Functional Response of the Right Ventricle to Myocardial Infarction: Dependence on the Site of Left Ventricular Infarction

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SUMMARY We previously showed that the extent of infarction is virtually identical in patients with anterior and inferior infarction despite the more favorable prognosis associated with the latter. We postulated that the damage associated with inferior infarction is shared by both ventricles, thereby causing less hemodynamic impairment than anterior infarction, which involves only the left ventricle. To further explore this hypothesis, global and regional function of both right and left ventricles was assessed by gated radionuclide ventriculography in 50 patients with infarction within 48 hours after admission and again on the tenth day. Radionuclide ventriculography was also performed in 10 normal subjects. In 22 patients who had anterior infarction, the mean global left ventricular ejection fraction was decreased (27 ± 15% [± SD] vs 64 ± 10% in normal subjects, p < 0.05), reflecting regional abnormalities, and increased only slightly by the tenth day (33 ± 11%, p < 0.05). The global right ventricular ejection fraction was decreased (28 ± 11% vs 43 ± 9% in normal subjects, p < 0.05), reflecting a uniform depression of function without localized abnormalities, and returned to normal by the tenth day (43 ± 12, p < 0.05). In 20 patients who had inferior infarction, global left ventricular ejection fraction was only slightly decreased (51 ± 11%), reflecting infarct-related, and did not change (55 ± 10). In contrast, global right ventricular ejection fraction was severely and persistently decreased (23 ± 9 vs 28 ± 9, p > 0.05), reflecting abnormalities primarily of the inferior region. The decreased right ventricular ejection fraction after inferior infarction correlated inversely with enzymatic estimates of infarct size (r = −0.85, p < 0.01), although there was no correlation between left ventricular ejection fraction and infarct size. Thus, the functional responses of the ventricles to myocardial infarction are markedly influenced by the site of damage. In patients with anterior infarction there was persistent regional and global impairment of left ventricular function but only transient impairment of the right ventricle, whereas inferior infarction was associated with severe, persistent regional and global impairment of the right ventricle. These results indicate that the site of infarction is a major determinant of ventricular function and its recovery and that right ventricular infarction is much more common with inferior infarction than is generally appreciated.

MORE PRECISE characterization of right ventricular function should improve our understanding of pathophysiology and permit more rational management of cardiac disorders. Although function can be evaluated accurately with contrast angiography, this invasive technique is not optimal for routine use. However, the increasingly widespread availability of radionuclide ventriculography provides a means to assess right and left ventricular function noninvasively.1,2 With this technique, global function, as reflected by the ejection fraction, can be determined for both ventricles from ventricular time-activity curves that reflect changes in ventricular volume in a manner virtually independent of ventricular geometry. Several studies show that measurements of global and regional left ventricular function determined by radionuclide ventriculography correlate closely with those obtained by contrast angiography.3,4 Using a similar approach, it is also possible to assess right ventricular function5,7 so that function of both ventricles can be assessed simultaneously in critically ill patients. Several investigators have evaluated left ventricular function in patients with acute infarction6,8 by this technique, but serial studies of the changes in right ventricular function during infarction are few,9 have dealt with global rather than regional function, and have used first-pass radionuclide angiography rather than equilibrium-gated blood pool imaging. The latter approach correlates closely with results of first-pass radionuclide angiography6,7 and is performed more readily with instruments presently available in most nuclear medicine facilities.

Proper interpretation of ventricular function requires knowledge of right and left ventricular function. Based on hemodynamic data,10,11 the right ventricle responds quite differently to inferior than it does to anterior infarction. Infarct size estimated enzymatically is virtually identical in patients with anterior and inferior infarction despite differing hemodynamics and a much lower mortality in patients with inferior infarction.12-14 We have postulated that with inferior infarction, the extent of damage and the hemodynamic impact are shared by both ventricles, whereas the left ventricle bears the full impact with anterior infarction. This hypothesis would require that damage to the right ventricle with inferior infarction is much more common than is generally appreciated,15 which is in keeping with recent hemodynamic16 and clinical16-18 studies.

To evaluate our hypothesis concerning the disparate...
prognostic results in patients with inferior vs anterior infarction, we undertook the present study to assess the sequential changes in global and regional function in both right and left ventricles. Ventricular function was studied scintigraphically with conventional, gated blood pool imaging during the acute and convalescent phases of myocardial infarction.

**Materials and Methods**

**Patients**

Radionuclide ventriculography was performed in 10 normal subjects and 50 consecutive patients with acute myocardial infarction. The normal subjects (six men and four women) were 38–64 years old. Six of the normal subjects had undergone cardiac catheterization for evaluation of chest pain and were found to have normal left and right ventricular function and coronary anatomy. The four other normal subjects had no history of cardiac disease and had normal physical examinations and ECGs.

Acute myocardial infarction was diagnosed when there was a history of typical chest pain lasting at least 15 minutes in conjunction with typical ECG changes and elevated plasma activity of total creatine kinase (CK) and MB-CK. Patients with historical or electrocardiographic evidence of myocardial infarction, coexisting congenital or acquired valvular disease or pulmonary hypertension were excluded. There were 37 men and 13 women, mean age 61 ± 12 years (± sd). ECGs showed the development of new Q waves indicative of transmural infarction in 44 patients (anterior in 22, inferior in 20 and lateral in two). ST-T abnormalities typical of nontransmural myocardial infarction developed in six patients. All patients received conventional therapy in the coronary care unit and there were no substantial differences in therapy among patients with respect to location of infarction.

Of the 50 patients with acute myocardial infarction categorized according to the Myocardial Infarction Research Unit classification (MIRU), 22 (44%) were class I (four anterior, 10 inferior, six subendocardial and two lateral), 20 (40%) were class II (11 anterior and nine inferior), and the remaining eight (16%) were class III (seven anterior and one inferior). The two patients with lateral infarction and the six with subendocardial infarction are not considered further in this report. Infarct size was estimated enzymatically in 20 of 22 patients with anterior infarction and 18 of 20 with inferior infarction. Blood samples for CK determinations were obtained every 2 hours for the initial 10 hours and every 4 hours thereafter until plasma CK activity had returned to baseline. Infarct size index was expressed as CK-gram-equivalents per square meter of body surface (CK-g-eq/m²).

**Scintigraphic Data Acquisition**

All studies were performed with red blood cells labeled in vivo by i.v. administration of 15.4 mg of stannous pyrophosphate, followed 20–30 minutes later by i.v. injection of 20–25 mCi of ⁹⁹ᵐTc-pertechnetate. Initial studies were performed within 48 hours of admission to the coronary care unit; the studies were repeated approximately 10 days after admission (10 ± 1.2 days).

The images were obtained with a mobile scintillation camera (25.4-cm diameter, 0.63-cm-thick NaI crystal). The camera was fitted with a low-energy, medium-resolution, parallel-hole collimator. For some studies, the camera was interfaced to a dedicated data collection device and data were collected in list mode and reformatted on a Varian V-76 minicomputer into 20–32 frames per cardiac cycle. In other studies, the camera was interfaced to a dedicated minicomputer system (Ohio Nuclear VIP 450). Multigated acquisition of scintigraphic data was achieved, as reported previously, using the technique of Burrows et al. For this purpose, the cardiac cycle was divided into 32 frames of equal duration.

Images were obtained in the anterior projection and in a 30–45° left anterior oblique projection with 15° caudal angulation of the detector. This projection optimally separated the two ventricles and the left ventricle from the left atrium. In most patients, a 70° left anterior oblique view was also obtained. The images were acquired or reformatted in a 64 x 64 matrix array; each image frame contained approximately 200,000 counts.

**Processing of Scintigraphic Data**

After initial collection and reformatting of data, the images were processed off-line on a Varian V-76 minicomputer. As the initial step, image frames were smoothed with use of a nine-point smoothing algorithm. To determine the appropriate level of background subtraction for each image, an activity profile along the center of the ventricle was generated from a horizontal region of interest 4 pixels wide. The value selected by the operator for background activity was the minimum point on the profile curve lateral to the ventricular edge or, if no clear minimum point was identifiable, the background was chosen as the point on the profile curve 2 pixels beyond the edge of the ventricle. Individual horizontal profiles were generated for both the left and right ventricles for determination of the appropriate background correction for each. Left and right ventricular time-activity curves were then generated using an algorithm that automatically detects the ventricular edge on each frame of the study. The operator first defines separate boxes surrounding the left and right ventricles using an electronic cursor. The boxes were chosen to provide the best possible separation of the ventricle from each other and from the atria. The operator then identifies the approximate center of each ventricle and the maximal distance from the center of each ventricle to its outermost edge. The ventricular edge is detected by scanning the data from the center of the ventricle along radial lines separated by 5° angles. The algo-
Algorithm searches along each radial line for a minimal point adjacent to a pixel with increased counts. The minimal pixel is considered the ventricular edge. Time-activity curves are then generated for each ventricle based on the activity within the varying regions of interest on each image frame, and the ejection fraction is calculated and expressed as a percentage. All calculations were performed on the images obtained in the 30–45° left anterior oblique projection.

This method has been validated in our laboratory. Measurements of left ventricular ejection fraction have been shown to correlate closely with those determined by single-plane, right anterior oblique contrast angiography ($r = 0.88$, $n = 22$, $p < 0.001$). The results of left ventricular ejection fraction calculated from separate data collections in the same patients separated by a 1-hour interval correlated closely ($r = 0.99$, $n = 12$, $p < 0.001$). The interstudy variation was 0.6 ± 2.4% (ejection fraction units). Repeat measurements of right ventricular ejection fractions by a single observer after 7–14 days correlated closely ($r = 0.90$, $n = 0.10$, $p < 0.01$), as did measurements performed independently by two experienced observers ($r = 0.91$, $n = 10$, $p < 0.01$). The results of right ventricular ejection fractions calculated from determinations 1 hour apart in the same patients also correlated closely ($r = 0.90$, $n = 10$, $p < 0.01$). The interstudy variation for global right ventricular ejection fraction was 3.5 ± 2.5%.

**Determination of Regional Ejection Fractions**

Regional ejection fractions for both the left and right ventricles were determined by use of a method similar to that reported by Maddox et al. In the modification we used, the longitudinal axis of each ventricle on the end-diastolic frame was first chosen by the operator using the outline of the ventricular edge generated as described above. The longitudinal axis of the ventricle (within the ventricular outline) was divided into four segments of equal length. Three equidistant minor axes perpendicular to the long axis were constructed, dividing the ventricle into eight regions. The two regions adjacent to the cardiac base were not used further, because these overlap the great vessels and the atria to some extent. The six remaining regions were combined into three larger regions: septal, inferior and lateral. For estimation of the regional ejection fractions of each ventricle, the background correction and the designation of end-diastolic and end-systolic frames were the same as those used to estimate global ejection fraction. The regional ejection fraction (EF$_r$) in each region was calculated from the formula $EF_r = (ED_r - ES_r)/(ED_r - background)$, where ED$_r$ is the regional activity at end-diastole and ES$_r$ is the regional activity at end-systole.

For separate determinations (1 hour apart) of regional ejection fractions in the same patients ($n = 12$), the interstudy variation was 0.0 ± 6.5% for the septum, 0.6 ± 7.5% for lateral wall and 1.8 ± 10.4% for the inferior wall of the left ventricle. The corresponding values for the right ventricle were 5.1 ± 2.9% for the septum, 5.3 ± 12.4% for the lateral wall and 5.0 ± 3.0 for the inferior wall ($n = 10$).

**Statistical Methods**

All data were expressed as mean ± SD. A comparison of the sequential changes detected between the acute and convalescent phases observed in either the right or left ventricular ejection fractions was performed using the $t$ test for paired samples. The comparison between groups (e.g., anterior vs inferior myocardial infarction) was performed using the unpaired $t$ test. Differences in group means were considered significant at $p < 0.05$.

**Results**

**Normal Subjects**

Global and regional ejection fractions of both ventricles were determined in 10 healthy, subjects (table 1). The global ejection fraction of the left ventricle averaged 64 ± 10% (range 49–80%). The regional ejection fractions of the left ventricle averaged 55 ± 11% for the septum, 64 ± 13% for the lateral wall and 85 ± 9% for the inferior wall. These values are similar to those reported by Maddox et al. The global ejection fraction of the right ventricle averaged 43 ± 9% (range 34–67%); regional ejection fractions for the right ventricle were 28 ± 10% for the septum, 53 ± 12% for the lateral wall and 79 ± 15% for the inferior wall. The mean regional ejection fraction of the right ventricular septal region is substantially less than that of the left ventricle during systole, and the only motion toward the center of the right ventricle is due to septal thickening. Thus, septal motion appears falsely paradoxical when viewed from the perspective of the right ventricle. However, the regional ejection fraction of the right ventricular septal area remains a positive number because of septal thickening during emptying of the right ventricle and shortening that occurs in the anteroposterior and longitudinal axes of the chamber.

**Anterior Myocardial Infarction**

Among the 22 patients with anterior myocardial infarction, global left ventricular ejection fraction within the first 48 hours was 27 ± 15% and improved slightly, to 33 ± 11% ($p < 0.05$) at 10 days (table 1). Both the early and late values were significantly less than those in control subjects. This improvement was due mostly to improvement in the regional ejection fraction of the lateral wall, which increased from 28 ± 9% initially to 36 ± 6% at 10 days after infarction ($p < 0.05$). However, no significant improvement in the inferior or septal regions of the left ventricle was noted (table 1, fig. 1).

The global right ventricular ejection fraction was 28 ± 11% early after infarction and improved sub-
change was seen in the lateral and septal regions of the left ventricle (fig. 1). However, the global right ventricular ejection fraction was severely depressed early after inferior infarction and remained depressed at 10 days, with only slight improvement, from 23 ± 9% to 28 ± 9% (p < 0.001). The ejection fractions of all regions of the right ventricle were depressed after inferior myocardial infarction, but the inferior and lateral walls were most severely depressed. The regional ejection fraction of the right ventricular septal area was depressed by approximately 30% compared with normal. In inferior regions it was decreased by 75% and in lateral zones by 55% compared with values for corresponding regions in the normal subjects (fig. 1).

The Influence of Septal Function on Global Right Ventricular Function

The decreased right ventricular function early after anterior myocardial infarction did not appear to reflect changes in the left ventricular septal region. Of the 22 patients with anterior myocardial infarction, the initial values for the left ventricular septal ejection fractions of five patients were nearly normal (43 ± 11%) and remained so (45 ± 10%) during the study. Nonetheless, global right ventricular ejection fraction was depressed in these patients and improved substantially during the study, from 30 ± 7% to 44 ± 15%. Eight patients had moderately depressed (23 ± 3%) left ventricular septal ejection fractions, which improved slightly (31 ± 8%). In these patients, global right ventricular ejection fraction was also depressed initially (30 ± 13%) and improved (41 ± 11%) in a manner analogous to that in patients with relatively normal septal function. Similarly, in the nine patients with severe depression of the left ventricular septal ejection fraction (5 ± 8%), which did not change during the study (8 ± 11%), comparable depression and improvement in right ventricular ejection fraction occurred (30 ± 13% to 41 ± 11%). Thus, initial depression and subsequent improvement of global right ventricular ejection fraction occurred in patients with normal, moderately impaired and severely impaired motion of the interventricular septum.

Relationship Between Enzymatic Estimates of Infarct Size and Ventricular Function

In patients with anterior myocardial infarction, the mean infarct size index (27 ± 14 CK-g-Eq/m²; n = 20) was virtually identical to that in patients with inferior myocardial infarction (25 ± 11 CK-g-Eq/m²; n = 18). Right ventricular ejection fraction in patients with anterior infarction did not correlate significantly with infarct size index. However, right ventricular ejection fraction in these patients did correlate significantly with left ventricular ejection fraction within the first 48 hours after infarction (r = 0.75, p < 0.001, fig. 2). Further, the improvement in right ventricular ejection fraction correlated closely with infarct size index; patients with the largest infarcts showed the most marked improvement (r = 0.81, p < 0.01).
in patients with anterior myocardial infarction, the left ventricular ejection fraction is depressed initially, and improves only slightly in the early convalescent phase. Somewhat surprisingly, the right ventricular ejection fraction is also severely depressed during the early postinfarction period, yet it returns dramatically toward normal within 10 days (table 1).

The explanation for the altered right ventricular function and its dramatic improvement during convalescence is uncertain, but several possibilities must be considered. Right ventricular function may be depressed after anterior infarction on a simple mechanical basis: impaired left, or right ventricular contractility secondary to increased afterload in the pulmonary vascular system. This hypothesis is partly supported by our finding of a significant correlation between the right and left ventricular ejection fractions measured within the first 48 hours after anterior infarction \((r = 0.75, p < 0.001)\). The improvement in right ventricular ejection fraction correlated closely with enzymatic estimates of the extent of damage (infarct size) \((r = 0.81, p < 0.001)\). Virtually all damage is in the left ventricle in patients with anterior infarction. Further, the greatest improvement in right ventricular function was observed in patients who had the most extensive damage to the left ventricle. Also, 56% of the patients were classified as class II or III, indicating the presence of mild-to-moderate ventricular failure. While pulmonary artery pressures were not obtained in all of these patients, it is known from other studies that pulmonary artery occlusive pressure and cardiac index improve after infarction within the first few days and that the degree of improvement tends to be greatest in patients with the most severe initial hemodynamic impairment. Therefore, it is likely that increased right ventricular afterload may play a partial role in its transient dysfunction. However, this is probably not the only explanation, because right ventricular dysfunction was present as often in patients in class I as those in class II and III.

The possible influence of drug therapy on ventric-

![Graph](https://via.placeholder.com/150)

**Figure 2.** Relationship between global right ventricular ejection fraction and left ventricular ejection fraction determined in 22 patients within the first 48 hours after anterior infarction.

In patients with inferior myocardial infarction, the left ventricular ejection fraction did not correlate with infarct size index. However, the ejection fraction of the right ventricle correlated negatively with the infarct size index \((r = -0.85, p < 0.01)\).

**Discussion**

**The Effect of Anterior Infarction**

Our results show that anterior and inferior infarction have markedly different effects on right and left ventricular global and regional function. Further, the site of infarction determines the nature of recovery of

| Table 1. Global and Regional Ventricular Ejection Fractions |
|---------------------------------|-----------------|-----------------|
|                                | Normal \(n = 10\) | Anterior infarction \(n = 22\) | Inferior infarction \(n = 20\) |
|                                | Day 0–2 | Day 10 | Day 0–2 | Day 10 |
| Left ventricle                 |         |       |        |        |
| Global                         | 64 ± 10 | 27 ± 15\* | 33 ± 11\*† | 51 ± 11\* | 55 ± 10\*† |
| Lateral                        | 64 ± 13 | 28 ± 9\* | 36 ± 6\*† | 64 ± 11 | 65 ± 10 |
| Inferior                       | 85 ± 19 | 30 ± 13\* | 21 ± 11\*† | 45 ± 10\* | 52 ± 11\*† |
| Septal                         | 55 ± 11 | 16 ± 10\* | 15 ± 12\* | 55 ± 12 | 53 ± 10 |
| Right ventricle                |         |       |        |        |
| Global                         | 43 ± 9  | 28 ± 11\* | 43 ± 12\† | 23 ± 9\* | 28 ± 9\*† |
| Lateral                        | 53 ± 12 | 16 ± 16\* | 36 ± 21\*† | 24 ± 7\* | 26 ± 17\* |
| Inferior                       | 79 ± 15 | 26 ± 7\* | 50 ± 15\*† | 21 ± 8\* | 21 ± 22\* |
| Septal                         | 28 ± 10 | 25 ± 17 | 35 ± 21\† | 19 ± 11\* | 32 ± 4\* |

\*\(p < 0.05\) vs normal.
\†\(p < 0.05\) vs day 2.
ular function must also be considered. No patient received digoxin or propranolol during the study. Isosorbide dinitrate was administered every 6 hours to 15% of the patients with inferior infarction and to 18% of the patients with anterior infarction. This drug was administered at the initial study and was continued throughout the study interval, including the repeat study. Furosemide, 20–60 mg/day, was administered to 10% of the patients with anterior infarction throughout the study interval and to 8% of the patients with inferior infarction. Thus, it is unlikely that drug therapy accounted for the depression or improvement in right ventricular function in patients with anterior infarction.

It is possible that abnormalities in septal contraction due to septal necrosis or ischemia accompanying anterior infarction contribute to the decrease in right ventricular ejection fraction. However, the regional ejection fraction of the septal segment of the left ventricle does not correlate with the degree of initial right ventricular impairment or its improvement during convalescence. Thus, impairment of septal contraction does not appear to be the primary cause of right ventricular dysfunction in these patients. In view of the rapid improvement in right ventricular function, it is tempting to postulate that reversible right ventricular ischemia is responsible for the initial transitory changes. It is possible that a coronary steal is produced from the right to the left coronary artery, producing right ventricular ischemia. It is also possible that humoral or metabolic mediators released into the blood or interstitial fluid from the ischemic area may temporarily depress contractility of normal myocardium. Relevant to this hypothesis may be the finding that after experimental infarction, the normal surviving myocardium was shown to be temporarily depleted of catecholamines and exhibited decreased contractility.

Our results are somewhat different from those reported by Reduto et al. These investigators found no significant impairment in right ventricular ejection fraction in 12 of 13 patients with anterior myocardial infarction and no significant change in right ventricular ejection fraction between admission to the coronary care unit and discharge (13 ± 3 days). The reasons for this difference are not clear. However, only three of their 13 patients with anterior infarction were in clinical class II and none were in class III, whereas 11 of our 22 patients were in class II and seven were in class III. The greater hemodynamic impairment of the left ventricle in our patients may explain the difference in the results of the two studies.

The Effect of Inferior Infarction

Global and regional left ventricular function was only minimally impaired in patients with inferior infarction, which is in keeping with our previous hypothesis for lower mortality in these patients than in those with anterior infarction with comparable infarct size. With anterior infarction, the injury is exclusively in the left ventricle, whereas inferior infarction is associated with injury to both ventricles, causing less impairment of left ventricular function despite an equivalent overall myocardial insult.

In patients with inferior myocardial infarction, right ventricular function is severely depressed initially and improves only slightly during the convalescent phase. These findings are in agreement with those reported by others and most likely reflect right ventricular infarction. Others have postulated, based on hemodynamic or pathologic data, that right ventricular infarction is present in a substantial fraction of patients with inferior infarction. In our patients with inferior infarction, the right ventricular ejection fraction correlated closely with enzymatically estimated infarct size ($r = -0.85$, $p < 0.01$). This is probably not due to hemodynamic compromise accompanying the impairment of left ventricular function, for the ejection fraction of the left ventricle is nearly normal in patients with inferior infarction and does not correlate with infarct size. Further support for right ventricular infarction is the persistent localized impairment of the inferior region. In contrast, after anterior infarction, impaired right ventricular function reflects uniform depression of function in all regions of the ventricle.

It is not known whether recognition of right ventricular infarction will alter our management of patients with acute infarction. However, right ventricular infarction often presents with elevated jugular venous pressure, a large V wave and a steep Y descent. This may be interpreted as pericardial tamponade or right ventricular failure. The therapeutic approach to tamponade would be inappropriate and possibly deleterious to patients with acute infarction. We previously showed that treatment of patients with right ventricular infarction with diuretics for a mistaken diagnosis of right-sided cardiac failure is deleterious and associated with reduced cardiac output and hypotension. On the contrary, patients with right ventricular infarction need hemodynamic monitoring and adequate fluids to maintain right ventricular filling pressure. Clinical awareness of right ventricular infarction is increasing rapidly despite the lack of a specific and convenient diagnostic marker. Further assessment of the diagnostic sensitivity and specificity of radionuclide angiography and other techniques should help in defining the clinical recognition and manifestations of right ventricular infarction.

In conclusion, our results show that inferior infarction is generally associated with persistent impairment of right ventricular function caused primarily by localized involvement of the inferior region. This suggests that right ventricular infarction is commonly associated with inferior infarction and is substantially more frequent than previously reported. The hemodynamic responses of the right and left ventricles to infarction as assessed by conventional equilibrium-mode radionuclide ventriculography are characteristic and distinctly different with anterior and with inferior infarction. Anterior infarction is associated with persistent left ventricular regional impairment and transient global right ventricular impairment, whereas inferior
infarction is associated with persistent right and left ventricular regional impairment.

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Functional response of the right ventricle to myocardial infarction: dependence of the site of left ventricular infarction.

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