The Influence of Occult Right Ventricular Infarction on Enzymatically Estimated Infarct Size, Hemodynamics and Prognosis

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SUMMARY Clinical and hemodynamic manifestations of overt right ventricular infarction differ markedly from those that involve injury confined exclusively to the left ventricle. However, the frequency of covert right ventricular infarction and its influence on overall enzymatically estimated infarct size, hemodynamics and prognosis have not been characterized. Accordingly, 249 patients with transmural anterior or inferior left ventricular infarction were studied prospectively (average follow-up 20.7 months). Enzymatically estimated infarct size (average and frequency distribution) was similar among patients in both groups (25 ± 3.0 and 24 ± 1.8 CK-g-Eq/m² [±SEM]). Sixty-two patients were studied with invasive hemodynamic monitoring. Judging from the increased ratio of right ventricular end-diastolic pressure to pulmonary artery occlusive pressure in patients with inferior compared with anterior infarction (0.47 ± 0.7 vs 0.26 ± 0.3), and the greater fraction of patients who had a ratio greater than 0.45 (43% vs 14%), inferior infarction was frequently associated with occult right ventricular infarction. Although there were no significant differences in ventricular ectopic activity among patients in the two groups during the first 24 hours after the onset of infarction, early mortality was substantially less with inferior than with anterior infarction (12% vs 23%, p < 0.05), as was mortality throughout the first 2 years of follow-up (p < 0.01). Thus, covert right ventricular infarction, reflected by hemodynamic criteria, frequently contributes to overall enzymatic estimates of infarct size among patients with inferior transmural infarction, and accounts in part for the substantially increased initial and long-term survival compared with patients with anterior infarction associated with equivalent overall injury confined exclusively to the left ventricle.

PROGNOSIS IN PATIENTS with acute myocardial infarction appears to be directly related to the extent of left ventricular necrosis. Thus, patients who die with cardiogenic shock exhibit necrosis in 40% or more of the entire left ventricle. Further, mortality early after infarction, the incidence and severity of ventricular dysrhythmia, and the extent of impairment of left ventricular performance have been found to correlate with enzymatically estimated infarct size, generally taken to reflect primarily left ventricular injury.

Patients who have anterior myocardial infarction die more often than those who have inferior transmural infarction, an observation often interpreted as implying that anterior infarctions are generally more extensive than inferior infarctions. However, enzymatic estimates of infarct size may reflect infarction involving the right as well as the left ventricle. Because the right coronary artery supplies both the right ventricle and the inferior and posterior portions of the left ventricle, it is likely that diaphragmatic and true posterior infarcts, in contrast to anterior or lateral infarcts, may often be associated with some right ventricular infarction. Hemodynamic, electrophysiologic and clinical consequences of right ventricular infarction are not necessarily the same as those associated with injury that involve the same amount of tissue but are confined exclusively to the left ventricle. Accordingly, we undertook this investigation to assess the frequency of covert right ventricular infarction and to determine whether early morbidity and mortality in patients with exclusively left ventricular infarction are different from morbidity and mortality associated with combined left and right ventricular involvement of comparable overall magnitude, judging from enzymatic estimates of infarct size.

We evaluated 249 consecutive patients with transmural myocardial infarction to assess the relationships among enzymatically estimated infarct size, site of infarction, early ventricular dysrhythmia, left and right ventricular performance and early mortality (i.e., within 1 month of the onset of infarction).

Methods

Patients

The population was composed of 249 patients admitted consecutively to the Barnes Hospital Cardiac Care Unit who gave informed consent within 12 hours after the onset of chest pain. There were 174 males and 75 females, with a mean age of 61 years (range 29-93 years). Transmural myocardial infarction was established on the basis of typical serial changes in the activity of conventionally measured plasma enzymes (CK, SGOT, LDH, HBDH) and the appearance of new pathologic Q waves (greater than 0.04 second) in serial ECGs. All patients had elevated plasma MB-
CK. Patients with subendocardial infarction, reflected by evolutionary ST-T abnormalities without the appearance of new Q waves, and patients with pre-existing left bundle branch block were excluded. In this study, the site of infarction, determined electrocardiographically, was classified as anterior if it was anteroseptal (Q waves in leads V1-V3), anterolateral (Q waves in anterior and lateral precordial leads or in leads I and aVL), or both. Infarction was classified as inferior if Q waves appeared in leads II, III, and aVF, with or without Q waves in V2 and V3, or if the R-wave amplitude increased in lead V1 (true posterior infarction). Infarction was anterior in 119 patients (group 1) and inferior in 130 patients (group 2). Group 1 included 80 men and 39 women, with a mean age of 62 years (range 29–92 years); group 2 included 94 men and 36 women, with a mean age of 61 years (range 36–93 years). The incidence of previous myocardial infarction (determined by historical and electrocardiographic criteria) was 24% in group 1 and 25% in group 2. Among hemodynamically monitored patients, the incidence of previous infarction was 25% in group 1 and 26% in group 2.

Standard Care

All patients received i.v. morphine as necessary for pain, i.v. furosemide for severe congestive heart failure, bolus injections of lidocaine (1 mg/kg i.v.) followed by continuous infusions of 1–4 mg/kg/min for five or more premature ventricular complexes (PVCs) per minute occurring during at least 2 consecutive minutes or more than three consecutive PVCs. Early mortality was defined for the purposes of this study as death within 1 month of admission. All patients were evaluated clinically throughout hospitalization and for at least 1 month thereafter. Most were followed again 3 months after discharge and then at 6-month intervals.

Estimation of the Extent of Infarction

Infarct size was estimated enzymatically as previously described, based on plasma CK activity in samples obtained with the use of an intravenous heparin lock hourly for the first 12 hours and every 4 hours thereafter for 72 hours.

Assessment of Ventricular Rhythm

Because ventricular dysrhythmia associated with acute myocardial infarction is most frequent and severe primarily early after its onset, data analysis pertinent to dysrhythmia in this study focused on the first 24 hours. Ventricular dysrhythmia was detected on continuous 24-hour Holter tape recordings and analyzed quantitatively with the Argus/H computer system, using human editor verification of all computer-identified ventricular ectopic beats. The reproducibility of results obtained with this system is within 1%. Recordings were initiated in all cases within 1 hour after admission, and were analyzed to determine the number of PVCs, peak PVC frequency, and the number of episodes of couplets and runs of ventricular tachycardia, defined as three or more consecutive PVCs.

Evaluation of Hemodynamics

Systemic blood pressure and heart rate were monitored conventionally. All 62 patients in Killip classes III and IV (35 in group 1 and 27 in group 2) were studied with invasive hemodynamic monitoring. Hemodynamic values were recorded within 4 hours of admission. Intracardiac pressures (pulmonary artery occlusive pressure, pulmonary artery systolic and diastolic pressure, right ventricular end-diastolic, and mean right atrial pressure) were obtained by right-heart catheterization with a Swan-Ganz thermodilution catheter inserted via an antecubital vein after venous cutdown, or via the femoral vein using the Seldinger technique, and advanced into the pulmonary artery under fluoroscopic control. Cardiac output was determined by the thermodilution method. Mean pulmonary artery occlusive pressure was measured as an index of left ventricular filling pressure. The ratio of right ventricular end-diastolic pressure to mean pulmonary artery occlusive pressure was calculated and used as an index of relative right-to-left ventricular functional integrity. A high value of this ratio has been found to reflect right ventricular hemodynamic impairment angiographically.

Statistical Procedures

The chi-square test was used to determine the significance of differences for discontinuous variables. The two-tailed t test for unpaired samples was used to assess the significance of differences for hemodynamic variables. Because data on the frequency of PVCs in a population do not conform to a normal distribution, values obtained after logarithmic transformation of the data were compared using the two-tailed t test. Late survival was evaluated using the life-table method, and significance was assessed with the Mantel-Cox test. Values are mean ± SEM.

Results

Early Mortality

The early mortality of all patients with transmural infarction was 17% (43 of 249); mortality among patients with anterior infarction significantly greater (23%, p < 0.05) than that among patients with inferior infarction (12%) (fig. 1). Among patients who died during the first month after infarction, mean infarct size was 36 ± 3 CK-g-Eq/m² compared with 25 ± 2 CK-g-Eq/m² in the 62 survivors (p < 0.02).

Infarct Size

Enzymatically estimated infarct size index was similar among patients with anterior (25 ± 3.0 CK-g-Eq/m²) compared with inferior infarction (24 ± 1.8 CK-g-Eq/m²) (fig. 2). The distributions of enzymatically estimated infarct size among patients in
FIGURE 1. Early mortality among patients with anterior and those with inferior myocardial infarction. Open bars represent the total patient population in each group. Shaded bars represent the number of patients who died within 1 month after infarction.

Each of the two groups were virtually superimposable (fig. 3). Among hemodynamically monitored patients, infarct size was similar in the two groups, averaging 27 and 29 CK-geq/m². Consistent with previous results, patients who died in the acute phase of myocardial infarction have larger infarcts (36 ± 2 CK-geq/m²) than patients who survived (25 ± 1 CK-geq/m²), although the difference was not statistically significant because the number of patients who died was so small. In contrast, a comparable difference in mortality within 1 month was statistically significant because the number of decedents was larger.

Although the elimination rate of CK from blood is not markedly affected by profound hemodynamic perturbations in dogs,^4^ values for this measurement could conceivably differ among patients with infarction involving different regions of the heart. However, values for the elimination rate were virtually identical among patients with anterior (9.7 × 10⁻⁴ min⁻¹ ± 0.3 × 10⁻⁴) compared with inferior infarction (9.5 × 10⁻⁴ ± 0.1 × 10⁻⁴).

Hemodynamics

There was no significant difference in either systolic or diastolic blood pressures in patients with anterior compared with inferior infarction. However, patients with inferior infarction had slower heart rates (80 ± 1.6 beats/min) than patients with anterior infarction (87 ± 1.7 beats/min, p < 0.001) (fig. 4). Cardiac output was similar in the two groups (fig. 5), 5.1 ± 0.2 l/min with anterior and 5.0 ± 0.2 l/min among patients with inferior infarction, although pulmonary artery occlusive pressure was significantly higher with anterior than with inferior infarction (14.5 ± 1.1 mm Hg, n = 35, and 11.4 ± 0.9 mm Hg, n = 27) (fig. 5). These results suggest that left ventricular function was more severely impaired among patients with anterior than with inferior infarction, because the former had higher left ventricular filling pressure without a concomitant increase in cardiac output. Conversely, patients with inferior myocardial infarction had higher (though not statistically significantly) right ventricular end-diastolic pressure than patients with anterior infarction (5.7 ± 0.9 mm
end-diastolic pressure to pulmonary artery occlusive pressure among patients with inferior infarction suggests a primary impairment of right ventricular function. These data suggest that the frequency of right ventricular involvement, reflected by a high ratio of right ventricular end-diastolic pressure to pulmonary artery occlusive pressure, was substantially greater among patients with inferior infarction.

Ventricular Dysrhythmia

To determine whether a difference in early incidence of ventricular dysrhythmia accompanies the difference in early mortality in patients with anterior and inferior infarction, the number of PVCs during the first 10 hours after admission and the number of patients with couplets or ventricular tachycardia were assessed. No significant differences were observed in the incidence of PVCs or in the percentage of patients in the two groups with at least one couplet (44% in group 1 vs 46% in group 2), one episode of ventricular tachycardia (33% and 32%) or either (48% and 54%).

Follow-up Data

Of the 249 patients initially included in this study, 13 were lost to follow-up, seven with anterior and six

FIGURE 4. Heart rate (left) and systemic arterial blood pressure (right) among patients with anterior and inferior myocardial infarction. Error bars indicate SEM. Both systolic and diastolic blood pressure values are depicted for the two groups in the right panel.

Hg compared with 4.0 ± 0.8 mm Hg (fig. 5). The ratio of right ventricular end-diastolic pressure to pulmonary artery occlusive pressure was significantly greater in patients with inferior infarction than in those with anterior infarction ($p < 0.01$) (fig. 6). In addition, only 14% of invasively monitored patients with anterior infarction had a ratio exceeding 0.45, in contrast to 43% of invasively monitored patients with inferior infarction ($p < 0.01$). Although altered left ventricular compliance accompanying infarction could influence right ventricular performance indirectly, the increase in the ratio of right ventricular

FIGURE 5. Pulmonary artery occlusive pressure (left), right ventricular end-diastolic pressure (center) and cardiac output (right) among patients with anterior and those with inferior myocardial infarction. Pulmonary artery occlusive pressure (left ventricular filling pressure) was significantly less in patients who had inferior infarction than in those who had anterior infarction, even though overall enzymatically estimated infarct size (right plus left ventricular injury) was similar among patients in the two groups (see figure 3).

FIGURE 6. The ratio of right ventricular end-diastolic pressure to pulmonary artery occlusive pressure in patients with anterior infarction compared with those with inferior myocardial infarction. This ratio was significantly greater in association with inferior infarction, suggesting relatively more impairment of right ventricular function (reflected by a greater value for the numerator) compared with left ventricular function (reflected by a lower value of the denominator).
with inferior myocardial infarction. The remaining patients, 111 with anterior and 125 with inferior infarction, were followed for an average of 20.7 months. Patients with anterior or inferior infarction had a similar incidence of angina pectoris at least 3 months after the index episode of infarction (35% vs 38%) and of symptoms and signs of congestive heart failure (26% vs 23%). Actuarial survival curves are depicted in figure 7. Patients with anterior myocardial infarction exhibited a significantly higher mortality than those with inferior infarction for the first 2 years after infarction (p < 0.01). Deaths associated with power failure, i.e., those preceded by cardiogenic shock or profound congestive heart failure, were common among patients in both groups (74% and 56%), in keeping with the prevalence of early rather than late mortality. The incidence of power failure as a cause of death was even greater among hemodynamically monitored patients in the two groups (82% and 76%), in keeping with the influence of patient selection for monitoring. Among all decedents in the two groups, the infarct size index was similar (42 ± 3 and 37 ± 4 CK-g-Eq/m²).

Discussion

Results of this study indicate that among patients with comparable overall extent of infarction, anterior myocardial infarction is associated with a greater mortality than inferior infarction. Thus, site of infarction appears to be a determinant of mortality in addition to overall enzymatically estimated infarct size.

The hemodynamic findings support the hypothesis that infarction, reflected in overall enzymatic estimates, includes both right ventricular and left ventricular injury. Although anterior infarction may result in damage confined virtually exclusively to the left ventricle, inferior infarction frequently appears to entail injury involving right as well as left ventricular tissue. These observations are compatible with recent reports suggesting a high frequency of right ventricular involvement accompanying inferior infarction, based on studies with 201T1 scintigraphy, blood pool imaging, and necropsy. Thus, for any given overall infarct size (based on enzymatic estimates) the extent of necrosis confined to the left ventricle may be greater with anterior than with inferior infarction. Because right ventricular injury exerts different influences on overall systemic hemodynamics than equivalent injury in the left ventricle, it is not surprising that manifestations of infarction would therefore differ in the two groups of patients studied.

The present results confirm an association between infarct size and early mortality, particularly among patients with anterior infarction. In addition, they support the hypothesis that right ventricular infarction frequently accompanies inferior infarction and that the site of infarction (i.e., right vs left ventricle) may be an independent additional determinant of outcome. Thus, interpretation of the impact of the overall extent of infarction estimated enzymatically and by other techniques should take into consideration the relative contributions from each ventricle. Procedures will soon be readily available for defining the extent of right ventricular infarction in individual patients based on the use of conventional radiopharmaceuticals and positron-emission tomography with cyclotron-produced tracers. Recognition and quantification of right ventricular involvement should be particularly helpful in stratifying patients for prospective studies concerned with assessing the therapeutic efficacy of interventions and for characterizing prognosis to improve the selection of candidates for invasive diagnostic studies and therapeutic modalities with known risk.

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