oblique projection alone.

For the 21 patients who underwent selective coronary angiography, the number, location, and severity of obstructive atherosclerotic lesions were recorded. Maximal luminal diameter narrowing for each of the three major epicardial arteries and their branches was estimated visually, with obstructions of 50% or more considered hemodynamically significant. The relative extent of jeopardized myocardium was estimated by the model of Dash et al.18

**Echocardiographic evaluation.** Two-dimensional echocardiographic (2DE) studies were obtained at the bedside in 23 patients when ventricular septal rupture was first suspected or on admission if the diagnosis had already been established at another hospital. A complete ultrasonic examination was performed as previously described19-26 and included parasternal, apical, and subcostal views. All studies thus produced were recorded on half-inch videotape with a Panasonic NV 8200 cassette recorder. These images were then available for display and analysis in a real-time, slow-motion, or single-frame format.

Echocardiographic images of the left ventricle were obtained by recording short- and long-axis scans through the basal, midventricular, and apical regions of the left ventricle. The left ventricular ejection fraction was assessed by methods previously reported from our laboratory.27 For purposes of left ventricular wall motion analysis, a method previously published by our group was used.21 The left ventricle was divided into 11 segments and each segment was graded on a five-point scale: hypokinetic, −1; normal, 0; hypokinetic, +1; akinetic, +2; or dyskinetic, +3. To obtain a measure of overall left ventricular function, a wall motion index was calculated by summing the scores for each segment analyzed and dividing by the number of segments analyzed.23 Thus, a normal left ventricle would have an index of 0, while the theoretical maximum wall motion index would be 3 if all segments were dyskinetic.

Right ventricular systolic function was evaluated in a similar fashion. As illustrated in figure 1, the nonseptal or free wall of the right ventricle was divided into three segments (i.e., base, midwall, and apex). Each segment was graded with the use of the same point scale and method as above. Characterization of regional right ventricular function was based on the amount of inward endocardial excursion and myocardial thickening during systole.21 Overall right ventricular function was assessed by deriving a wall motion index and noting the presence or absence of right ventricular enlargement. Finally, a separate determination of isolated septal function was obtained by summing the scores of the basal and distal anterosepal segments, as depicted in figure 1.

**Clinical follow-up of hospital survivors.** After hospital discharge, survivors were followed by their private physicians, who regulated therapy. No attempt was made to standardize treatment or rehabilitation strategy. Long-term follow-up was obtained by phone contact with the patient or his or her family or private physician. Information obtained included: activity level, recurrence of angina or reinfarction, presence or absence of congestive heart failure, cardiac medications, interim develop-
ment of significant noncoronary illness, or occurrence of cardiac or noncardiac death.

Interpretation of data and statistical analysis. All test data were interpreted by two experienced reviewers without knowledge of patient identity or other test results. In cases of discordant interpretation, a consensus reading with a third observer was used.

Continuous data are recorded as the mean ± SD. To determine differences between means of independent observations, analysis of variance and Duncan’s multiple-range test were used. Discrete or noncontinuous variables were analyzed in contingency tables to determine differences between proportions with appropriate chi-square statistics or Fisher’s exact test for small cell size. Univariate predictors of adverse outcome (nonsurvival) were subjected to Duncan-Walker multiple stepwise discriminant analysis to identify independent variables predictive of nonsurvival.

Results

Our study cohort included 13 men and 12 women with a mean age of 65 ± 9 years (range 44 to 81). In all cases, the index infarction was associated with the development of new pathologic Q waves and involved the inferior wall in 15 and the anterior wall in 10. Death occurred in 14 patients (56%) 14 ± 10 days (range 1 to 41) after onset of myocardial infarction and was due to progressive pump failure in 13. The remaining patient died of postoperative sepsis. Intracoracic balloon counterpulsation was used in 13 patients, nine of whom had cardiogenic shock at the time of insertion of the balloon. In only three of these patients was transient clinical-hemodynamic improvement documented.

Eleven of the 15 patients with inferior myocardial infarction died during hospitalization compared with only three of 10 with anterior myocardial infarction (73% vs 30%, p < .05). As table 1 illustrates, this difference in mortality based on the site of index infarction could not be attributed to poorer left ventricu-

![Diagram of heart with labeled segments]

**FIGURE 1.** Echocardiographic model used for determination of right ventricular (RV) wall motion index and anteroseptal wall motion score from the apical four-chamber view. B = basilar septum; M = mid septum; LA = left atrium; LV = left ventricle; RA = right atrium.

**SCORE CODE**

- 1 = HYPERKINETIC
0 = NORMAL
1 = HYPOKINETIC
2 = AKINETIC
3 = DYSKINETIC

**RV FREE WALL MOTION INDEX = SUM OF FREE WALL SCORES**

\[
\text{SUM OF FREE WALL SCORES} = \frac{\text{NO. SEGMENTS ANALYZED}}{\text{RV FREE WALL MOTION INDEX}}
\]

**TABLE 1**

Pertinent clinical characteristics based on site of index infarction

<table>
<thead>
<tr>
<th></th>
<th>Anterior (n=10)</th>
<th>Inferior (n=15)</th>
<th>p value</th>
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</thead>
<tbody>
<tr>
<td><strong>Premorbid</strong></td>
<td></td>
<td></td>
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<tr>
<td>Age (yr)</td>
<td>65 ± 7</td>
<td>66 ± 10</td>
<td>NS</td>
</tr>
<tr>
<td>Sex (% male)</td>
<td>60</td>
<td>47</td>
<td>NS</td>
</tr>
<tr>
<td>Prior angina or MI (%)</td>
<td>50</td>
<td>33</td>
<td>NS</td>
</tr>
<tr>
<td>Prior CHF (%)</td>
<td>0</td>
<td>7</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>50</td>
<td>47</td>
<td>NS</td>
</tr>
<tr>
<td>NYHA class</td>
<td>1.4 ± 0.7</td>
<td>1.2 ± 0.4</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Before VSD</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Admission Killip class</td>
<td>2.5 ± 1.1</td>
<td>2.7 ± 1.0</td>
<td>NS</td>
</tr>
<tr>
<td>Peak CK (IU/l)</td>
<td>2422 ± 1283</td>
<td>1890 ± 1243</td>
<td>NS</td>
</tr>
<tr>
<td>No. complications</td>
<td>2.3 ± 1.2</td>
<td>2.3 ± 0.9</td>
<td>NS</td>
</tr>
<tr>
<td>Time to VSD (days)</td>
<td>11 ± 9</td>
<td>4 ± 3</td>
<td>&lt; .03</td>
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<tr>
<td><strong>VSD onset</strong></td>
<td></td>
<td></td>
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<tr>
<td>New murmur (%)</td>
<td>100</td>
<td>100</td>
<td>NS</td>
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<tr>
<td>Relative hypotension (%)</td>
<td>70</td>
<td>80</td>
<td>NS</td>
</tr>
<tr>
<td>New or ↑ rales (%)</td>
<td>80</td>
<td>87</td>
<td>NS</td>
</tr>
<tr>
<td>Chest x-ray deterioriation (%)</td>
<td>90</td>
<td>87</td>
<td>NS</td>
</tr>
<tr>
<td>Cardiac shock (%)</td>
<td>20</td>
<td>60</td>
<td>&lt; .05</td>
</tr>
<tr>
<td>Mortality (%)</td>
<td>30*</td>
<td>73b</td>
<td>&lt; .05</td>
</tr>
</tbody>
</table>

**MI** = myocardial infarction; **CHF** = congestive heart failure; **VSD** = ventricular septal rupture.

*Two of three patients who died had extended index MI inferiorly before onset of VSD.

Five of 11 patients who died had right ventricular infarction syndrome before onset of VSD.
lar function as assessed by history and examination on admission, or to more extensive acute infarction. Of interest, two of the three patients with anterior myocardial infarction who died suffered inferior extensions before the development of ventricular septal rupture. Thus, 13 of the 14 patients who died (93%) had inferior wall damage before septal rupture as confirmed by the MB-CK level.

The same variables listed in table 1 were analyzed with respect to hospital survival. No differences between survivors and nonsurvivors were found for any of these variables except inferior location of myocardial infarction (three of 11 [36%] vs 11 of 14 [79%], p = .05), time to onset of ventricular septal rupture (11 ± 9 vs 4 ± 3 days, p < .03), hypotension coincident with or shortly after onset of ventricular septal rupture (five of 11 [45%] vs 13 of 14 [93%], p = .01), and cardiogenic shock (one of 11 [9%] vs 10 of 14 [71%], p = .004). Of the 11 patients who developed cardiogenic shock, nine (82%) had inferior myocardial infarction and two (18%) had anterior myocardial infarction (p = .05). Among the nine patients who developed cardiogenic shock within 24 hr of the onset of ventricular septal rupture, mortality was 100%.

**Hemodynamic and angiographic correlations.** The effective forward cardiac index was significantly lower in nonsurvivors than in survivors (1.2 ± 0.5 vs 2.1 ± 0.5, p < .001). Moreover, 13 of 14 nonsurvivors (93%) had an effective cardiac index of 1.75 liters/min/m² or less and all 13 of these patients died of progressive pump failure. The remaining nonsurvivor with an index of 2.6 died of postoperative sepsis 41 days after acute infarction. In contrast, only two of 11 survivors (18%) had an effective forward cardiac index of 1.75 or less; one of these two patients with a markedly depressed index who survived underwent immediate surgery without left heart catheterization.

The size of the left-to-right shunt as estimated by the Qp/Qs was similar in nonsurvivors and survivors (3.4 ± 1.4 vs 2.8 ± 0.9, p = NS) and in patients with inferior and those with anterior myocardial infarction (3.3 ± 1.4 vs 3.0 ± 1.1, p = NS). Those who died during hospitalization were similar to survivors with respect to parameters of left ventricular function (figure 2), including ejection fraction (42% vs 45%, p = NS), end-diastolic pressure (24 vs 22 mm Hg, p = NS), the echocardiographically derived wall motion index (0.78 ± 0.4 vs 0.83 ± 0.4, p = NS), and pulmonary capillary wedge pressure (23 vs 21 mm Hg, p = NS).

When the 21 patients who underwent coronary angiography were compared, the 11 nonsurvivors could not be distinguished from the 10 survivors based on either the extent or distribution of coronary disease. These two groups were similar with respect to the prevalence of multivessel disease (64% vs 70%, p = NS), the number of vessels with 50% or more stenosis (1.8 ± 0.8 vs 1.9 ± 0.7, p = NS), and the amount of myocardium judged to be at risk by the Dash jeopardy score (4.9 ± 3.4 vs 6.8 ± 3.2, p = NS). These same variables were analyzed based on the site of index infarction and no differences were found between the patients with inferior and those with anterior myocardial infarction.

**Assessment of right ventricular function.** Twenty-three of our 25 patients (92%) had abnormally elevated right atrial and right ventricular end-diastolic pressures. However, mean right atrial and right ventricular end-diastolic pressures were significantly higher in the 14 nonsurvivors than the 11 survivors (16 ± 3 vs 10 ± 6 mm Hg, p < .01; 17 ± 6 vs 11 ± 6, p = .019). Importantly, these differences could not be attributed
to higher pulmonary arterial pressure in the nonsurvivors. The nonsurvivors had pulmonary systolic (51 ± 14 vs 45 ± 10, p = NS), mean (32 ± 5 vs 30 ± 7, p = NS), and diastolic pressure measurements (22 ± 4 vs 23 ± 6, p = NS) similar to those in survivors. In figure 3, the mortality risk based on the combination of mean right atrial pressure and effective forward cardiac index is shown. In all 25 patients, both measurements were obtained at the bedside shortly after ventricular septal rupture was first suspected. As can be seen, mortality was 100% for the 12 patients with a right atrial pressure of 12 mm Hg or more and an effective cardiac index of less than 1.75 liters/min/m².

Significant differences between groups were also noted when echocardiographic parameters of right ventricular dysfunction were assessed (figure 4). Among the 23 patients who underwent complete 2DE examinations, only six (26%) demonstrated normal (n = 1) or hyperkinetic (n = 5) free wall function and one (4%) showed mild impairment. Of interest, all seven of these patients survived. By comparison, 12 of the 16 patients (75%) with moderate or severe right ventricular dysfunction (i.e., wall motion index ≥ 1.0) died and 11 of these deaths were due to progressive pump failure. Finally, nonsurvivors had a higher 2DE-derived right ventricular wall motion index than survivors (1.7 ± 0.5 vs 0.6 ± 0.9, p < .001).

When mortality risk was assessed on the basis of the right ventricular free wall index and anteroseptal wall motion scores, several observations suggested an important relationship between these two parameters (figure 5). Among the eight patients with significant impairment of both right ventricular and anteroseptal function (right upper quadrant), the mortality was 100%. In contrast, none of the seven patients with hyperkinetic (n = 5), normal (n = 1), or only minimally abnormal (n = 1) right ventricular function died (right lower quadrant), despite markedly impaired septal contractility. In these seven patients, the anteroseptal dysfunction was attributed to anterior infarction. Lastly, among the eight patients (left upper quadrant) who suffered inferior myocardial infarction, all of whom had substantial right ventricular dysfunction by echocardiography, the overall mortality was 50%. All four survivors in this group had hyperkinetic anteroseptal function, whereas the four nonsurvivors demonstrated either normal (n = 2) or impaired (n = 2) septal contractility.

When assessment of right ventricular function was restricted to the inferior infarction group, significant differences between survivors and nonsurvivors were also evident. Specifically, subset analysis revealed

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**FIGURE 3.** Mortality rates based on cardiac index and mean right atrial (RA) pressure.

**FIGURE 4.** Echocardiographic (2DECHO) right ventricular (RV) wall motion index in survivors and nonsurvivors. Percentages represent the overall mortality rate based on the presence or absence of significant RV dysfunction. Group data are represented as mean ± SEM.
that the 11 nonsurvivors, compared with the four survivors, had a significantly higher mean right atrial pressure (16 ± 3 vs 9 ± 4 mm Hg, p < .004), higher right ventricular end-diastolic pressure (16 ± 4 vs 10 ± 4 mm Hg, p < .02), and, importantly, a higher mean peak CK level (2109 ± 1326 vs 1090 ± 179 IU/liter, p = .03). Additionally, nonsurvivors had a significantly lower mean effective forward cardiac index (1.2 ± 0.6 vs 2.0 ± 0.7 liters/min/m², p < .05).

Surgical observations and follow-up. Operative repair was undertaken in 22 patients 9 ± 12 days after onset of ventricular septal rupture (21 were via an left ventricular incision with infarctectomy, and one was through an right ventricular incision). None of these patients required mitral valve repair or replacement for significant mitral regurgitation. The extent of revascularization, as determined by the number of aortocoronary bypass grafts, was similar between survivors and nonsurvivors. Routine clinical and hemodynamic monitoring, e.g., Swan-Ganz catheter measurements, after surgery revealed no evidence of unsuccessful closure of the ventricular septal rupture.

Thirteen of the 22 surgically treated patients had suffered inferior myocardial infarction and nine had anterior myocardial infarction, including one with subsequent inferior wall extension. Overall mortality was 50%, but was higher in the inferior than the anterior myocardial infarction group (9/13 [69%] vs 2/9 [22%], p = .04). Cardiogenic shock was present in eight patients before surgery, seven of whom had suffered inferior wall myocardial infarction. As might be expected, mortality was greater in the eight patients with preoperative shock than in the 14 without shock (7/8 [88%] vs 4/14 [29%], p = .01). Operative repair was not undertaken in three patients; two had inferior myocardial infarction and one had anterior myocardial infarction with subsequent inferior wall extension. All three of these patients were in cardiogenic shock and died within 2 weeks of onset of septal rupture as a result of myocardial failure. Eleven of the 22 patients who underwent operative repair had surgery within 24 hr of ventricular septal rupture; in all 11 cases, the decision to perform emergency repair was based on parameters of hemodynamic instability. Nine of these 11 patients (82%) died, including one of three (33%) with anterior myocardial infarction and eight of eight (100%) with inferior infarction (p = .05).

As a group, the surgical survivors underwent operative repair much later after acute infarction than the nonsurvivors (27 ± 12 vs 5 ± 4 days, p < .001). Among the 14 patients who underwent surgery within 21 days of myocardial infarction, there were 11 deaths, for a mortality rate of 79%. Eight patients had sufficiently stable courses to permit elective late operative

FIGURE 5. Mortality rates based on the presence or absence of significantly abnormal RV function (horizontal dotted line) and elevated anteroseptal wall motion score (vertical dotted line) by two-dimensional echocardiography (2DECHO). The crosshatched regions indicate normal values. See text for details.
repair (i.e., >21 days) and no hospital deaths occurred in this group.

During a mean follow-up of 43 ± 20 months (range 21 to 75), only one death among the 11 hospital survivors was recorded. This occurred 12 months after discharge and was sudden. Of the remaining 10 patients, one reported symptoms of stable angina pectoris, three indicated intermittent symptoms of congestive heart failure, and one was receiving amiodarone for recurrent ventricular tachycardia. There were no enzyme-confirmed reinfections and all patients were NYHA class II or less.

**Multivariate analysis for prediction of outcome.** Among the 133 clinical, 2DE, hemodynamic, and angiographic variables, univariate analysis identified 33 that were predictive of nonsurvival. To eliminate redundant or interrelated information, these univariate predictors of outcome were subjected to stepwise discriminant function analysis. This technique sequentially assesses the independent predictive effect of each variable, including the most important, then reassesses the remainder until all important variables have been identified. As table 2 illustrates, this multivariate regression analysis identified four independent predictors of nonsurvival. When these four variables were considered, all 25 patients were correctly classified as survivors or nonsurvivors. Importantly, the 22 patients who underwent surgery would have been properly classified as either survivors or nonsurvivors before surgery was undertaken.

**Discussion**

**Historical perspective.** Ventricular septal rupture complicates 1% to 3% of all infarctions and reportedly accounts for 5% of all peri-infarction deaths. When medical therapy alone is used, most patients deteriorate rapidly and 25% die from cardiogenic shock within 24 hr. Since few patients have heart failure that is mild enough to permit substituting medical treatment for surgical repair, it is not surprising that the mortality approaches 90% at 2 months in medically managed patients. Even if surgical repair is carried out promptly, the mortality in patients with ventricular septal rupture remains high, especially when rupture complicates inferior wall infarction. The explanation for this unexpectedly poor surgical outcome after inferior myocardial infarction is not clear. In part, this is because comprehensive analyses of clinical and hemodynamic data from consecutive patient series are few, most previous studies are retrospective and involve chart reviews, and published reports conflict. Several studies have shown that the clinical status of the patient rather than the timing of surgery or technical failure represents the dominant factor determining outcome. Furthermore, recent autopsy data indicate that ruptures associated with inferior myocardial infarction are more complex and may pose greater surgical challenges.

**Clinical, hemodynamic, and functional correlates of outcome.** Our data demonstrate that ultimate outcome was not primarily related to infarct size as estimated by peak CK levels, the degree of left ventricular dysfunction, the amount of left-to-right shunting, or the severity of underlying coronary artery disease. A significant difference, however, was noted between survivors and nonsurvivors in effective forward cardiac index. Specifically, nonsurvivors were much more likely to have values of 1.75 liters/min/m² or less. This categorical index of biventricular pump performance was highly correlated with impending or frank preoperative cardiogenic shock, and ultimately with more severe preoperative multisystem failure culminating in irreversible end-organ damage. Moreover, an effective cardiac index of 1.75 liters/min/m² or less proved to be the single most powerful predictor of nonsurvival.

**Influence of infarct location and right ventricular function on survival.** In agreement with our original hypothesis, we found that inferior infarction complicated by ventricular septal rupture was associated with a higher mortality. Compared with patients with anterior infarction, more patients with inferior myocardial infarction had an effective cardiac index of 1.75 or less after onset of ventricular septal rupture (40% vs 73%), and more developed cardiogenic shock. In the absence of obvious technical factors precluding a successful operative repair and outcome, our data provide strong hemodynamic, angiographic, and echocardiographic evidence to support a causal relationship between right ventricular dysfunction, a markedly depressed cardiac index, and the excess mortality in the inferior myocardial infarction group.

The present study is the first to demonstrate in a consecutive series of prospectively identified patients a significant difference in right ventricular hemodynamics in survivors and nonsurvivors of ventricular

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**TABLE 2**

<table>
<thead>
<tr>
<th>Variable</th>
<th>p value</th>
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</thead>
<tbody>
<tr>
<td>(1) Cardiac index ≤1.75 l/min/m²</td>
<td>.0001</td>
</tr>
<tr>
<td>(2) Right ventricular free wall-septal motion index ≥1.0</td>
<td>.0029</td>
</tr>
<tr>
<td>(3) Right atrial pressure ≥12 mm Hg</td>
<td>.0094</td>
</tr>
<tr>
<td>(4) Ventricular septal rupture onset ≥6 days</td>
<td>.0100</td>
</tr>
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</table>

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septal rupture. Although the majority of our patients demonstrated elevated right heart filling pressures, nonsurvivors had significantly higher mean right atrial and right ventricular end-diastolic pressures. Furthermore, this notable difference could not be explained by the size of the left-to-right shunt, measures of right ventricular afterload, or clinically recognized tricuspid regurgitation. Failure of prior studies to note this finding may be explained by the fact that right atrial and right ventricular pressures were not recorded in a large majority of patients. For example, Radford et al. did not observe a difference in right heart filling pressures in survivors and nonsurvivors, but these measurements were made in only 36% of nonsurvivors and 23% of those with cardiogenic shock. The importance of the differences in right heart filling pressures that were observed in the present study is strengthened by our echocardiographic findings of greater right ventricular segmental dysfunction among nonsurvivors (figure 4).

If the higher mortality observed among patients with ventricular septal rupture and inferior infarction is due mainly to severe right ventricular dysfunction, rather than greater left ventricular dysfunction, then it is logical to expect that nonsurviving patients might show evidence of more extensive right ventricular infarction. Indeed, compared with the four survivors with inferior infarction, the 11 nonsurvivors had a significantly lower mean effective forward cardiac index, higher right ventricular filling pressures, and a larger infarct size as determined by peak CK levels. Moreover, the four survivors of inferior infarction all demonstrated preserved function of the anterior right ventricular free wall on contrast opacification of the right ventricle during left ventriculography in the left anterior oblique projection. Also, three of these four patients who survived ventricular septal rupture demonstrated right coronary artery occlusion at or distal to the acute margin with preserved circulation to the anterior free wall of the right ventricle via moderate- to large-caliber right ventricular branches.

Our data suggest that right ventricular dysfunction is not limited exclusively to patients with inferior infarction since all three of our patients with anterior myocardial infarction who died had echocardiographic evidence of significant right ventricular dysfunction. It is important to note, however, that two of these three patients had inferior wall extensions before onset of septal rupture. Since the left anterior descending artery can supply up to 33% of the right ventricular myocardium and is a prime source of collateral supply to the right ventricle in patients with atherosclerotic right coronary artery lesions, patients with anterior infarc-
tion and necrosis extending beyond the primary laceration of the ventricular septum. Of interest, 80% of all complex ruptures occurred in patients with inferior infarction. Furthermore, among patients with inferior infarction, 69% of ruptures were complex as opposed to only 21% of those in patients with anterior infarction. While echocardiographic distinction between complex and simple ruptures may not be possible, the demonstration of more severe septal dysfunction (remote from the perforation) observed in nonsurvivors may be a reflection of more extensive myocardial disruption, with hemorrhage into neighboring tissue from complex ruptures leading to contractile dysfunction.

Interaction and interdependence of the right ventricle and interventricular septum has been demonstrated in canine preparations. Whereas cauterization of the free wall of the right ventricle alone does not produce a significant impairment of right-sided circulation, exclusion of the entire right ventricular free wall and interventricular septum uniformly results in death. The similarity between this experimental preparation and the clinical condition of septal rupture with extensive myocardial disruption and right ventricular dysfunction would seem to allow analogous conclusions to be drawn.

Surgical considerations. The role, technique, and timing of surgery after ventricular septal rupture was not a primary subject of our investigation. Nevertheless, our data do support an inverse relationship between the timing of surgery and mortality. They also indicate that the high mortality associated with early closure of the ventricular septal rupture is directly related to the physiologic status of the patient rather than to timing of surgery per se. The unselected and consecutive nature of our study cohort would seem to eliminate any bias derived from determining surgical candidacy on the basis of natural selection that results from delaying surgery for 6 to 8 weeks.

Despite our aggressive surgical approach employing early repair of the defect and revascularization of diseased coronary arteries, mortality was still quite high. In view of our foregoing discussion, refractory pump failure due to right ventricular dysfunction rather than obvious technical failure seems to account for this high mortality, especially among the 15 patients with inferior or infarction. While we cannot exclude the possibility that operative repair per se placed an increased hemodynamic burden on the right ventricle, it is noteworthy that traditional surgical techniques were employed in our cohort, i.e., 95% of the repairs were via a left ventricular incision, and postoperative assessments revealed no evidence of residual ventricular septal rupture. We should also emphasize that the parameters listed in table 2 would have identified all cardiac deaths before surgery. Thus, although the high perioperative mortality among patients with inferior myocardial infarction may be related to the greater surgicoanatomic challenge in repairing inferoposterior defects, our data and those of others indicate that mortality remains high despite successful closure of the ventricular septal rupture. Moreover, only a minority of reported surgical deaths have been attributed to technical failure alone.

To our knowledge, there are insufficient data that clearly establish improved overall survival with surgery among the subgroup of elderly patients with inferior myocardial infarction, preoperative shock, and multisystem failure. While we cannot presume to dictate surgical practice, application of the preoperative criteria in table 2 should serve to identify a patient population at extremely high risk for subsequent death with or without surgery, thereby providing the physicians attending the patient and family with a realistic prediction of subsequent outcome. Given this information, an aggressive and costly surgical approach may not be prudent in all cases and will require individualization to each situation. If surgical repair is planned in the critically ill patient, it should be performed without undue delay to avoid further multisystem deterioration. Whether left heart catheterization, ventriculography, and coronary angiography are mandatory preoperatively is controversial and remains unproven. Although the trend has been toward complete revascularization, documentation that this results in improved survival is lacking.

Methodologic considerations. While our data indicate a significantly lower overall mortality in patients with ventricular septal rupture complicating anterior infarction, which we have attributed to the lower incidence of right ventricular dysfunction, we cannot exclude the possibility that, as a result of the tertiary nature of our clientele, a significant number of patients with septal rupture and anterior infarction suffer early deaths at outside hospitals as a result of overwhelming extensive left ventricular dysfunction. However, the consecutive nature of the study cohort probably reflects that our population is similar to those of other surgical referral centers and makes our conclusions no less applicable to comparable patient populations.

Several possibly important variables were not included in our analysis, e.g., pump time, timing of surgery, and measurements of right and left ventricular function during the early postoperative period. While current surgical techniques that involve left ventricular
incision and infarctectomy may place an increased burden on the right ventricle or further compromise overall pump function, the preoperative parameters listed in table 2 should serve to identify a subset of patients in whom traditional operative techniques fail to reverse a highly fatal preoperative scenario.

Clinical implications. In summary, ventricular septal rupture that complicates inferior wall infarction is associated with a very high mortality. Based on information that is readily obtainable at the bedside, nonsurvivors can be identified, and the prediction of outcome is highly accurate, when the following variables are considered: (1) an effective forward cardiac index of 1.75 liters/min/m² or less, (2) echocardiographic evidence of significant right ventricular and septal dysfunction as evidenced by an abnormal right ventricular wall motion index of 1.0 or greater and an elevated septal wall motion score, (3) a mean right atrial pressure of 12 mm Hg or more, and (4) the early occurrence (i.e., ≤6 days) of ventricular septal rupture after onset of infarction. Although a cardiac index of 1.75 liters/min/m² was found to be the most powerful predictor of death, this hemodynamic measure of biventricular pump performance appears unrelated to left ventricular infarct size, parameters of left ventricular dysfunction, or shunt size. Conversely, the presence of right ventricular dysfunction and extensive septal dysfunction are closely linked to this measure of severe myocardial failure and have a substantial impact on mortality risks. Therefore, the interaction, interdependence, and function of the right ventricle and interventricular septum appear to be important determinants of ultimate outcome in the setting of postinfarction ventricular septal rupture.

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