Quantitative analysis of right and left ventricular infarction in the presence of postinfarction ventricular septal defect

ROBIN G. CUMMINGS, M.D., KEITH A. REIMER, M.D., PH.D., ROBERT CALIFF, M.D., DONALD HACKEL, M.D., JANE BOSWICK, M.S., AND JAMES E. LOWE, M.D.

ABSTRACT To quantitate the amount of right and left ventricular infarction in patients dying with postinfarction ventricular septal defect (PIVSD), hearts from 54 patients with anterior or inferior myocardial infarction were studied at autopsy. Fifteen hearts had myocardial infarction with PIVSD and 39 hearts had infarction without PIVSD and were used as a comparison group. All infarcts were sized histologically and the percent of each ventricle infarcted was quantitated by computer-assisted planimetry. The pathologic substrate for PIVSD was diffuse coronary artery disease with acute thrombosis resulting in transmural confluent infarction. Within the PIVSD group, there was significantly more left ventricle involved in anterior infarctions than in inferior infarctions (p<.04). Conversely, there was more right ventricular infarction in inferiorly located myocardial infarctions with resulting PIVSD (p = .059). When infarctions resulting in PIVSD were compared with infarctions not resulting in PIVSD, the PIVSD group was characterized by larger left and right ventricular infarcts irrespective of infarct location (p<.003). The incidence of right ventricular infarction was 100% in the PIVSD group (p<.0001). Twelve of the 15 patients with PIVSD (80%) developed cardiogenic shock within 48 hr of septal rupture. The high incidence of shock and the rapid deterioration may have been secondary to right ventricular infarction in these patients. Therefore, infarcts resulting in PIVSD and subsequent death are characterized by a high incidence of right ventricular infarction. Significantly more infarction of the right ventricle is seen in either anterior or inferior infarctions resulting in PIVSD compared with infarctions not resulting in PIVSD. PIVSD complicating inferior infarctions is associated with the greatest amount of right ventricular infarction.


MANY FACTORS, both in the clinical management and pathophysiology of postinfarction ventricular septal defect (PIVSD) have been postulated to affect subsequent outcome. Clinically, those patients who develop cardiogenic shock after ventricular septal rupture and those patients with inferior infarction by electrocardiogram have been noted to have a higher mortality.1-4 Postmortem studies have noted factors important in PIVSD to be first infarction, transmural infarction, complete and sudden occlusion of a coronary artery, limited collateral blood flow, alterations of septal geometry, infarct extension, and left ventricular hypertrophy.5-11 The importance of right ventricular infarction on subsequent outcome has only recently been recognized.2, 3, 12-15

The present study investigated the clinical and pathologic findings in a series of patients with PIVSD and determined, in a quantitative fashion, the amount of right and left ventricular infarction in patients dying with postinfarction ventricular septal rupture. The association of right and left ventricular infarction was further characterized by comparison with a group of infarcts not resulting in PIVSD.

Methods

Patient selection. From 1969 to 1984, a total of 1023 hearts of adult patients dying from a variety of causes were submitted to the Cardiovascular Pathology Laboratory at Duke University. A retrospective review resulted in a total study group of 13 hearts (1.3%) with the diagnosis of PIVSD. The original pathology reports and medical records of these patients were reviewed to determine pathologic findings, medical history, and clinical course.

All hearts were examined by a routine that began with weigh-
ing and x-ray ing on receipt in the Duke Cardiovascular Pathology Laboratory. The coronary arteries were cannulated and injected with a barium-gelatin mixture and the hearts again x-rayed. The arteries were then cut at 2 mm intervals and examined grossly, and cross sections were taken for histologic examination at marked points of narrowing.

Quantitation of infarct size. Cross sections of the ventricles were made from apex to base, resulting in four to five transverse slices of approximately equal thickness. To quantitate infarct size, the basal aspect of each of these slices was photographed. A thin section was then taken from the apical surface of each slice so as to encompass the entire circumference of the ventricles. The tissues were embedded in paraffin and 6 μm thick sections were stained with Masson’s trichrome stain. An average of nine blocks was required to process each of the circumferential slices for microscopic examination. The histologic slides were then compared with the photograph of the adjacent basal surface of each subsequent slice. Based on the combined gross and microscopic appearances, the outline of each infarct was drawn on the photograph of the heart slices. For old infarcts, a correction was made for loss of infarct mass due to the removal of necrotic muscle, as evidenced by wall thinning. In regions where the infarct was patchy, an estimate of the amount of infarcted myocardium was made to the nearest 25%. Subsequently, tracings of the photographs of each heart slice with the outlined boundaries of the infarct were drawn on an x-y digitizer coupled to a DEC-Vax 11-80 for calculation of the percentage of the left and right ventricular myocardium infarcted.16

Generation of comparison group. To further characterize the amount of right and left ventricular infarction in PIVSD, a comparison group of hearts was examined. Our pathology laboratory had received 74 hearts through cooperation in the Multicenter Investigation of the Limitation of Infarct Size (MILIS) clinical trial. Patients enrolled in the MILIS study had electrocardiographic, clinical, and enzymatic evidence of myocardial infarction. After death, either following the initial infarction or after subsequent infarctions, all hearts from enrolled patients were submitted to our laboratory for detailed autopsy and infarct sizing. Two of the hearts had a PIVSD and were included with the 13 hearts originating from within our institution. Within the MILIS group, hearts excluded from further analysis included: nine from patients with combined infarctions involving both anterior and inferior locations, one from a patient with aortic valvular stenosis, five from patients with left ventricular wall rupture, and 18 from patients with infarctions that were nonconfluent, patchy, and difficult to ascribe to one major coronary artery distribution. Thus, a total of 39 hearts were available to serve as a comparison group to 15 hearts with postinfarction septal rupture. In all cases of PIVSD, there was no pathologic evidence of previous infarction. Therefore, analysis of right and left ventricular infarct size in the comparison group was limited to first infarctions to avoid possible interference in the eventual size of later infarctions from previous infarctions and to characterize only infarctions resulting in PIVSD and infarctions not resulting in PIVSD.

Statistical analysis. Included in the analysis were 15 patients with PIVSD and 39 patients without PIVSD. The Wilcoxon Mann-Whitney two-sample test was used as a nonparametric tool for evaluation of the relationship observed within and between groups. Unless otherwise noted, values are expressed as the mean ± SD.

Results

Clinical findings. There were 15 patients included in the PIVSD group: seven men and eight women with a mean age of 65 years (51 to 75 years). Premorbid history was significant for a history of hypertension in nine patients, adult-onset diabetes mellitus in two patients, cigarette smoking in nine patients, and angina in three patients. There was no history of previous myocardial infarction or congestive heart failure in any patient. Seven patients were medically treated and eight patients had undergone surgery. Medical treatment was elected in seven patients because deterioration was rapid and the opportunity for surgical intervention was not available or patients were transferred to our facility late in the course of their illness and surgical therapy was believed to be inappropriate. The location of infarction by electrocardiography and subsequently confirmed at autopsy was anterior in eight patients and inferior in seven patients.

The median time from infarction to appearance of PIVSD was 2 days. One patient developed ventricular septal rupture within 4 hr of the onset of pain and electrocardiographic changes marking his infarction. The latest appearance was at 13 days after infarction. Fourteen of the 15 patients (93%) developed a holosystolic murmur that marked the appearance of septal rupture. All patients were diagnosed by Swan-Ganz oximetry with O2 step-up at the bedside. Seven of 15 patients (47%) had associated thrills with their murmurs. Ten of 15 patients (67%) had recurrent chest pain at the time of murmur appearance. Six patients developed new electrocardiographic changes after PIVSD including: first-degree block (one patient), second-degree block (three patients), right bundle branch block (one patient), and left bundle branch block (one patient).

For the most part, every patient’s course consisted of a stable period before PIVSD followed by a rapid and progressive deterioration in hemodynamic status after PIVSD. Fourteen of 15 patients (93%) experienced shock after the appearance of PIVSD (figure 1). Shock was defined as: (1) systolic blood pressure less than 80 mm Hg or mean arterial pressure less than 60 mm Hg, with evidence of end-organ hypoperfusion (obtundation, decreased urine output, elevated creatinine or BUN, cool clammy skin) or (2) the requirement for mechanical or pharmacologic interventions to maintain blood pressure and end-organ perfusion. With the appearance of a new holosystolic murmur, all patients developed relative hypotension involving a 10 mm Hg or greater drop in systemic blood pressure. Seven patients went on to develop shock within 24 hr after PIVSD, with an additional five patients developing shock over the following 24 hr. One patient developed shock after 4 days and an additional patient at 67 days. Therefore, 12 of 15 patients, or 80%, developed shock within 48 hr of the appearance of PIVSD.
Pathologic findings. The mean value of the greatest diameter of ventricular septal rupture was 1.7 cm, with a range of 0.3 to 4 cm (table 1). The mean size in anterior locations was 1.5 cm compared with a mean size of 1.8 cm in inferiorly located infarctions.

In each of the eight patients operated on, the repaired septal ruptures were found to be closed. In two patients, however, a new septal defect was found that occurred in a different area of the interventricular septum than the initial septal rupture. In a third patient, there was dissection by blood through the septum just beyond the suture line, suggesting a second rupture was imminent at the time of death. Thus, of eight patients undergoing surgery, three (38%) demonstrated evidence of recurring interventricular septal rupture at the time of death despite adequate surgical closure of the original defect. All three patients were operated on within 24 hr of VSD appearance.

Coronary artery disease. In all patients in the PIVSD group, occlusion of a single major coronary artery resulted in infarction of tissue within the distribution of the occluded vessel. Inferior myocardial infarction resulted from occlusion of the right coronary artery, while anterior myocardial infarction resulted from occlusion of the left anterior descending artery. All but one heart had a right dominant coronary artery distribution. Fourteen hearts showed infarction resulting from acute thrombotic occlusion superimposed on significant (>75% stenosis) coronary artery disease (table 1).

Overall coronary artery disease in these patients was extensive. One patient (5) had an anterior infarction with only a 50% narrowing of the left anterior descending coronary artery (LAD) and one patient (6) had significant disease limited to one major coronary artery. The remaining 13 patients had either one-vessel disease with 50% or more involvement of the remaining two vessels (two patients), two-vessel disease with involve-

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Infarct location</th>
<th>Size of VSD (cm)</th>
<th>Heart weight (g)</th>
<th>Coronary artery disease (% stenosis)</th>
<th>Infarct size (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Anterior</td>
<td>1.5</td>
<td>557</td>
<td>LM 25 95^ a 75 35</td>
<td>26.0 2.8</td>
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<tr>
<td>2</td>
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<td>2.0</td>
<td>476</td>
<td>LAD 75 75^ a 75</td>
<td>b b</td>
</tr>
<tr>
<td>3</td>
<td>Inferior</td>
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<td>454</td>
<td>RCA 90^ a 95</td>
<td>22.3 71.1</td>
</tr>
<tr>
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<td>Inferior</td>
<td>4.0</td>
<td>700</td>
<td>LCX 95 75^ a 95</td>
<td>13.9 22.0</td>
</tr>
<tr>
<td>5</td>
<td>Anterior</td>
<td>4.0</td>
<td>483</td>
<td>Anterior 50 —</td>
<td>31.1 23.9</td>
</tr>
<tr>
<td>6</td>
<td>Anterior</td>
<td>1.0</td>
<td>321</td>
<td>Anterior 95^ a —</td>
<td>18.4 4.9</td>
</tr>
<tr>
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<td>Anterior</td>
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<td>436</td>
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<td>b b</td>
</tr>
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<td>663</td>
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<td>31.5 26.2</td>
</tr>
<tr>
<td>9</td>
<td>Anterior</td>
<td>0.5</td>
<td>375</td>
<td>Anterior 95^ a 65 50</td>
<td>26.4 16.6</td>
</tr>
<tr>
<td>10</td>
<td>Inferior</td>
<td>1.0</td>
<td>509</td>
<td>Anterior 95^ a 95 90</td>
<td>22.0 41.2</td>
</tr>
<tr>
<td>11</td>
<td>Anterior</td>
<td>0.3</td>
<td>323</td>
<td>Anterior 95^ a 85 25</td>
<td>39.5 11.4</td>
</tr>
<tr>
<td>12</td>
<td>Anterior</td>
<td>1.0</td>
<td>573</td>
<td>Anterior 95^ a 75 75</td>
<td>36.6 2.4</td>
</tr>
<tr>
<td>13</td>
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<td>23.0 1.3</td>
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<td>14</td>
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<td>310</td>
<td>Anterior 80 80^ a 80</td>
<td>15.1 26.5</td>
</tr>
<tr>
<td>15</td>
<td>Anterior</td>
<td>2.5</td>
<td>620</td>
<td>Anterior 95^ a 99 85</td>
<td>48.0 7.0</td>
</tr>
</tbody>
</table>

LM = left main coronary artery; LCX = left circumflex artery; LV = left ventricle; RV = right ventricle.

^Complete occlusion by thrombus.

bNot specified.
ment of both the LAD and right coronary artery (RCA) (three patients), or three-vessel disease (eight patients). The distribution of coronary artery disease was such that in the 11 patients with significant two- or three-vessel disease, the coronary artery that potentially would have supplied collateral flow to the area of infarction was involved by significant disease. In two additional patients, the system opposite the infarction had 50% or greater stenotic lesion. None of the patients had significant left main disease and none had isolated RCA disease.

Quantitation of right and left ventricular infarction in PIVSD. In the 15 patients with PIVSD, accurate quantitation of left ventricular and right ventricular myocardium involved by infarction was determined as previously described. Two hearts were not used because of inadequate preservation. In the remaining 13 hearts, the percentage of left ventricle involved by infarction ranged from 13.9% to 48.0%, with a mean value of 27.2 ± 9.1% (table 1). The percentage of right ventricle involved by infarction ranged from 1.3% to 71.1%, with a mean value of 19.8 ± 19.5%.

The amount of left and right ventricular infarction examined relative to infarct location is summarized in figure 2. In anterior infarcts with complicating septal rupture 32.3 ± 9.9% of the left ventricle was involved by infarction, and 9.9 ± 8.0% of the right ventricle was involved. In inferior locations, 21.3 ± 6.3% of the left ventricle was infarcted with 31.4 ± 23.3% of the right ventricle involved. The percentage of left ventricle involved by infarction in anterior locations was significantly greater than the percentage associated with inferior locations (p<.04). Conversely, inferiorly located infarctions, although involving a smaller amount of left ventricle, involved a much larger amount of right ventricular myocardium (p = .059). In all cases, infarction of the anterior right ventricle was associated with left ventricular anterior wall infarction, while infarction involving the posterior right ventricle was associated with inferior wall infarction of the left ventricle.

Comparison of right and left ventricular infarct size in hearts with and without PIVSD. To further investigate the question of infarct size as well as right ventricular involvement in PIVSD, a comparison group (table 2) of hearts was analyzed for specific differences. In both groups, each heart had evidence of at least one myocardial infarction. In all hearts in the PIVSD group there was evidence of one infarction with septal rupture and ensuing death. In contrast, within the comparison group, 27 of 39 hearts (69%) had pathologic evidence of more than one infarction.

The distribution of location of infarction in the two groups was comparable (table 3). All infarcts in the PIVSD group were transmural, confluent, and predominantly in the distribution of one major coronary artery, either the RCA or LAD. In contrast, only 77% of infarcts in the comparison group were transmural.

![Figure 2](http://circ.ahajournals.org/)

**TABLE 2**

<table>
<thead>
<tr>
<th>Baseline characteristics of PIVSD and comparison groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
</tr>
<tr>
<td>-----</td>
</tr>
<tr>
<td>65</td>
</tr>
<tr>
<td>60</td>
</tr>
<tr>
<td>60</td>
</tr>
<tr>
<td>13</td>
</tr>
<tr>
<td>Coronary artery disease (%) with disease indicated</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>1 vessel</td>
</tr>
<tr>
<td>2 vessel</td>
</tr>
<tr>
<td>3 vessel</td>
</tr>
<tr>
<td>Left main</td>
</tr>
</tbody>
</table>

The PIVSD group differed from the comparison group in two ways. There was a higher percentage of women with PIVSD. In addition, 50% of the comparison group had a history of adult-onset diabetes mellitus, while only 13% of the PIVSD group had a history of diabetes. Overall, prevalence of coronary artery disease was similar in the two groups, with the exception of a higher percentage of left main disease within the comparison group.
Because hearts considered for inclusion in the comparison group were eliminated if infarctions were patchy and nonconfluent or were evenly distributed between the anterior and inferior positions, i.e., anterior-inferior location, infarcts in both groups were similar in these respects.

The percentage of left ventricular infarctions in hearts with PIVSD, without reference to location, was 27.2 ± 9.1% (table 3). In the comparison group, the mean percent of left ventricle infarcted was 16.9 ± 14.1% (p<.003). Thus, PIVSD occurred after myocardial infarctions that involved significantly more left ventricle than was found for infarctions not associated with subsequent PIVSD. When infarctions were considered by location (table 4), within both groups anterior location was associated with significantly more left ventricular infarction than was an inferior location. Specifically, within the PIVSD group, the mean percent of left ventricle infarcted was 32.3 ± 9.9% in anterior locations compared with 21.3 ± 6.3% in inferior locations (p<.04). Within the comparison group, anterior location was associated with 26.0 ± 16.0% compared with 9.9 ± 6.9% (p<.0001).

The incidence of right ventricular infarction, defined as greater than 1% infarcted tissue, was 100% in the PIVSD group compared with 28% in the comparison group (p<.0001). In neither group was a case of isolated right ventricular infarction found. In the PIVSD group, the percent of right ventricle involved by infarction was 19.8 ± 19.5% (table 3), as compared with 1.9 ± 5.1% involvement of the right ventricle in the comparison group (p<.0001). Therefore, infarctions resulting in PIVSD were associated with a greater amount of infarction of the right ventricle. If infarctions were considered by location, PIVSD was associated with greater right ventricular infarction in either the anterior or inferior location and furthermore, inferior infarctions with PIVSD were associated with greater right ventricular infarction than inferior infarctions without PIVSD (table 4). As previously noted in hearts with PIVSD, inferiorly located infarcts were associated with greater right ventricular infarction than anteriorly located infarcts. The relationship of inferior location and the percentage of right ventricle infarcted was much less strong in the comparison group (p = .972).

### Discussion

The present data support findings from previous studies indicating a relatively high prevalence of women experiencing PIVSD, the lack of a significant premorbid history of manifestations of coronary artery disease, and an early mean time from infarction to appearance of PIVSD being associated with a high incidence of shock.1–5, 8–15, 17–23 However, the present study is unique in that it is the first attempt to accurately quantitate the association of right and left ventricular infarction in patients with PIVSD and to further characterize this association by use of a comparison group. These results show that within the PIVSD group, there is significantly more left ventricle involved in anterior infarctions than in inferior infarctions. Conversely, there is significantly more right ventricular infarction in inferiorly located myocardial infarctions with resulting PIVSD. Because it was not reasonable to assume a normal distribution with our data, the Wilcoxon Mann–Whitney nonparametric two-sample test was used to evaluate the relationship observed between anterior and inferior infarctions and between PIVSD and comparison groups. The resulting p values from this test tend to be slightly conservative if normality is satisfied. When normality cannot be assumed, this is a preferable approach. The p value of .059 obtained in testing the difference between right ventricular infarction in inferior locations compared with anterior locations in association with PIVSD represents a strong trend in the data in view of the small sample sizes in the two groups. Infarctions resulting in PIVSD compared with infarctions not resulting in PIVSD are characterized by greater left and right ventricular infarction, irrespective of location. Moreover, PIVSDs complicating inferior infarctions are associ-

### TABLE 3

**Characteristics of infarctions with and without PIVSD**

<table>
<thead>
<tr>
<th></th>
<th>PIVSD group (%)</th>
<th>Comparison group (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior</td>
<td>53.0</td>
<td>46.0</td>
</tr>
<tr>
<td>Inferior</td>
<td>47.0</td>
<td>54.0</td>
</tr>
<tr>
<td>LV infarct size</td>
<td>27.2 ± 9.1</td>
<td>16.9 ± 14.1</td>
</tr>
<tr>
<td>RV infarct size</td>
<td>19.8 ± 19.5</td>
<td>1.9 ± 5.1</td>
</tr>
<tr>
<td>Transmural</td>
<td>100.0</td>
<td>77.0</td>
</tr>
<tr>
<td>Associated RV infarction</td>
<td>100.0</td>
<td>28.0</td>
</tr>
</tbody>
</table>

LV = left ventricular; RV = right ventricular.

### TABLE 4

**Summary statistics by group and location**

<table>
<thead>
<tr>
<th></th>
<th>Anterior</th>
<th>Inferior</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>PIVSD group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left ventricular infarction</td>
<td>7</td>
<td>32.3 ± 9.9</td>
</tr>
<tr>
<td>Right ventricular infarction</td>
<td>7</td>
<td>9.9 ± 8.0</td>
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<tr>
<td>Comparison group</td>
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<tr>
<td>Left ventricular infarction</td>
<td>17</td>
<td>26.0 ± 16.0</td>
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<tr>
<td>Right ventricular infarction</td>
<td>17</td>
<td>1.3 ± 3.1</td>
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</table>
ated with the greatest amount of infarction of the right ventricle. Importantly, the strong association of inferior infarction and the percentage of right ventricle infarcted seen in the PIVSD group was not present in the comparison group. The incidence of right ventricular infarction was 100% in infarctions resulting in PIVSD compared with 28% in infarctions not complicated by PIVSD.

The pathologic substrate in this group of patients dying with PIVSD was diffuse coronary artery disease with acute thrombosis resulting in transmural confluent infarction. However, as seen in one patient without significant coronary artery disease and another patient with only one-vessel disease, PIVSD can occasionally occur without diffuse coronary artery disease. In patients with multivessel disease, the coronary artery that potentially would have supplied collateral flow to the infarcted region was affected by significant disease in 11 patients and greater than 50% lesions in two additional patients.

**Right ventricular infarction in PIVSD.** Autopsy series have indicated that isolated infarction of the right ventricle is rare, occurring in 1.7% to 4.6% of all patients with myocardial infarction.24–26 However, right ventricular infarction associated with left ventricular infarction is more common, with autopsy series reporting an incidence of 14% to 43%.26–29 Even within autopsy series, ischemic damage to the right ventricle is more frequent that suspected grossly when the right ventricle is examined microscopically.30 Clinically, right ventricular dysfunction has been noted to occur in up to 40% of patients with acute infarctions.31,32 The relative immunity of the right ventricle to infarction has been explained in a number of ways, including a lower oxygen requirement for the right ventricle because of its smaller mass and lower intracavitary pressure, greater systolic coronary artery blood flow, a more developed Thebesian system, and a more extensive network of collateral vessels.27,33

Fananapazir et al.12 reviewed several series of patients with PIVSD treated surgically and noted that overall survival of patients with anterior infarctions was significantly greater than that of patients with inferior infarctions. Patients with PIVSD after inferior infarction had an even higher incidence of right ventricular dysfunction than patients with anterior infarction, although poor right ventricular function was noted in almost half of anterior infarctions.12 Our study showed significantly more right ventricular infarctions in inferior locations. Furthermore, significantly more right ventricular infarctions in an anterior location with PIVSD than in an anterior location without PIVSD were seen. The rapid deterioration in our group of patients with septal rupture could be attributed to the sudden volume and pressure overloading of an already impaired right ventricle with associated left ventricular infarction contributing to the progression to cardiogenic shock.

The association of right ventricular infarction with PIVSD as seen in this and other studies is interesting in that many of the pathologic substrates that appear to predispose to right ventricular infarction are also implicated in the pathogenesis of PIVSD. Isner and Roberts28 noted right ventricular infarction to be a complication among their patients exclusive of transmural posteroseptal left ventricular infarction. In the study of Ratliff and Hackel,29 all of the right ventricular infarcts were seen to be associated with transmural infarction of the posterior left ventricle or the interventricular septum or both. Thus, in both studies, right ventricular infarction was associated with transmural infarctions and infarctions that involved the interventricular septum. Other investigators have observed right ventricular infarction in association with anterior infarction.34 The present study is in agreement in that right ventricular infarction was observed in association with posteroseptal as well as anteroseptal infarction. In any event, right ventricular infarction and PIVSD appear to occur when infarctions are transmural and involve the septum.

The common pattern of atherosclerosis in the present series was significant stenosis of the LAD and RCA resulting in compromised blood flow to the right ventricle and to the interventricular septum. Other autopsy studies,10,11,35 as well as clinical series,2,3 have noted an incidence of 70% to 100% of two- or three-vessel coronary artery disease in patients experiencing PIVSD. Indeed, because of the rich anastomotic network of vessels supplying the human interventricular septum, it is not surprising that multiple narrowings in the major coronary arteries are observed in most patients with septal rupture.17 Similarly, in patients with right ventricular infarction. multivessel disease is common. Wade26 emphasized that in cases of RCA occlusion, the right ventricle receives much of its blood supply from the left coronary artery, particularly through branches that traverse the septum and supply the anterior third of the right ventricle. He further emphasized the importance of preexisting lesions in the LAD in the pathogenesis of right ventricular infarction. Other pathologic series have revealed that in cases of right ventricular infarction, severe stenoses or occlusion of the LAD and RCA are present.28,29 Haupt et al.33 recognized the importance of collateral flow from
the LAD to the right coronary system in preventing right ventricular infarction. Thus, both right ventricular infarction and PIVSD primarily occur in coronary circulations compromised by significant coronary artery disease in two or three vessels.

In this series, all except one patient experienced infarction as a result of an acute coronary arterial thrombotic lesion. In the one remaining patient a single 50% lesion of the LAD was found at autopsy. It was thought that infarction resulted from apparent vasospasm in that no thrombus was present to explain the location of the infarct and none was believed likely to have been present previously. An embolic cause of the infarct with subsequent lysis or distal migration of the embolus could not be completely ruled out, but was thought to be unlikely because of the absence of embolic sources. This represents the fifth patient reported in the literature with apparent coronary spasm in infarction with associated ventricular septal rupture.12, 14, 36, 37

Previous reports of patients with PIVSD have noted a high incidence of acute thrombotic lesions precipitating the infarctions that subsequently result in septal rupture.10, 17, 22, 23, 35 It has been suggested that an abrupt, relatively large reduction in flow such as that produced by thrombosis or spasm could cause the intense necrosis later responsible for rupture.2 Bloor and White38 showed that in a compromised coronary circulation with complex collateral flow, an acute occlusion will result in an abrupt reduction in collateral flow throughout the system. Likewise, right ventricular infarction complicates infarctions caused by acute coronary arterial thrombosis.26, 28, 29 Ratliff and Hackel29 suggested that acute coronary arterial lesions might lead to the development of right ventricular infarction by causing an abrupt decrease in collateral blood flow in severely atherosclerotic coronary arteries. Thus, for example, acute thrombosis of the right coronary results in a significant decrease in blood flow to the right ventricle with little opportunity for collateral blood flow because of obstructions involving the LAD. Likewise, this would hold true in cases of infarction with resulting septal rupture involving the RCA and LAD blood supply to the interventricular septum.

In summary, right ventricular infarction and PIVSD may have certain pathophysiologic factors in common, including transmural infarction, involvement of the interventricular septum by infarction, impairment of collateral blood flow to the ischemic region, and acute coronary arterial occlusion.

**Hemodynamic effects of right ventricular infarction in PIVSD.** Starr et al.39 first popularized the idea that the right ventricle was not necessary to maintain cardiac hemodynamics. Recent experimental and clinical studies have demonstrated that a normally contractile right ventricular free wall is not essential for cardiac performance at rest. However, under conditions of hemodynamic instability, overall cardiac performance becomes increasingly dependent on the right ventricle.40-45 For example, Cohn et al.41 and others42 have described a unique clinical and hemodynamic syndrome associated with right ventricular infarction. Marmour et al.45 examined the global and regional function of both right and left ventricles after anterior and inferior infarction and noted that the site of infarction was a major determinant of ventricular function. Right ventricular infarction was much more common with inferior infarction than previously appreciated. They postulated that the transient right ventricular dysfunction seen in association with anterior infarctions was due to reversible right ventricular ischemia, while the more persistent dysfunction associated with inferior infarction was due to actual infarction of the right ventricle.

Goldstein et al.44 investigated the genesis of low-output syndrome secondary to right ventricular infarction in a dog preparation model in which selective infarction of the right ventricle was produced. A profound depression of right ventricular function with a resulting marked decrease in left ventricular preload, left ventricular stroke volume, and left ventricular stroke work was observed. The marked reduction in left ventricular preload was attributed to right ventricular dysfunction secondary to infarction. Importantly, experiments were conducted with the pericardium open as well as intact. It was noted that elevated intrapericardial pressure secondary to right ventricular dilatation further reduced left ventricular preload and produced diastolic pressure equalization. Pericardiectomy after right ventricular infarction improved left ventricular filling and resulted in increased cardiac output. Therefore, the hemodynamic changes observed resulted from isolated right ventricular systolic dysfunction and elevated intrapericardial pressure. The comprehensive effects of these mechanisms would obviously be exacerbated in the presence of abnormal left ventricular function and indeed a degree of right ventricular systolic dysfunction that might have trivial effects on a normal left ventricle could have significant impact on cardiac performance in the presence of significant left ventricular dysfunction. Shah et al.52 detected scintigraphically predominant right ventricular dysfunction in 40% of patients with acute inferior infarction and noted that this dysfunction resulted in a
reduced left ventricular preload, as indicated by a reduced left ventricular end-diastolic volume index. The decreased left ventricular end-diastolic volume index was thought to have resulted from reduced right ventricular output. This study demonstrated that scintigraphically detected predominant right ventricular dysfunction occurred with near-normal left ventricular ejection fraction and yet produced a low-output syndrome, often in the absence of clinically detectable right ventricular failure.

The presence of shock in PIVSD has been suggested to be largely due to right ventricular impairment.\(^2\)\(^{12}\) PIVSD precipitates acute severe volume and pressure overload of the right ventricle and indeed right ventricular dysfunction in PIVSD is probably a consequence of right ventricular infarction, right ventricular ischemia, and/or pressure-volume abnormalities.\(^15\) The role of right ventricular dysfunction in PIVSD has been elucidated by experiments in which the right ventricular wall was not only damaged but actually excised and replaced with a noncontractile prosthetic patch. The hemodynamic status generally deteriorated to such an extent that any additional stress could not be tolerated. The survival of some animals was believed to be due to an intact interventricular septum. Moreover, when a complete exclusion of the right ventricle was accomplished (right ventricular free wall and interventricular septum), life could not be supported for any length of time.\(^46\)

**Correlation of infarct size with PIVSD.** Attempts to quantitate left ventricular infarction complicated by PIVSD have resulted in much disagreement. No attempt to quantitate right ventricular infarction has been made. Schuster and Bulkley\(^11\) examined 24 patients with cardiac rupture, including nine with ventricular septal defect and 15 with free wall rupture. The percent of left ventricular infarction was quantified in a manner similar to our method. The percent of left ventricle involved by acute myocardial infarction was 16% in the 24 patients with rupture compared with 28% in 86 patients with acute myocardial infarction but no rupture. Indeed, it was noted that the high mortality in patients experiencing cardiac rupture was especially troubling because these patients had small transmural infarctions. In contrast, Hutchins\(^10\) performed pathologic studies on 10 patients who died of acute myocardial infarction and PIVSD. Infarcts were sized based on results of gross as well as microscopic examinations. The average percent of left ventricular infarction in the 10 patients was 28% compared with 16% in a group of patients without PIVSD studied in a similar manner. The percent of left ventricular infarction in our PIVSD group (27.2 ± 9.1%) was very similar to that noted by Hutchins. In anterior infarctions, Hutchins found 33% of the amount of left ventricle to be involved by infarction compared with our value of 32.3 ± 9.9%. In inferiorly located infarctions, Hutchins noted 26% of the left ventricle to be involved by infarction compared with 21.3 ± 6.3% in our group. Furthermore, his value of 16 ± 12% is comparable to our value of 16.9 ± 14% for infarctions not resulting in PIVSD. Therefore, the present findings support Hutchins' conclusions that infarcts resulting in perforation of the interventricular septum are relatively large, transmural, first infarcts.

Radford et al.\(^2\) examined the hearts of 16 patients at autopsy and noted grossly the proportion of left and right ventricular free wall and interventricular septum infarcted. Although this study was limited by its semi-quantitative method, the findings suggested that in patients with inferior infarction, shock was related to extensive right ventricular infarction, while in patients with anterior infarction, a relationship existed between shock and massive septal infarction. Cardiogenic shock was seen to be the most important determinant of postoperative survival, but was not explained by the state of left ventricular function. These investigators concluded that right ventricular dysfunction might be the major determinant of the development of cardiogenic shock in some patients with septal rupture. A lower mean pulmonary arterial pressure in patients with shock was noted compared with that in those without shock. The findings in the present study of 31.4 ± 23.3% infarction of the right ventricle for inferior infarctions and 9.9 ± 8.0% infarction of the right ventricle for anterior infarctions indicates a significant role of right ventricular infarction in death in patients with PIVSD.

**Accentuation of left ventricular dysfunction secondary to infarction by RVI and PIVSD.** The present data indicate that PIVSD tends to compound the clinical effects of the amount of infarcted left ventricular tissue. Lundy et al.\(^47\) noted a close correlation between the amount of left ventricular infarction and cardiac index in patients dying with acute myocardial infarction. Thus, a cardiac index greater than 2 liters/min/m\(^2\) was associated with 22.0 ± 10% left ventricular infarction, compared with 46 ± 14% left ventricular infarction in patients with a cardiac index less than 2. Page et al.\(^48\) in a classic study examining the amount of left ventricular infarction and the presence or absence of cardiogenic shock in patients dying with acute myocardial infarction, revealed that in 20 patients with shock, 40% or more of the left ventricle was involved by infarction.
while only one of 14 patients without shock had lost 40% or more of the left ventricle due to infarction. The remainder of the latter group lost 35% or less.\textsuperscript{48} Interestingly, among 13 cases of acute myocardial infarction resulting in PIVSD in our study, only two patients had approximately 40% of the left ventricle involved by infarction. Indeed, Page et al. noted a range of 40% to 70% of left ventricle in his patients, while the highest percentage of left ventricle in our group was 48%. Our overall value of 27% is much lower than the reported range of infarcted left ventricle in his group dying of cardiogenic shock, despite the fact that a very high incidence of cardiogenic shock was noted in our PIVSD group. This observation may relate to accentuation of left ventricular infarction by right ventricular infarction per se or by right ventricular dysfunction due to the pressure and volume overload in these patients.

In summary, the results of the present study show that PIVSD resulting in death is a complication of myocardial infarctions that are transmural, relatively large, first infarctions. The pathologic substrate is diffuse coronary artery disease, with acute thrombosis precipitating the infarction. More importantly, acute infarctions resulting in PIVSD are associated with a 100% incidence of right ventricular infarction. Furthermore, significantly more infarction of the right ventricle is seen in either anterior or inferior infarctions resulting in ventricular septal rupture compared with infarctions not resulting in ventricular septal rupture. PIVSDs complicating inferior infarctions are associated with the greatest amount of infarction of the right ventricle. Right ventricular infarction appears to be an important determinant of subsequent clinical course in patients dying with PIVSD complicating anterior and especially inferior infarctions.

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