Value of Noninvasive Techniques for Predicting Early Complications in Patients With Clinical Class II Acute Myocardial Infarction

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Twenty-six consecutive patients with acute clinical class II myocardial infarction were prospectively evaluated to assess the ability of two-dimensional echocardiography and gated equilibrium radionuclide angiography to predict early morbidity and mortality. Within 48 hours of the onset of symptoms, right heart catheterization, two-dimensional echocardiography and radionuclide angiography were performed. Serious in-hospital complications developed in 7 patients (27%, Group I), while the remaining 19 patients (Group II) had no complications.

Mean left ventricular stroke work index was the only hemodynamic variable that differed significantly between Group I and Group II. (28 ± 8 [standard deviation] vs. 39 ± 13 g-m/m², respectively, p < 0.02). Also, Group I compared with Group II had a significantly lower mean left ventricular ejection fraction by two-dimensional echocardiography (26 ± 5 vs. 51 ± 10%, p < 0.001) or by radionuclide angiography (29 ± 9 vs. 46 ± 12%, p < 0.001). Similarly, Group I had a higher average wall motion index than Group II by both techniques (2.2 ± 0.2 vs. 1.7 ± 0.3, p < 0.001 by two-dimensional echocardiography, and 2.1 ± 0.3 vs. 1.7 ± 0.3, p < 0.001 by radionuclide angiography). Selected stepwise multiple regression analysis demonstrated that left ventricular ejection fraction or wall motion index, by two-dimensional echocardiography or radionuclide angiography, had additional value to a history of prior myocardial infarction for predicting in-hospital complications in patients with class II infarction.

It is concluded that either two-dimensional echocardiographic or radionuclide angiographic left ventricular ejection fraction and wall motion index have additional predictive value to a history of prior myocardial infarction for identifying those patients with clinical class II myocardial infarction at risk for developing early complications.
has not been shown; nor has a systematic study been performed to assess the relative value of invasive and noninvasive variables for predicting in-hospital complications in the subgroup of patients with clinical class II infarction. Accordingly, the purposes of this study were: 1) to assess the comparative value of invasive and noninvasive variables for predicting in-hospital complications in patients with a clinically defined class II myocardial infarction; and 2) to compare two-dimensional echocardiographic estimates of left ventricular performance and regional wall motion with those obtained from radionuclide angiography in the same patients.

Methods

Study patients. The study group consisted of 26 prospectively evaluated male patients ranging in age from 46 to 71 years (mean 60). Myocardial infarction was documented by the presence of all of the following criteria: 1) a history, or electrocardiographic evidence, or both, of a prior myocardial infarction; 2) evolution of diagnostic Q waves or ST-T wave changes, or both, by surface electrocardiography (19); and 3) a characteristic rise and fall of serum creatine kinase (CK) and CK-MB isoenzyme levels. The infarction location by electrocardiography was anterior transmural in 9 patients, inferior transmural in 15 and nontransmural in 2. All patients were examined by at least two of the investigators, who agreed that each patient was in clinical class II when two or more of the following criteria were present: 1) a left ventricular third heart sound (26 patients); 2) pulmonary rales covering less than 50% of the posterior lung fields (24 patients); or 3) evidence of pulmonary venous congestion by chest roentgenography (25 patients). Eleven patients had a history, or electrocardiographic evidence, or both, of a prior myocardial infarction.

The therapeutic regimen at the time of the study included digoxin in 5 patients, propranolol in 11, diuretic drugs in 8 and nitrates in 3 patients. All patients gave written informed consent on a form approved by our Institutional Review Board. The three diagnostic procedures were all performed within 2 hours of each other and within 48 hours of the onset of symptoms.

Hemodynamics. Right heart catheterization was accomplished using a balloon-tipped flow-directed 7 thermocatheter. Using a Statham P23Db transducer leveled at the mid-calf, calibrated recordings of the pulmonary artery wedge pressure (PAWP) and electrocardiogram were made simultaneously. Blood pressure was measured with a cuff sphygmomanometer. Cardiac output (CO) was determined in triplicate by the thermodilution technique using an Edwards 9520A cardiac output computer. From these data, the cardiac index (CI), stroke volume index (SVI) and left ventricular stroke work index (LVSWI) were calculated as: CI = CO/BSA (liters/min per m²); SVI = CI/HR × 1,000 (ml/min per m²); LVSWI = SVI × (MAP-PAWP) × 0.0136 g-m/m²; where BSA = body surface area (m²), HR = heart rate and MAP = mean systemic arterial pressure calculated as: systolic pressure + (2 × diastolic pressure)/3.

Two-dimensional echocardiography. A two-dimensional echocardiogram was performed using a commercially available phased array ultrasonograph equipped with a 2.25 MHz transducer having a minimal sector angle of 84°. Particular emphasis was placed on obtaining high quality views from the parasternal long and short axes and from the apical four chamber and long-axis projections (20). Images were recorded on videotape simultaneously with 1 cm vertical and horizontal calibration grids and an electrocardiogram. In 23 (88%) of the 26 patients, high quality echocardiograms were obtained for analysis.

Images were processed for left ventricular volumes and ejection fraction using the method validated previously in this laboratory in comparison with biplane cineangiography (21). In brief, with the use of a microprocessor-controlled video light pen system, each image was calibrated for analysis using the simultaneously recorded grid system. Images were viewed in real-time, slow motion and stop-frame formats. Using the stop-frame mode and the reference echocardiogram, an observer employed the light pen to trace the outline of the left ventricular endocardium at end-diastole (defined as the peak of the R wave on the electrocardiogram) and end-systole (defined as the maximal inward motion of the left ventricle) in both the apical four chamber and long-axis projections. Long axes were measured from the left ventricular apex to the midpoint of the mitral valve plane. These data were averaged over three sinus beats and a modified Simpson’s rule algorithm was used to calculate end-diastolic and end-systolic volumes. Left ventricular ejection fraction was obtained in the standard manner.

Radionuclide angiography. Good quality gated equilibrum radionuclide angiographic images were obtained in the anterior and 45° left anterior oblique projections in all 26 patients after in vivo red blood cell labeling with 20 mCi of technitium-99m. Images were acquired under electrocardiographic control using a single crystal gamma scintillation camera (Ohio Nuclear 420). Count information in consecutive corresponding 40 ms segments of each cardiac cycle was summed and stored as images in the dedicated computer memory until each frame contained at least 300,000 counts. Nine point spatial smoothing was performed on each image of the composite cycle. A semiautomated edge detection program defined a left ventricular region of interest for each left anterior oblique image. From these regions of interest, a left ventricular time-activity curve was generated after background (obtained manually from a left ventricular end-diastolic paraventricular region of interest) was subtracted. The left ventricular ejection fraction was calculated by subtracting end-systolic from end-diastolic counts and dividing by end-diastolic counts. This radionuclide angio-
graphic method of obtaining left ventricular ejection fraction has been validated previously (21) in this laboratory in comparison with biplane cineangiography (correlation coefficient \( r = 0.93 \)).

Wall motion analysis. Left ventricular wall motion for each noninvasive study was analyzed independently by at least two of the investigators in a blinded fashion. Seven corresponding left ventricular segments were identified and each segment was evaluated for the degree of dyssynergy for each noninvasive technique (Fig. 1). In 1 of the 23 patients studied by two-dimensional echocardiography and in 8 of the 26 patients studied by radionuclide angiography, only six of the seven segments were visualized adequately. Therefore, in the 26 patients studied, 160 (88%) of a possible 182 left ventricular segments were evaluated by two-dimensional echocardiography and 174 (96%) of 182 left ventricular segments were analyzed by radionuclide angiography. Interobserver concordance in the grade of dyssynergy was observed in 111 (69%) of the 160 left ventricular segments on two-dimensional echocardiography and in 128 (74%) of the 174 left ventricular segments on radionuclide angiography. The remaining left ventricular segments differed by only one grade of dyssynergy in the two noninvasive techniques. The scores of all identified segments for each patient were then added, and the total score was divided by the total number of segments visualized to obtain a left ventricular wall motion index.

**Figure 1.** The left ventricular regions for wall motion analysis by radionuclide angiography from the anterior (ANT) and left anterior oblique (LAO) views and by two-dimensional (2D) echocardiography from the apical long-axis, apical four chamber and parasternal short-axis views are shown. The seven left ventricular regions for wall motion analysis by each technique include: 1, anterobasilar; 2, anterior; 3, apical; 4, inferior; 5, inferobasilar; 6, septal; and 7, posterolateral. Wall motion was scored from 1.0 to 4.0 as indicated.

### Results

**Hospital complications.** The in-hospital course of each patient was monitored closely for complications. Seven patients (Group I) developed one or more serious in-hospital complications: sudden death (one patient), recurrent infarction (two patients), progression to cardiogenic shock (three patients, one of whom subsequently died) or angina decubitus refractory to medical management and requiring early cardiac catheterization (four patients). The remaining 19 patients (Group II) had an uncomplicated in-hospital convalescence. The only demographic predictor variable identified for in-hospital complications was a history of or electrocardiographic evidence for a prior myocardial infarction \( (p = 0.01) \).

**Hemodynamics.** There was a broad range of hemodynamic findings in the total group of patients. The pulmonary artery wedge pressure ranged from 7 to 35 mm Hg (mean 20 ± 6). The cardiac index varied between 1.3 and 3.2 liters/min per m² (mean 2.5 ± 0.8) and the stroke volume index ranged from 14 to 53 ml/min per m² (mean 31 ± 9). In addition, left ventricular stroke work index varied from 12.8 to 65.1 g-m/m² (mean 36 ± 13).

**Two-dimensional echocardiographic and radionuclide angiographic data.** The noninvasive estimates of left ventricular ejection fraction and dyssynergy also varied considerably in the entire group of patients. Left ventricular ejection fraction ranged from 19 to 65% (mean 43 ± 14) for two-dimensional echocardiography and from 16 to 68% (mean 41 ± 14) for radionuclide angiography. Similarly, the extent of left ventricular dyssynergy, as estimated by the wall motion index, ranged from 1.1 to 2.6 (mean 1.8

### Statistical analysis

Data are presented as the mean ± 1 standard deviation. Continuous variables were compared between patient groups with and without in-hospital complications using a nonpaired \( t \) test. A probability value \( (p) \) of 0.05 or less was considered significant. Correlation coefficients, regression equations, 95% confidence intervals and standard errors of the estimate were obtained using least squares linear regression analysis. To identify the best variables for predicting in-hospital complications, categorical data and break-point analysis of continuous data were performed utilizing Fischer’s exact test. A Pearson’s correlation matrix was generated to determine how well each of the potential predictor variables correlated with the predicted variable, that is, in-hospital complications. Finally, selected stepwise multiple regression analysis was employed to determine the optimal ordering of variable inclusion in the regression equation. Several methods were used for stepwise ordering of predictor variables as suggested by the correlation matrix, to determine the additive value of individual and sequentially added invasive and noninvasive predictor variables to demographic predictor variables (22).
± 0.4) for two-dimensional echocardiography and from 1.1 to 2.7 (mean 1.8 ± 0.4) for radionuclide angiography. The left ventricular ejection fraction and wall motion index estimates obtained from two-dimensional echocardiography correlated with the corresponding values obtained from radionuclide angiography (r = 0.86 and 0.92, respectively) (Fig. 2A and B).

Predictive value of hemodynamic and noninvasive variables. Hemodynamic variables. When the complicated (Group I) and uncomplicated (Group II) patient groups were compared, individual values for hemodynamic variables demonstrated considerable overlap. Whereas mean pulmonary artery wedge pressure was slightly higher and cardiac index and stroke volume index were slightly lower in Group I compared with Group II patients, these differences were not statistically significant. However, the average left ventricular stroke work index in Group I was significantly lower than that in Group II (28 ± 8 vs. 39 ± 13 g·m/m², respectively, p < 0.02) (Fig. 3). In addition, two hemodynamic predictor variables for in-hospital complications were identified by break-point analysis: a pulmonary artery wedge pressure of more than 20 mm Hg (p < 0.05) and a left ventricular stroke work index of less than 30 g·m/m² (p < 0.02). Four of the 26 patients had both of these hemodynamic predictor variables present and all 4 had one or more complications.

Noninvasive measurements. By contrast, the individual left ventricular ejection fraction and wall motion index measurements obtained by either noninvasive method better discriminated between Group I and II patients. The mean two-dimensional echocardiographic left ventricular ejection fraction for Group I (26 ± 5%) was significantly lower than that for Group II (51 ± 10%) (p < 0.001) (Fig. 4A). The mean radionuclide angiographic left ventricular ejection fraction for Group I (29 ± 9%) was also significantly lower than that for Group II (46 ± 12%) (p < 0.001) (Fig. 4B). The mean two-dimensional echocardiographic wall motion index for Group I (2.2 ± 0.2) was significantly higher than that for Group II (1.7 ± 0.3) (p < 0.001) (Fig. 5A). Also, the mean radionuclide angiographic wall motion index for Group I (2.1 ± 0.3) was significantly higher than that for Group II (1.7 ± 0.3) (p < 0.001) (Fig. 5B). Moreover, the noninvasive predictor variables for in-hospital complications identified by break-point analysis were a left ventricular ejection fraction of 40% or less by two-dimensional echocardiography (p < 0.001) or radionuclide angiography (p < 0.01) and a left ventricular wall motion index of 2.0 or more by either noninvasive method (p < 0.01 and p < 0.001, respectively).

The Pearson correlation matrix identified six individual predictor variables that correlated significantly with in-hospital complications, including a history of or electrocardiographic evidence for prior myocardial infarction, a left ventricular stroke work index of less than 30 g·m/m² and a left ventricular wall motion index obtained from radionuclide angiography and two-dimensional echocardiography are shown in a similar manner.
ventricular ejection fraction of 40% or less, or a left ventricular wall motion index of 2.0 or more by either two-dimensional echocardiography or radionuclide angiography (Table 1). After selecting prior myocardial infarction as the initial predictor variable, stepwise multiple regression analysis was used to add the hemodynamic and noninvasive variables individually and sequentially to determine whether they improved the predictive value for in-hospital complications beyond that observed for the demographic predictor variable alone ($r = 0.53$). The only hemodynamic variable that individually improved the prediction of in-hospital complications was left ventricular stroke work index ($r = 0.68$). However, all four noninvasive variables individually improved the prediction of complications. Two-dimensional echocardiographic left ventricular ejection fraction and wall motion index improved prediction to $r = 0.81$ and 0.71, respectively, and radionuclide angiographic left ventricular ejection fraction and wall motion index improved prediction.

**Table 1. Pearson’s Correlation Matrix: Univariate Predictors of Complications**

<table>
<thead>
<tr>
<th>Predictor Variables</th>
<th>$r$ Value</th>
<th>Nonpredictor Variables</th>
<th>$r$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of myocardial infarction</td>
<td>0.50</td>
<td>History of angina pectoris</td>
<td>-0.12</td>
</tr>
<tr>
<td>Left ventricular stroke work index</td>
<td>-0.45</td>
<td>History of congestive heart failure</td>
<td>-0.31</td>
</tr>
<tr>
<td>2DE LV wall motion index</td>
<td>0.59</td>
<td>Site of new myocardial infarction</td>
<td>-0.12</td>
</tr>
<tr>
<td>2DE LV ejection fraction</td>
<td>-0.80</td>
<td>Heart rate</td>
<td>0.32</td>
</tr>
<tr>
<td>RNA LV wall motion index</td>
<td>0.66</td>
<td>Pulmonary artery wedge pressure</td>
<td>0.22</td>
</tr>
<tr>
<td>RNA LV ejection fraction</td>
<td>-0.61</td>
<td>Cardiac index</td>
<td>0.16</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Stroke volume index</td>
<td>-0.27</td>
</tr>
</tbody>
</table>

$LV =$ left ventricular; $RNA =$ radionuclide angiography; $2DE =$ two-dimensional echocardiography.
to \( r = 0.71 \) and 0.74, respectively. The sequential addition of two-dimensional echocardiographic left ventricular ejection fraction to wall motion index did not improve the prediction observed for two-dimensional echocardiographic left ventricular wall motion index alone.

**Discussion**

Although clinical findings are the basis for the Killip and Kimball classification (1) of patients with acute myocardial infarction, signs of mild left ventricular failure have been shown to be relatively poor predictors of an individual patient’s hemodynamic status. Riley et al. (23) examined the relation between a left ventricular third heart sound and end-diastolic pressure in 27 patients with acute myocardial infarction. In patients with a third heart sound, left ventricular end-diastolic pressure ranged from 7 to 60 mm Hg and 10 patients had filling pressures less than 20 mm Hg. Wolk et al. (2) also reported a poor correlation between clinical findings and left ventricular end-diastolic pressure in patients with acute infarction. In addition, chest roentgenographic evidence of pulmonary venous hypertension may not reflect the corresponding left ventricular end-diastolic pressure or wedge pressure (24,25). Therefore, patients with acute myocardial infarction with clinically defined mild left ventricular failure may be better characterized by an invasive or noninvasive study.

**Role of hemodynamic monitoring.** Invasive hemodynamic monitoring is valuable for characterizing patients with myocardial infarction into low and high risk subsets (2–6). Henning et al. (6) reported that patients with myocardial infarction with a cardiac index less than 2.0 liters/min per m², a stroke volume index less than 25 ml/min per m² or a pulmonary artery wedge pressure greater than 20 mm Hg had a significantly higher 30 day mortality rate than did patients without these hemodynamic abnormalities. Verdoux et al. (3) evaluated 122 patients with acute myocardial infarction and observed that a pulmonary artery wedge pressure exceeding 20 mm Hg was a “threshold value” that helped to identify patients at risk for early mortality. However, Wolk et al. (2) reported that in patients with clinical class II myocardial infarction the only hemodynamic variable that differentiated between those whose condition improved and those with subsequent deterioration was the average left ventricular stroke work index. Therefore, although hemodynamic variables were valuable predictors of morbidity and mortality in studies that evaluated patients with myocardial infarction of all clinical classes, their predictive value in the subset of patients with clinical class II infarction remains unclear.

The present study of patients with clinical class II infarction suggests that hemodynamic variables are of limited predictive value. Whereas mean pulmonary artery wedge pressure was slightly higher and mean cardiac index and stroke volume index were slightly lower in the complicated compared with the uncomplicated patient group, these differences were not statistically significant. Left ventricular stroke work index was significantly lower in the complicated patient group and was the only hemodynamic variable predictive of complications by selected stepwise regression analysis. However, four of the seven patients with complications had both a pulmonary artery wedge pressure of more than 20 mm Hg and a left ventricular stroke work index of less than 30 g·m/m². Thus, individual hemodynamic variables have limited value for identifying patients with class II infarction who may develop complications early after myocardial infarction.

**Prognostic role of radionuclide angiographic ejection fraction.** In patients with acute myocardial infarction, initial left ventricular ejection fraction determinations by radionuclide angiography have been of particular value in identifying high risk patients (7,10,11). Shah et al. (10) studied 56 patients with a first myocardial infarction and found that mean left ventricular ejection fraction was lower in the patients who developed serious complications than in the patients whose hospital course was uncomplicated (34 ± 10 vs. 52 ± 13%, respectively, \( p < 0.001 \)). Subsequently, Sanford et al. (11) studied 100 patients with acute myocardial infarction and reported that the Killip classification correlated poorly with left ventricular ejection fraction in individual patients. Moreover, they found that the range of left ventricular ejection fraction estimates among patients with clinical class II infarction was wide (9 to 76%). Schelbert et al. (7) reported that such patients had a significantly lower mean left ventricular ejection fraction than did patients with class I infarction (40 ± 5 vs. 52 ± 5%, respectively, \( p < 0.001 \)), and that all early deaths were in patients with a reduced left ventricular ejection fraction.

**Prognostic role of echocardiographic wall motion abnormalities.** Two-dimensional echocardiography has also been used to categorize patients with acute myocardial infarction. Heger et al. (13) observed a correlation between infarct location by electrocardiography and two-dimensional echocardiographic left ventricular wall motion abnormalities. They also reported (14) that left ventricular wall motion abnormalities correlated with the measured hemodynamic variables of left ventricular function. In addition, Gibson et al. (18) found that two-dimensional echocardiographic wall motion abnormalities in patients with myocardial infarction were useful in determining the risk for subsequent hemodynamic deterioration. Therefore, from these initial noninvasive myocardial infarction studies, it appears that left ventricular ejection fraction and wall motion abnormalities obtained by radionuclide angiography or two-dimensional echocardiography may be of value for predicting complications in patients with myocardial infarction. However, the
ability of two-dimensional echocardiography to quantitate left ventricular performance in patients with acute myocardial infarction and the value of both techniques for predicting complications in the selected subgroup of patients with clinically defined class II myocardial infarction have not been evaluated systematically.

**Role of either noninvasive technique.** The present study demonstrates that qualitative and quantitative radionuclide angiographic and two-dimensional echocardiographic variables can predict complications in patients with clinical class II acute myocardial infarction. A left ventricular ejection fraction of 40% or less and a wall motion index of 2.0 or more by either noninvasive technique were each shown to be a valuable predictor variable for in-hospital complications in those patients with clinical class II infarction by selected stepwise multiple regression analysis. The present study also demonstrates that left ventricular ejection fraction and wall motion index measurements obtained by two-dimensional echocardiography in patients with acute myocardial infarction correlate with the corresponding values obtained by radionuclide angiography. Therefore, either two-dimensional echocardiography or radionuclide angiography is valuable for rapid assessment of the extent of left ventricular dysfunction and, as a result, for characterizing a subgroup of patients with clinical class II acute infarction at risk for early complications.

**Limitations.** Some potential limitations of this study should be noted. First, several of our patients had a prior myocardial infarction, were treated with digitalis or had an acute anterior transmural myocardial infarction that may have affected independently the occurrence of early complications. However, the distribution of digitalis therapy and acute infarction location did not differ between the groups with and without in-hospital complications. Despite the presence of the demographic predictor variable or prior myocardial infarction, the selected stepwise multiple regression analysis demonstrated the additive predictive value of one hemodynamic and all four noninvasive variables. Second, not all patients had two-dimensional echocardiograms of sufficient quality for qualitative and quantitative interpretation. However, only 3 (12%) of the 26 patients with acute myocardial infarction did not have high quality studies. This success rate in acutely ill patients is similar to that reported by other investigators (13,17). Finally, radionuclide angiography did not allow for the careful evaluation of the inferobasilar segment of the left ventricle in all patients because of the overlapping right ventricle. This is an important consideration in the present study because of the large number of patients with acute inferior transmural myocardial infarction. A left lateral or left posterior oblique projection might have enhanced our ability to evaluate qualitatively the inferobasilar region.

**Clinical implications.** Either two-dimensional echocardiography or radionuclide angiography can be used both qualitatively or quantitatively to assess the extent of left ventricular dysfunction in patients with acute clinical class II myocardial infarction. From these data, patients with class II infarction can be stratified into a high risk subset prone to in-hospital complications on the basis of a history of prior myocardial infarction and the noninvasive predictor variables of a left ventricular ejection fraction of 40% or less or a left ventricular wall motion index of 2.0 or more. However, the two-dimensional echocardiographic left ventricular ejection fraction was a better predictor of complication than the two-dimensional echocardiographic wall motion index. In addition, difficulties in visualizing all left ventricular regions for wall motion analysis coupled with the variability in observer interpretation of wall motion by either noninvasive technique potentially limit the value of the wall motion index compared with the left ventricular ejection fraction determination by either noninvasive method.

These noninvasive predictor variables appear to be more useful in patients with clinical class II infarction than most hemodynamic variables. Therefore, a subgroup of patients with clinical class II infarction, in whom more aggressive therapy may be indicated to alter this prognosis, may be identified immediately by either two-dimensional echocardiography or radionuclide angiography.

References


10. Shah PK, Pichler M, Berman DS, Singh BN, Swan HJe. Left ventricular ejection fraction determined by radionuclide ventriculography.


