Clinical and Echocardiographic Correlates of Health Status in Patients with Acute Chest Pain

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OBJECTIVE: To assess the ability of echocardiographic data to predict important functional status outcomes in patients with chest pain.

DESIGN: Prospective cohort study.

SETTING: A large, urban teaching hospital.

PATIENTS: Three hundred thirty-three patients admitted from the Emergency Department for evaluation of chest pain.

MEASUREMENTS AND MAIN RESULTS: Patients underwent two-dimensional and Doppler echocardiography as well as a face-to-face interview during their initial hospitalization and a telephone interview 1 year thereafter. The interview included the Medical Outcomes Study 36-Item Short Form (SF-36) health inventory, a generic health status instrument with a physical function subscale. The relation between clinical and echocardiographic factors and functional status was explored by univariable and multivariable linear regression and logistic regression analyses. Multiple clinical and echocardiographic factors correlated significantly with functional status measures at 1 year. For the SF-36 score at 1 year, age, male gender, white race, the presence of rales, and a comorbidity score were independently predictors in multivariate analysis; echocardiographic findings of severe left ventricular dysfunction (parameter estimate [PE] -27.6 ; 95% confidence interval [CI] -43.1 , -12.2) and aortic insufficiency (PE -16.7 ; 95% CI -26.4 , -7.0) added independent predictive information. Explanatory power (r^2) for models using clinical and demographic variables was .27 and increased after inclusion of echocardiographic data to an r^2 of .35. Results in the subset of patients ($n = 148$) with acute coronary syndromes such as unstable angina or myocardial infarction were qualitatively similar. Selected factors (rales on examination, electrocardiographic changes suggestive of ischemia, and moderate to severe mitral regurgitation) also predicted which patients would die or have a decline in their functional status. In multivariate analysis, only rales remained an independent predictor of poor outcome (odds ratio 2.4; 95% CI 1.2, 4.5).

CONCLUSIONS: Echocardiographic data are correlated with measures of functional status in patients with chest pain, but the ability to predict future functional status from clinical or echocardiographic information is limited. Because functional status cannot be predicted adequately from either patients' characteristics or echocardiographic testing, it must be assessed directly.

KEY WORDS: chest pain; echocardiography; functional status; prognosis.

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Echocardiographic factors such as left ventricular (LV) function and the presence of significant mitral regurgitation are important predictors of mortality in patients with myocardial infarction (MI) or an acute chest pain syndrome.¹⁻⁵ There is growing appreciation, however, of other outcomes, such as functional status, that contribute significantly to patient satisfaction and health-related quality of life and may also be useful as prognostic indicators. Several instruments are available to allow physicians to measure patients' perception of their physical functioning in a manner that correlates well with objective testing,⁶ and is sensitive to therapeutic changes.⁷ The relation between these functional status measures and the echocardiographic evaluation often obtained in patients with chest pain is not clear, although some information is available from studies of patients with congestive heart failure (CHF).⁸⁻¹¹

The strength of the correlation between results of noninvasive imaging and functional status has important repercussions for clinical assessment of these patients and for trials of pharmacologic or therapeutic interventions. For example, if LV function strongly predicts functional status, particularly in patients with acute coronary syndromes such as unstable angina or MI, this information may help guide clinical decisions about further assessment or intervention. Physiologic measures such as LV ejection fraction are also often used in addition to mortality or as surrogate end points in clinical trials, but their ability to predict vital functional status outcomes remains uncertain. Conversely, a weak correlation between echocardiographic information and future functional status suggests that echocardiography and measures of functional status provide different, complementary information concerning patient outcome and that direct measurement of functional status is necessary. To determine the relation between echocardiographic factors and self-reported measures of functional status, we prospectively studied 333 patients with acute chest pain.

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METHODS

Patients 30 years of age or older presenting to the Emergency Department with a chief complaint of chest pain in the absence of trauma or chest x-ray abnormalities were eligible for enrollment in the Chest Pain Study, a multiphase investigation of optimal diagnostic and treatment strategies in this population.^{12–20} Patients were eligible for the current study if they were admitted to a monitored setting for evaluation on enrollment days between October 1991 and December 1992. Of the 709 eligible patients who visited on enrollment days, 40 patients (6%) were not approached, for example, because the patient had been discharged previously or because the physician caring for the patient requested that the patient be excluded. In 164 (23%) of the cases, patients declined to participate. In the remaining 505 patient visits (71%), echocardiographic studies could not be performed owing to logistic difficulties in 12 cases, and 27 studies were technically insufficient for accurate interpretation, leaving a cohort of 466 patient visits associated with interpretable echocardiograms. In 333 cases, patients consented to a face-to-face interview during their initial hospitalization and a telephone interview at 1 year after hospitalization. The interview included the Medical Outcomes Study 36-Item Short Form (SF-36) health inventory,²¹ a generic health status instrument with a physical function (PF) subscale. The PF subscale generates a numeric score between 0 and 100, with 100 denoting optimal function. Patients were asked to answer questions about their health status for the period of the month prior to the chest pain episode. At 1 year, survival status information was available for 96% of the cohort, and 14 patients (4%) had died. Seventy-one percent of the survivors completed the 1-year follow-up interview.

Clinical data for each patient were collected prospectively by the Emergency Department physician or by a research nurse using the data collection protocol of the Chest Pain Study.¹² The electrocardiograph (ECG) findings were considered new unless their presence previous to the index presentation could be documented. Early two-dimensional and color Doppler echocardiography was also completed on each patient on the day of or the day after admission, either on clinical grounds or for the purposes of this study (mean 21.0 h, median 22 h). Standard views, including parasternal long and short-axis, apical four- and two-chamber views, were recorded on Hewlett-Packard Sonos 1000 and 1500 machines (Hewlett-Packard Co., Andover, Mass.).

Echocardiographic Analysis

Echocardiograms were analyzed independently by two experienced echocardiographers without knowledge of the clinical information. Qualitative categorical data such as those routinely used in clinical practice were collected concerning left and right ventricular (LV and RV) function, and valvular disease such as aortic, stenosis,

aortic regurgitation, mitral stenosis, and mitral and tricuspid regurgitation. For example, LV function was defined as normal (estimated ejection fraction >50%), mildly depressed (ejection fraction 40%–50%), moderately depressed (ejection fraction 30%–39%), or severely depressed (ejection fraction <30%). Mitral regurgitation was graded visually as none, mild, moderate, or severe, predominantly on the basis of the color Doppler appearance of the jet in relation to left atrial size.²²

Regional myocardial function was assessed by a wall motion scoring system modified from Edwards et al. and Nishimura et al.^{23–25} The LV was divided into 14 segments, and each was assigned a score (1 = normal, 2 = hypokinetic, 3 = akinetic, 4 = dyskinetic). Segment scores were added and then divided by the number of segments analyzed, generating a “wall motion index” (WMI) ranging from 1 to 4. Data from both observers were combined, and discrepancies in these categorical data or in individual segment scores were resolved by a third independent reader. Intraobserver and interobserver variabilities for this cohort have been reported previously,²⁶ and were good to excellent with concordance rates of 77% to 99%. Intraclass correlation coefficients for continuous variables ranged from 87% to 96% with weighted κ of 0.61 to 0.95 for categorical variables.

Left ventricular size was estimated visually. One reader also measured M-mode or two-dimensional septal and posterior wall thickness and end systolic and end diastolic dimensions.

Definitions

Detailed data concerning definitions of outcomes in the Chest Pain Study have been published previously.^{13,15} The presence of acute MI was based on these criteria, including characteristic evolution in serum enzyme levels, ECG changes, or sudden unexplained death. In addition, acute MI was diagnosed in patients who received reperfusion therapy with intravenous thrombolysis or primary coronary angioplasty if the patient had new ST-segment elevation that evolved over the next day, and if the patient had 100% occlusion of the infarct-related artery, an echocardiographic wall motion abnormality that corresponded to the acute ECG changes, or an elevated total creatine kinase level and an MB isoenzyme above 2.5% of the total creatine kinase level with characteristic evolution.

Analysis

The population distribution of clinical, echocardiographic, and functional status measures was assessed by proportions for categorical variables and means and standard deviations for continuous variables. Patients who died before the 1-year time point were assigned a PF subscale score of 0 at 1 year, as suggested by Fletcher et al.²⁷ The unadjusted relation between clinical and echocardiographic factors and functional status was explored by

univariable linear regression analyses using 1-year functional status indices as the dependent variable and was considered significant at a level of $p < .05$ (SAS Institute, Cary, NC). Because multiple variables were explored, one would normally adjust p values with a Bonferroni correction, for example. However, to minimize the chances of missing potential confounders, we included all explanatory variables with conventional p values $< .05$ as candidate variables in our multivariate analyses, as well as potential confounders that did not achieve this p value. Therefore, p values marginally smaller than $.05$ should be interpreted with caution.

Multivariable modeling was also performed in a stepwise forward selection process (entry criteria $p < .05$, retention criteria $p < .05$) to identify clinical and echocardiographic factors that were independent predictors of functional status at 1 year. A "best" clinical model was created using the clinical factors identified through this process, and the ability of echocardiographic factors to improve on the predictive capabilities of this model was assessed by a stepwise forward selection process of echocardiographic variables. Candidate clinical and echocardiographic variables included all factors associated with the outcome to a level of $p \leq .20$ in univariate analysis. A similar analysis was conducted in the subset of patients with acute coronary syndromes as defined by a discharge diagnosis of unstable angina or MI.

Changes in functional status over the year between initial presentation and follow-up were analyzed in two ways. In the first, the SF-36 PF score at 1 year was subtracted from the score at initial presentation to create a change score, with deaths assigned a 1-year score of 0. Clinical and echocardiographic predictors of this change score were identified by univariable and multivariable regression analysis. In addition, an index designed to identify patients with a worsened functional outcome over the course of the year was created and tested by logistic regression. This index was considered positive if patients died or if survivors decreased more than 6.5 points in self-reported PF score, as a change of more than 6.5 points in the PF subscale is considered outside the 95% confidence interval (CI) for an individual patient score.²⁸ This latter approach has the advantage of avoiding potentially undue influence in change scores by assigning deaths a score of 0 at 1 year. All models are presented as parameter estimates or odds ratio (OR) with 95% CI.

RESULTS

Baseline Characteristics

Average age in the study cohort was 60 years with a slight predominance of men (Table 1). The cohort was racially mixed. Twenty-eight percent had a history of MI while 41% reported prior angina. In the Emergency Department, 19% had rales on examination, and 36% had ECG changes consistent with ischemia. Just under half

left the hospital with a discharge diagnosis of MI or unstable angina. For echocardiographic variables, 21% had abnormal global ventricular function, and LV size was enlarged in 19%. One hundred fifty patients had mitral regurgitation, including 29 patients with moderate insuf-

Table 1. Baseline Characteristics of Cohort ($n = 333$)

Characteristic	Values
Demographics & emergency department data	
Age, mean years $\pm$ SD	60 $\pm$ 13.5
Male gender, n (%)	181 (54)
Race*, n (%)	
White	229 (69)
African American	74 (22)
Hispanic	25 (8)
Asian/other	1 (<1)
Past angina, n (%)	94 (28)
Past MI, n (%)	135 (41)
Rales, n (%)	64 (19)
Ischemic changes on ECG, n (%)	121 (36)
Hospital data, n (%)	
Admission triage	
Coronary/intensive care unit	43 (13)
Stepdown	286 (86)
Other	4 (1)
Discharge diagnosis	
Myocardial infarction	36 (11)
Unstable angina	112 (34)
Echocardiographic data	
Left ventricular dysfunction, n (%)	
None	264 (79)
Mild	34 (11)
Moderate	14 (4)
Severe	21 (6)
Left ventricular enlargement, [†] n (%)	
None	269 (81)
Mild	36 (11)
Moderate	20 (6)
Severe	6 (2)
Right ventricular dysfunction, n (%)	
Absent	315 (95)
Present	18 (5)
Mitral regurgitation, [‡] n (%)	
None	178 (54)
Mild	114 (35)
Moderate	29 (9)
Severe	7 (2)
Tricuspid regurgitation, [§] n (%)	
None	201 (62)
Mild	104 (32)
Moderate	15 (4)
Severe	6 (2)
Wall motion index, mean $\pm$ SD with (5%, 95%)	1.2 $\pm$ 0.4 (1.0, 2.4)

*Data unavailable in 4 patients.

[†]Data unavailable in 2 patients.

[‡]Data unavailable in 5 patients.

[§]Data unavailable in 7 patients.

iciency and 7 with severe regurgitation. The average WMI was 1.2 ± 0.4 with 90% of values falling in the range of 1.0 to 2.4 on a scale of 1 to 4.

Distribution of Functional Status Measures

Functional status scores at the time of initial presentation included an average PF subscale score of 60 ± 31 points on a scale of 0 to 100 (Table 2). When initial functional status was compared for patients with and without 1-year functional status data, no significant differences were noted. At 1 year, the average PF subscale score was slightly higher at 62 points. In 69 cases, patients had a worsened functional outcome as defined previously (death or > 6.5 -point decrease in PF scale).

One-Year Functional Status

Clinical and echocardiographic predictors of PF scores at 1 year (Table 3) included age; gender; race; history of angina or MI; Charlson Comorbidity Index score; rales on examination; WMI; LV function, size, and wall thickness; LV dimensions; RV function; and the presence of substantial aortic, mitral, or tricuspid regurgitation. However, the single strongest predictor for the 1-year value of the PF subscale was the score at initial presentation with an r^2 value of .44. A discharge diagnosis of acute MI, unstable angina, or an acute coronary syndrome (acute MI or unstable angina) was not predictive of PF score at 1 year.

Multivariable models using 1-year functional status measures as the dependent variable are shown in Table 4. Demographic and clinical characteristics such as age, gender, race, the presence of rales, and the degree of comorbidities all were independent predictors of the PF score at 1 year. In addition, the presence of aortic insufficiency or of severe LV dysfunction on echocardiogram was an independent predictor of the PF subscale score. On average, patients with aortic insufficiency had PF scores that were lower by 16.7 points in this model, and patients with severe ventricular dysfunction had scores almost 28 points lower. These parameter estimates exceeded those for clinical factors such as rales (parameter estimate [PE] -10.7 ; 95% CI -20.1 , -1.4) or comorbidity score (PE -7.5 ; 95% CI -10.0 , -4.9). Models using only clinical and demographic variables had modest explanatory power expressed as an r^2 of .27. Inclusion of echocardiographic

Table 3. Univariable Linear Regression Analysis for Physical Function Subscale

Variable*	1-Year Physical Function Score	
	Parameter Estimate† (95% CI)	p Value
Clinical		
Age (per year)	-0.7 (-1.0 , -0.3)	.0001
Male gender	15.3 (7.0 , 23.6)	.0004
History of MI	-13.0 (-22.5 , -3.5)	.008
History of angina	-15.1 (-23.5 , -6.6)	.0005
Charlson comorbidity score	-8.8 (-11.6 , -6.0)	.0001
Rales	-25.6 (-35.5 , -15.7)	.0001
White	10.0 (0.4 , 19.7)	.04
Echocardiographic		
WMI (per unit from 1 to 4)	-17.3 (-26.9 , -7.7)	.0005
LV dysfunction	-19.2 (-29.6 , -8.8)	.0004
LV enlargement	-25.8 (-36.4 , -15.1)	.0001
RV dysfunction	-27.0 (-46.3 , -7.7)	.007
ESD (per cm)	-7.9 (-12.5 , -3.4)	.0008
EDD (per cm)	-7.9 (-13.8 , -2.1)	.008
PWT (per cm)	-3.0 (-5.1 , -1.0)	.004
SWT (per cm)	-2.3 (-4.2 , -0.4)	.02
Aortic insufficiency	-22.9 (-33.1 , -12.7)	.0001
Moderate/severe MR	-33.3 (-45.7 , -20.9)	.0001
Moderate/severe TR	-28.7 (-44.4 , -13.0)	.0004

*WMI indicates wall motion index; LV, left ventricle; RV, right ventricle; ESD, end systolic dimension; EDD, end diastolic dimension; PWT, posterior wall thickness; SWT, septal wall thickness; MR, mitral regurgitation; TR, tricuspid regurgitation.

†Parameter estimate indicates absolute change in physical function subscale score on a 0–100 scale.

data raised the r^2 to .35. If a variable accounting for a discharge diagnosis suggesting an acute coronary syndrome (i.e., acute MI or unstable angina) was forced into the clinical model, aortic insufficiency and severe LV dysfunction remained independent predictors and parameter estimates changed only slightly. If the PF score at the time of initial presentation was included in modeling, then four factors, male gender (PE 7.8; 95% CI 1.4, 14.2), comorbidity score (PE -4.0 ; 95% CI -6.3 , -1.6), aortic insufficiency (PE -10.8 ; 95% CI -18.8 , -2.8), and severe LV dysfunction (PE -20.6 ; 95% CI -34.2 , -7.0), remained independent predictors. Cross-generalizability of the final model (Table 4) was assessed by means of a bootstrap analysis, and an analysis using 500 bootstrapped samples yielded qualitatively similar results.

Predictors of Change in Functional Status

Univariable clinical and echocardiographic predictors of change scores in physical function included ischemic changes on ECG (PE -7.8 ; 95% CI -14.7 , -0.9), severe LV dysfunction (PE -15.4 ; 95% CI -30.2 , -0.5), and substantial valvular regurgitation such as moderate to severe aortic insufficiency (PE -38.4 ; 95% CI -64.4 , -12.4) or severe tricuspid regurgitation (PE -24.2 ; 95% CI -47.7 , -0.6). In multivariate modeling, ECG changes suggesting

Table 2. Distribution of Physical Function (PF) Subscale Score (Mean $\pm$ SD) at Baseline and 1 Year

Baseline (n = 333)		
With 1-Year Data* (n = 242)	Without 1-Year Data† (n = 91)	1-Year Follow-Up† (n = 242)
58 ± 32	64 ± 30	62 ± 34

*PF subscale score unavailable in 4 patients.

†PF subscale score unavailable in 1 patient.

Table 4. Multivariable Model for 1-Year Physical Function Score

Variable	1-Year Physical Function Subscale Score ($r^2 = .35$)	
	Parameter Estimate (95% CI)	p Value
Intercept	78.2 (58.8, 97.5)	.0001
Age (per year)	-0.2 (-0.5, 0.1)	.2
Male gender	11.5 (4.0, 19.0)	.003
White	9.5 (1.3, 17.8)	.03
Rales	-10.7 (-20.1, -1.4)	.02
Charlson comorbidity score	-7.5 (-10.0, -4.9)	.0001
Aortic insufficiency	-16.7 (-26.4, -7.0)	.0009
Severe left ventricular dysfunction	-27.6 (-43.1, -12.2)	.0005

ischemia (PE -7.9; 95% CI -14.7, -1.1) and moderate or severe aortic insufficiency (PE -37.5; 95% CI -63.3, -11.7) remained independent predictors, but the model explained only 6% of the variability in change scores. Even when functional status at initial presentation was included, the resultant model explained only 21% of the variability in change scores.

Selected clinical and echocardiographic factors also predicted which patients in the overall cohort would die or suffer a decline in their functional status. These included rales on examination (OR 2.4; 95% CI 1.2, 4.5), ECG changes suggestive of ischemia (OR 1.8; 95% CI 1.0, 3.1), or moderate to severe mitral regurgitation (OR 2.5; 95% CI 1.1, 5.5). In multivariable analysis, only rales remained significantly correlated with patients who died or survivors in whom functional status declined substantially (OR 2.4; 95% CI 1.2, 4.5).

Subset Analysis in Patients with Unstable Angina or Myocardial Infarction

In the 148 patients with a discharge diagnosis of unstable angina or MI, results were qualitatively similar to those in the cohort overall. Several clinical and echocardiographic factors predicted 1-year functional status including gender, race, comorbidity score, rales on examination, WMI, LV function and size, aortic insufficiency, and mitral insufficiency. In multivariable analysis of this smaller subset, three clinical factors, gender, comorbidity score, and rales on examination, remained independent predictors. The presence of aortic insufficiency and severe LV dysfunction added incremental predictive information (model $r^2 = .44$).

DISCUSSION

Echocardiographic factors such as LV function and the presence of significant mitral regurgitation provide important and incremental information on patients' risk

of mortality in several clinical populations, including the patient with MI or with acute chest pain syndromes.¹⁻⁵ In addition, echocardiography can help predict short-term outcomes such as the risk of in-hospital complications in these patients.²⁶ However, the relation between these variables and other important outcomes such as functional status has been much more circumspect. Studies in patients with CHF have documented relatively poor correlation between LV function as measured by ejection fraction and exercise tolerance during treadmill testing.^{8,9}

More recent data from large multicenter trials of CHF patients such as the Studies of Left Ventricular Dysfunction,¹⁰ and Veterans Administration Heart Failure Trial study,¹¹ also found limited correlation between ejection fraction and a battery of self-reported and observed functional status measures. In stable patients presenting to a large academic medical center for cardiac catheterization and subsequent revascularization, Nelson and colleagues found that the angiographic extent and severity of disease showed only weak correlation with functional status as measured by the Duke Activity Status Index (DASI) and that angiographic variables did not add independent information in predicting functional status after factors such as age and gender had been considered.²⁹

The current study explores the relation of echocardiographic information to self-reported health status in patients with acute chest pain and in the subset of patients with documented acute coronary syndromes. Several echocardiographic factors correlated significantly with physical function at 1 year, but coefficients were modest, implying that echocardiography and measures of functional status provide different, complementary information concerning patient health status. In multivariable models, clinical factors such as age, race, rales, and the presence of comorbidities were independent predictors, but were only moderately predictive of functional status at 1 year. Regurgitant valvular disease or severe LV dysfunction were also independent predictors associated with large parameter estimates, but with relatively small incremental improvement in the predictive capabilities of the model. These conclusions held true for the subset of patients with acute coronary syndromes as well as for the cohort overall. This suggests that direct measurement of functional status is necessary to provide more complete evaluation of patient outcome and for studies of the impact of therapeutic interventions.

As in other studies,²⁹ women reported lower PF subscale scores than men even when age was taken into account. Although the reasons for this gender discrepancy cannot be elucidated from the current study, the findings emphasize the importance of obtaining baseline values for functional status from which change can be measured.

Neither clinical nor echocardiographic factors were accurate predictors of change in functional status over the course of the ensuing year. This was true regardless of whether change was assessed in terms of change scores over the course of the year following presentation

or in terms of logistic regression for an end point of death or significant decline in functional status.

A potential limitation of this study is bias related to the study cohort and to patients in whom functional status information at 1 year could not be obtained. Although every attempt was made to enroll patients meeting the criteria specified, not all patients ultimately participated, allowing for potential selection bias. Although information on survival status at 1 year was 96% complete, 1-year health status information could not be obtained for all patients. However, baseline functional status, the most potent single predictor of future functional status, was not significantly different for patients with and without 1-year data, suggesting that the two groups are comparable.

In summary, echocardiographic data are correlated with self-reported measures of functional status in patients with chest pain, even after adjustment for clinical data. However, the overall correlation is not strong, and the ability to predict future functional status from either clinical or echocardiographic information is limited, even in patients with acute coronary syndromes. As functional status cannot be predicted adequately either from patient characteristics or echocardiographic testing, it must be assessed directly.

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