Natural History of Severe Left Ventricular Dysfunction after Myocardial Infarction*

Angel Castañer, M.D., F.C.C.P.; Amadeo Betriu, M.D.; Ginés Sanz, M.D.;
J. Carlos Pare, M.D.; Santiago Coll, M.D.; Juan Soler, M.D.;
Eulàlia Roig, M.D.; and Francisco Navarro-López, M.D., F.C.C.P.

The prevalence and prognosis of severe left ventricular dysfunction after infarction was prospectively analyzed in a series of 259 male patients aged 60 years or less surviving an acute myocardial infarction. All patients underwent coronary angiography 30 days after the acute event and were followed up for a mean period of 34 months (range, 15 to 55 months). Forty-five patients (17 percent) were found to have severe left ventricular dysfunction (ejection fraction ≤30 percent). Comparison of patients with and without severe impairment of left ventricular function showed the former to have a lower cardiac index (p<0.001), higher left ventricular end-diastolic volume index (p<0.001), and a higher prevalence of three-vessel disease (p<0.025) and of total or subtotal occlusion of at least one coronary artery (p<0.025). While the occurrence of congestive heart failure was higher in patients with severe left ventricular dysfunction (p<0.001), the probability of developing angina was similar in both groups. Cox's regression analysis showed ejection fraction to be the only independent predictor of survival in patients with severe impairment of left ventricular function. An ejection fraction of 20 percent or less identified a subset of patients with the highest mortality (62 percent at four years), significantly different from that of patients whose ejection fraction was between 21 and 30 percent (28 percent) (p<0.001).

The term, "bad ventricle," graphically characterizes the situation of severe myocardial dysfunction resulting from oclusive coronary arterial disease. Survivors of infarction showing a poorly contracting ventricle at angiography are known to have a high mortality,1-8 however, since available series deal with selected population samples, they are unlikely to represent the natural history of this condition. Lack of prospective studies explains why even the prevalence of severe left ventricular dysfunction following myocardial infarction is unknown. Similarly, the incidence of nonfatal new coronary events in these patients and the influence of baseline clinical and angiographic variables on survival are important questions waiting for an answer. Identification of predictors of the clinical course of these patients appears mandatory to design strategies for management.

The present study was therefore undertaken to assess the natural history of severe left ventricular dysfunction after myocardial infarction. To achieve this goal, a series of 259 consecutive patients who were catheterized one month following infarction and followed up for a mean period of 34 months. Data on the 45 patients of this group who presented with an ejection fraction of ≤30 percent were analyzed separately and are the subject of this report. Specific aims of the study were as follows: (1) to define the prevalence of severe left ventricular dysfunction after infarction; (2) to characterize the coronary anatomy of this population; (3) to determine the rate of occurrence of nonfatal new coronary events; and (4) to identify independent predictors of survival by using Cox's regression analysis.

MATERIALS AND METHODS

Patients

From December 1975 to March 1979, a total of 300 male patients aged 60 years or less were admitted to our coronary care unit with a definite myocardial infarction. A detailed description of the study protocol for myocardial infarction has been published elsewhere.9,10 There were 284 survivors; 21 of them were excluded from the prospective protocol on the basis of their refusal to undergo coronary angiography. Four additional patients were excluded due to the coexistence of a disease with decreased life expectancy (two patients had cancer and two others severe cor pulmonale). The mean follow-up was 34 months (range, 15 to 55 months).

Only 16 patients (6 percent) died before coronary angiography. Nonsurvivors had a higher prevalence of Killip's class 3 and 4 congestive heart failure (11/16 or 69 percent; p<0.001). No differences in mean age, previous infarction, the infarct's location, or prevalence of risk factors were found between participants (259) and nonparticipants (25). Inferior infarcts were more prevalent among nonparticipants (75 percent [19/25] vs 42 percent in participants, p<0.001).

Forty-five of the 259 participants had severe left ventricular dysfunction defined as an ejection fraction of 30 percent or less and they form the basis of the present report. The study's protocol was approved by the Committee for Human Research at our institution. Informed consent was obtained for all patients.
Criteria for Diagnosis of Myocardial Infarction

Acute myocardial infarction was diagnosed when at least two of the following were present: ischemic chest pain lasting more than 20 minutes; typical rise and fall of enzyme levels; and evolving Q-wave abnormalities with acute ST-T wave changes on the electrocardiogram. Previous infarction was diagnosed in the presence of a hospitalization for a documented myocardial infarction or Q waves in the ECG diagnostic of an old infarct.

Catheterization and Angiographic Procedures

Four weeks after infarction, right and left cardiac catheterization and coronary angiography by the percutaneous femoral approach were performed. Single-plane left ventriculography was performed in the 30° right anterior oblique projection. Coronary arteriograms were obtained in multiple projections including angulated views in the sagittal plane. All angiographic images were recorded on 35-mm film at 50 frames per second and reviewed on a projector (Tagarno). Left ventricular volumes and ejection fraction were determined using the area-length method of Sandler and Dodge modified for single-plane calculations. To assess regional wall motion, five areas of interest were considered: anterobasal, anterolateral, apical, diaphragmatic, and posterobasal. They were constructed by drawing a longitudinal axis from the midpoint of the aortic valve to the apex and bisecting it by equidistant chords. The two apical areas were combined and treated as a single region. The systolic change for each region was measured as the segmental ejection fraction.

All angiograms were assessed by two independent observers who coded the degree and location of coronary arterial lesions. Discrepancies were resolved by caliper measurement of percent reduction of luminal diameter in the projection showing maximal stenosis. Lesions of less than 50 percent were considered to be nonobstructive. Each patient was classified as having one-vessel, two-vessel, or three vessel coronary arterial disease. Obstructions of diagonal or marginal branches were considered lesions of the left anterior descending or circumflex artery, respectively. Collateral vessels were judged to be well developed when the diameter of the receiving artery measured more than 1 mm and the sending vessel showed no obstructive lesions. Complete revascularization by collaterals was assumed when all vessels with total or subtotal occlusion were filled by well-developed collaterals. The scoring system of Gensini was used and its result entered in the calculations as an independent variable.

Exercise Test

Six months after infarction, bicycle ergometry was performed in the erect position using an electrically braked ergometer (Elema Schonander EM 370). A standard 12-lead ECG was recorded prior to the test. During exercise a CM1 lead was continuously monitored and recorded at three-minute intervals and at the end point. A test was judged positive in the presence of angina or significant ST-T changes. The latter were defined by either a 1-mm horizontal or downward sloping depression for at least 0.08 second.

Statistical Analysis

A total of 17 variables were identified in each patient from the clinical history, cardiac catheterization, and angiographic data. These variables were age, hypertension, previous infarction, dyslipemia, diabetes, peak creatine phosphokinase (CPK) value, peak lactic dehydrogenase level, the infarct’s location, severe congestive heart failure (Killip’s class 3 or 4) complicating the acute phase of the infarct, left ventricular end-diastolic pressure, cardiac index, ejection fraction, end-diastolic volume index, number of abnormally contracting segments, number of involved vessels, and the Gensini score. Differences between patients with and without severe left ventricular dysfunction were analyzed using the Statistical Package for Social Sciences, applying Student’s t-test, Fisher’s exact test, or the χ2 test when appropriate. A p value less than 0.05 was considered significant.

The occurrence of new coronary events was compared between patients with and without severe left ventricular dysfunction by constructing Kaplan-Meier actuarial curves for the two groups. Statistical differences were assessed by the log-rank test. To assess the factors determining late mortality in patients with severe left ventricular dysfunction, univariate analysis was used to compare the long-term survivors with patients dying during the follow-up. In addition to the variables reaching statistical significance in the univariate analysis (ie, dyslipemia, ejection fraction, and congestive heart failure in the acute phase), a history of previous infarct, left ventricular end-diastolic pressure, cardiac index, the number of affected vessels, and the Gensini score were tested for independent predictive value on survival by multivariate analysis. Cox’s regression technique was used, and the regression coefficients were estimated by a maximal likelihood method. These coefficients indicate the degree of association of each variable with survival time, after adjusting for the effects of other covariates in the model.

Results

Prevalence

A total of 45 patients were found to have an ejection fraction of 30 percent or less. Thus, the prevalence of severe left ventricular dysfunction was 17 percent in this series.

Clinical and Hemodynamic Data

A previous history of myocardial infarction was more frequent in patients with severe left ventricular dysfunction (p<0.001). Also, anterior or combined (anterior plus inferior) infarcts were more common in this group (p<0.001). Patients with an ejection fraction of less than 30 percent had higher CPK values at the time of the acute event than their counterparts (p<0.05). Age, the prevalence of diabetes mellitus, high blood pressure, dyslipemia, or a previous history of angina

Table 1—Clinical Findings*

<table>
<thead>
<tr>
<th>Ejection Fraction</th>
<th>Data</th>
<th>≤30 percent</th>
<th>&gt;30 percent</th>
<th>p†</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>45</td>
<td>214</td>
<td>. .</td>
<td></td>
</tr>
<tr>
<td>Age, yr</td>
<td>50 ± 7</td>
<td>50 ± 8</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>12 (26)</td>
<td>15 (7)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Previous angina</td>
<td>21 (47)</td>
<td>81 (38)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>15 (33)</td>
<td>70 (32)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Dyslipemia</td>
<td>25 (55)</td>
<td>93 (43)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>5 (11)</td>
<td>42 (19)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Infarct’s location</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>28 (62)</td>
<td>79 (37)</td>
<td>≤0.002</td>
<td></td>
</tr>
<tr>
<td>Inferior</td>
<td>10 (22)</td>
<td>111 (52)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Combined</td>
<td>7 (16)</td>
<td>14 (6)</td>
<td>≤0.05</td>
<td></td>
</tr>
<tr>
<td>Nontransmural</td>
<td>0</td>
<td>10 (5)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Severe congestive heart failure in acute phase</td>
<td>10 (22)</td>
<td>4 (2)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Peak CPK level‡</td>
<td>1,352 ± 980</td>
<td>1,001 ± 722</td>
<td>&lt;0.05</td>
<td></td>
</tr>
</tbody>
</table>

*Table values are numbers of patients; numbers within parentheses are percents.
†NS, Not significant.
‡Mean ± SD.
were not significantly different between the groups with and without severe left ventricular dysfunction (see Table 1). Cardiac index was lower (p<0.001) and left ventricular end-diastolic pressure and volume higher (p<0.001) in patients with an ejection fraction less than 30 percent (Table 2).

**Coronary Anatomy**

As shown in Table 2, three-vessel disease was more prevalent among patients with an ejection fraction less than 30 percent (p<0.025). While 41 patients (91 percent) with severe left ventricular dysfunction had lesions of 90 percent or more in at least one coronary artery, such a degree of stenosis was found in 153 (72 percent) of the cases with an ejection fraction greater than 30 percent (p<0.025). Total or subtotal lesions in more than one vessel were also more prevalent in the former group (p<0.001).

Collateral vessels identified in a total of 115 patients were equally prevalent in patients with or without severe left ventricular dysfunction. Figure 1 represents the percentage of patients with coronary arterial lesions greater than 90 percent found to have collateral channels on angiography. Well-developed collateral vessels were prevalent among patients with an ejection fraction greater than 30 percent (p<0.05).

Patients with severe left ventricular dysfunction after an anterior myocardial infarction had lower regional systolic wall motion in anterior as well as in inferior segments (p<0.001) than those with a lesser degree of dysfunction. The latter group showed motion in diaphragmatic and posterolateral segments to be within the normal range. Patients with inferior myocardial infarction and severe left ventricular dysfunction had more depressed wall motion in anterobasal (p<0.001), anterolateral (p<0.001), apical (p<0.001), and diaphragmatic (p<0.05) segments, whereas no difference with patients showing a better left ventricular function was found in posterobasal wall motion. In combined infarcts, patients with severe impairment of left ventricular function showed significantly more depressed wall motion in all segments (see Fig 2).

**Exercise Test**

An exercise test could be performed only in 30 of the 45 patients with severe left ventricular dysfunction. The remaining 15 were excluded because of poor physical condition (ten) or death before six months of follow-up (five). Double product was 214 ± 59 mm Hg x beats per minute x 10^-3, similar to that found in the group of 214 patients showing better ejection fraction (216 ± 63 mm Hg x beats per minute x 10^-3). Maximal work load was lower in the former group (58 ± 20 kpm/kg/min vs 68 ± 23 kpm/kg/min; p<0.02).

**Follow-Up**

Eleven of the 45 patients died during follow-up. The probability of survival at 48 months was higher (p<0.001) in patients with an ejection fraction over 30 percent. While the probability of developing angina on follow-up was similar in both groups and close to 40 percent at 30 months, congestive heart failure was prevalent among patients with severe left ventricular...
dysfunction (p<0.001).

The 45 patients with an ejection fraction of 30 percent or less were independently analyzed to search for predictors of survival. Of the 17 variables considered (see methods), only ejection fraction, dyslipemia, and the development of severe congestive heart failure in the acute phase of the infarct were found to be univariate predictors of survival. Although a previous infarct, cardiac index, left ventricular end-diastolic pressure, the number of involved vessels, and the Gensini score were not statistically different between the dead and survivor groups, they were also entered in the multivariate analysis to test their value as predictors of survival. Cox’s regression analysis identified the ejection fraction as the only variable carrying independent information to predict survival in this group of patients (p<0.005).

Figure 3 shows Kaplan-Meier survival curves in patients with severe left ventricular dysfunction. No significant differences were found with regard to the presence of one-vessel, two-vessel, or three-vessel disease; however, a subgroup was identified with an ejection fraction of 20 percent or less who had a 62 percent mortality at four years, significantly higher (p<0.005) than that of patients whose ejection fraction was between 21 and 30 percent (28 percent mortality).

**Figure 2.** Regional wall motion in anterior, inferior, and combined infarcts. Open circles represent patients with ejection fraction less than 30 percent, and closed circles represent group with severe left ventricular dysfunction. Notice more severe depression of regional ejection fraction in infarcted and noninfarcted segments, in patients with ejection fraction less than 30 percent, independently of infarct's location. Shaded area represents normal range of wall motion. Anterobasal, anterolateral, apical, diaphragmatic, and posterobasal segments are numbered 1, 2, 3, 4, and 5, respectively. Single asterisk indicates p<0.05; double asterisk indicates p<0.025; triple asterisk indicates p<0.001; and quadruple asterisk indicates p<0.0001; MI, Myocardial infarction.

**Figure 3.** Survival curves in different subsets of patients with severe left ventricular dysfunction. Left panel shows probability of survival in patients with one-vessel (IV) (n = 10), two-vessel (2V) (n = 16), or three-vessel (3V) (n = 18) disease. Right panel compares survival rates of patients with ejection fraction (EF) of 20 percent or less (n = 10) with that of those with EF between 21 and 30 percent (n = 35). NS, Not significant.
DISCUSSION

Prevalence of Severe Left Ventricular Dysfunction

The prevalence of severe left ventricular dysfunction after infarction has not previously been analyzed in unselected groups of patients. Since prior studies are either retrospective or exclude a variable number of potential candidates, our series which includes 91 percent of the candidates for angiography represents the first attempt to assess the prevalence of this condition on a prospective basis. Although we analyzed a limited age group of men, our series included 70 percent of all patients admitted to our cardiac care unit with myocardial infarction. Thus, our results are not likely to be distorted by selection criteria.

Clinical and Angiographic Characterization of Severe Left Ventricular Dysfunction

Anterior wall location (p<0.001), previous history of infarction (p<0.001), three-vessel involvement (p<0.025), and total or subtotal stenosis in more than one vessel (p<0.001) were found to be more prevalent in this group. Thus, it appears that both the severity and extent of coronary arterial lesions are determinants of left ventricular performance after infarction.

Experimental data indicate that early reperfusion after coronary arterial occlusion improves left ventricular function. In patients with myocardial infarction, spontaneous reperfusion could be achieved by reopening the occluded vessel or through collateral vessels. In view of the prevalence of total occlusion and the lack of adequate collateralization observed in the setting of severe left ventricular dysfunction, neither of these mechanisms seems to be operative in these patients.

When regional wall motion was compared in patients with and without severe left ventricular dysfunction (Fig 2), the former group showed a more severe impairment in both infarcted and noninfarcted areas. Therefore, it appears that these patients sustain larger infarcts with more severe transmural necrosis and involvement of more ventricular segments. The observed dysfunction of noninfarcted areas may be accounted for by the extent of coronary arterial disease or the association of a previous infarct (or both).

Prognostic Significance of Severe Left Ventricular Dysfunction

The best predictors of survival in patients with coronary arterial disease have been demonstrated to be ejection fraction and the number of diseased vessels. In agreement with previous observations, our data indicate that the probability of survival after infarction is significantly reduced in patients with severe left ventricular dysfunction; however, when this group is separately analyzed besides ejection fraction, no other variables influencing survival could be identified by multivariate analysis. In keeping with our data is the observation of Vlieesta et al., who found by linear discriminant analysis that the prognostic value of ejection fraction on mortality was not improved when the number of diseased vessels was considered. Taylor et al showed by multivariate analysis that previous myocardial infarction and low ejection fraction (<40 percent) were the only predictors of mortality. The predicting value of previous infarction is probably linked to the lower ejection fraction that the association of two infarcts determines. This may well explain why Cox's regression analysis failed to identify old myocardial infarction as an independent variable influencing mortality in our series.

An ejection fraction of 20 percent or less identified a subset of patients whose prognosis was significantly worse than that of the population showing ejection fraction between 21 and 30 percent (63 percent vs 22 percent mortality at 30 months; p<0.001). Although we failed to demonstrate three-vessel disease associated with severe left ventricular dysfunction to play any significant role as an independent predictor of survival at 60 months, the mortality in this subgroup was high (44 percent). The borderline p value obtained by comparing the probability of survival in patients with one-vessel and three-vessel disease strongly suggests that a longer follow-up may disclose significant differences.

Clinical Implications

Surgical management of patients with poor left ventricular function remains controversial in spite of recent reports showing its feasibility at an acceptable risk. Manley et al., in a retrospective study, compared the effects of surgical treatment on survival in patients with coronary arterial disease and severe left ventricular dysfunction. Patients with an ejection fraction of 20 percent or less had a four-year mortality of 70 percent in the medically treated group and of 58 percent in the surgical cohort. These figures closely resemble the observed mortality in the present series (62 percent at four years) for patients with comparable degrees of left ventricular dysfunction. Therefore, and according to our interpretation of the present data, we believe that surgical management of patients whose ejection fraction is lower than 20 percent should be restricted to cases with intractable angina or congestive heart failure due to resectable aneurysms (or both). Interestingly, none of these patients in our series had a localized scar amenable to surgical correction. On the other hand, patients with an ejection fraction between 21 and 30 percent had a four-year mortality of 28 percent, significantly higher than the 5 percent observed in individuals with better left ventricular function (p<0.001). The suggestion that these pa-
tients—even if asymptomatic—would be candidates for myocardial revascularization is supported by data from large retrospective series. These studies indicate that patients with multivessel disease and moderate impairment of ventricular function may have an improved outlook when treated surgically. We found congestive heart failure to be prevalent among patients with severe left ventricular dysfunction. No differences were observed with regard to the occurrence of angina between patients with and without severe left ventricular dysfunction. As only one of the 45 patients with an ejection fraction below 30 percent suffered a nonfatal reinfarction, analysis of factors determining its occurrence could not be carried out.

In conclusion, severe left ventricular dysfunction after myocardial infarction is not uncommon (17 percent) and is prevalent among patients with either a previous infarction or severe extensive coronary arterial disease. While congestive heart failure in the follow-up was more commonly observed in these patients, the occurrence of angina was independent of the degree of impairment of ventricular function. The four-year survival did not appear to be related to the number of involved arteries. An ejection fraction of 20 percent or less identifies a subset with the highest mortality (62 percent at four years), significantly different from that of patients whose ejection fraction was between 21 and 30 percent (28 percent mortality).

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