Serial changes in systolic and diastolic echocardiographic indices as predictors of outcome in patients with decreased left ventricular ejection fraction

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Echocardiography; Outcome; Decreased ejection fraction

Abstract  Background: Echocardiographic estimation of left ventricular ejection fraction aids in predicting adverse outcomes in coronary artery disease. However, in patients with impaired left ventricular function, further risk stratification is difficult.

Methods: A 2 year retrospective review was performed to identify patients with ejection fraction ≤30%. Echocardiographic measures of systolic and diastolic function were independently performed offline. Outcome information, which included MI, stroke, or death, was obtained. The patient cohort identified those with follow-up having 1) a single echocardiogram and a subset 2) with an initial echocardiogram and a second echocardiogram at greater than one year follow-up.

Results: This study included 110 patients, ages 20–94. Mean follow-up time was 29 ± 9 months. Ejection fraction did not predict cardiovascular events. LV mass predicted of mortality (p = 0.03). Diastolic indexes of mitral inflow E wave was a significant predictor of outcome (p = 0.05). Impaired diastolic filling grade 2, 3, or 4 showed a 76% event rate. Decreases in ejection fraction at follow-up were seen in those who had an event, with an average decrease in ejection fraction of 17% versus those who lived with no event of 1%. Changes in mitral inflow E wave and changes in E/A ratio were both significant predictors of outcome.
Conclusions: These data indicate that echocardiographic measures of both systolic and diastolic function aid in risk stratifying patients with decreased ejection fraction. The change detected in serial echocardiographic information may be important in treatment and secondary prevention of future events.

Introduction

With five million Americans currently living with congestive heart failure (CHF), about 550,000 newly diagnosed each year, and 287,200 attributable deaths in 1999, heart failure remains a major public health concern. The strongest predictors of mortality in patients with CHF in previous studies are New York Heart Association (NYHA) functional class, left ventricular function, and echocardiographic wall motion score index (WMSI). Those with decreased ejection fraction are at higher risk of sudden cardiac death, stroke, MI, and progression to heart transplant. CHF ranks second in cardiogenic stroke risk after atrial fibrillation with a two to threefold increased relative risk. Beattie et al. reported transthoracic echocardiographic abnormality in between 7–14% of patients with cerebral ischemia without known cardiac disease. Crawford et al demonstrated the presence of left ventricular (LV) thrombus in patients with an ejection fraction (EF) ≤35% was associated with an increased risk of stroke.

Echocardiography has become the gold standard for the evaluation of patients with heart failure because it is an inexpensive, highly reproducible, widely available, and relatively extensive method for assessing left ventricular systolic and diastolic function. Significant proportions (10–50%) of those suffering from CHF by clinical diagnosis have preserved systolic function with at least one abnormal echocardiographic index of diastolic function. Consequently, echocardiography is an invaluable tool for assessing diastolic function in the setting of heart failure.

Data regarding the predictive value of serial echocardiography in clinical outcome measures is limited. Although the usefulness has been demonstrated post MI, serial measurements in CHF has not been well explored. Accordingly, the aim of this study was to confirm the predictive value of baseline echocardiographic measures of LV systolic and diastolic function as well as assess the importance of serial changes in predicting two-year composite risk of MI, stroke, or cardiovascular death.

Methods

A 2 year retrospective review of patients with EF ≤30% was performed. Echocardiographic images were retrieved and measures of systolic and diastolic function were independently performed on each echocardiogram using an offline analysis system (Digisonics, Houston, TX). A total number of 110 patients were included from a cohort of 455. Most patients were excluded secondary to lack of follow up data, non-cardiac death, or echocardiogram not available.

Patients

Patients were eligible for inclusion if they underwent at least one transthoracic echocardiogram with a measured ejection fraction ≤30%. Outcome information, which included MI, stroke, or death, was obtained by cross referencing hospital electronic medical record and/or contact with the patient or family by phone. Those who died from non-cardiovascular causes were excluded in data analysis.

The patient cohort was divided into two groups. Group 1 comprised those who underwent one echocardiogram with long-term follow-up. Group 2 was a subset of group one who underwent the initial echocardiogram with a one year follow-up echo to provide serial echocardiographic data.

Echocardiography

Systolic measurements

Simpson’s biplane method quantitatively determined LVEF and provided volume and functional measures. M-mode measurements of size and thickness were completed of the left ventricle. LV mass was calculated using recommended methods from the American Society of Echocardiography: 

\[
LV mass (g) = 1.04[(IVSd + LVIDd + PWTd)\text{^3} - LVIDd\text{^3}]_{20,21}
\]

Diastolic measurements

Diastolic function was assessed by Pulsed-wave (PW) Doppler, PW Doppler tissue imaging (DTI), continuous wave assessment of isovolumic
relaxation time (IVRT), and color M-mode flow propagation imaging. PW Doppler interrogated systolic and diastolic pulmonary vein velocities. PW Mitral inflow measurements included early and late peak diastolic velocities which measured E/A ratio, and deceleration time.\(^{22}\) DTI assessed diastolic function by quantifying myocardial peak systolic, early and late diastolic velocities sampled from the lateral annulus of the mitral valve.\(^{23}\) Finally, color M-mode provided flow propagation information by measuring the slope of the inflow velocities.\(^{24}\) Grading of diastolic dysfunction was performed using standard grading criteria for E/A ratio, deceleration time, IVRT, pulmonary veins.\(^{25}\) Impaired relaxation was defined as E/A ratio $<1$, deceleration time $>220$ ms, IVRT $>100$ ms, and systolic/diastolic pulmonary vein ratio $>1$. Pseudonormal was defined as E/A ratio $1-2$, deceleration time of $150-220$ ms, IVRT of $60-100$ ms, and systolic/diastolic pulmonary vein ratio $<1$. Restrictive filling was defined as E/A ratio $>2$, deceleration time $<150$ ms, IVRT $<60$ ms, and systolic/diastolic pulmonary vein ratio $<1$.

**Statistical analysis**

Continuous data are expressed as mean $\pm$ SD. Comparisons of correlation were computed using Pearson’s correlation coefficient. Logistic regression was used to test significant predictors. Unpaired $t$-test was used to assess differences in values between initial echocardiogram and follow-up echo.

**Results**

This study included 110 patients, ages 20–94 and a mean age of $62 \pm 15$, of which 57% are male, 44% are Caucasian, and 42% are African-American. At follow-up, 48% ($n=57$) were alive with no event, 30% ($n=34$) were dead from cardiovascular etiologies, 7% ($n=8$) had a stroke, 7% ($n=8$) had a myocardial infarction, and 3% ($n=3$) continued to heart transplant. Analysis included comparison of those patients alive without event to those who had an event (including cardiovascular death, stroke, MI, or transplant) at follow-up.

Group 1 comprised the complete cohort with an initial echocardiogram with mean follow-up of $29 \pm 9$ months. Baseline structural measurements of LV size and function are included in Table 1. Although there were significant differences in EF and LV size between those with and without events, these were not predictors of those alive without event versus those patients with events at follow-up. LV mass was the only structural predictor of mortality $p=0.03$. Those who were not alive at follow-up had a mean LV mass of 550 g with an average of 281 g in those alive. Diastolic indexes of mitral inflow E wave $>1.5$ m/s was a significant predictor of outcome ($p=0.05$). When grade of diastolic impairment was used to assess events, those patients with impaired diastolic filling grade 2, 3, or 4 had a 76% event rate. Half of those patients with events had diastolic dysfunction graded as phase 3 and 4.

Group 2 ($N=35$) included as subset of patients from the group 1 cohort who underwent an initial echocardiogram as well as a one year follow-up echo to provide serial echocardiographic data. Mean time between serial echo examination was $16 \pm 5$ months. Table 2 summarizes the diastolic measurements performed at baseline in comparison to the measurements from the second echo performed. Three patients had a decrease in EF.

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<th>Table 1 Baseline structural measurements of left ventricular size and function</th>
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<td>LV end diastolic volume</td>
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<td>LV end systolic volume</td>
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<td>LV mass</td>
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<th>Table 2 Baseline and serial echo summary of diastolic measurements</th>
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<td><strong>Parameter</strong></td>
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<td>Mitral valve E wave (cm/s)</td>
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<td>Mitral valve E/A ratio</td>
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by greater than 10%. The EF did not change by greater than 10% in 17 patients. The remaining pa-
tients had an improvement in EF greater than 10%. Three patients had a decrease in LVdiastolic diam-
eter (LVDd) of greater than 1 cm, 2 patients had an increase in LVDd, and the remaining patients did not have a significant change in LV diastolic size. In 8 patients the diastolic filling worsened, in 6 patients the filling improved, and the remaining patients had no change in diastolic filling. Additional interval decreases in ejection fraction at follow-up were seen in those who had an event, with an average additional decrease in ejection fraction of 17% versus those who lived with no event of a 1% further decrease in ejection fraction (Fig. 1). Significant differences were also seen in those patients who had a decrease in E/A ratio with associated follow-up events. With the exception of ejection fraction, no structural measure-
ments were predictive of those with and without follow-up events (Fig. 2). Diastolic indexes of de-
creases in mitral inflow E wave velocities corre-
sponding to decreases in E/A ratio were both significant predictors of outcome.

Discussion

Systolic predictors

These data show that in a population with poor LV function, EF and left ventricular size differs from those with and without events, but does not further predict cardiovascular outcomes. Although LV end-diastolic diameter (LVIDd) has been corre-
lated with increased mortality and cardiac events in patients with symptomatic heart failure and low EF, our study indicated in a population with baseline reduced LV function, only LV mass was corre-
related to outcome.26,27

Our findings reconfirm that increased LV mass is an independent predictor of mortality as reported by Sunstrom which indicated LV mass by echo more than LVH criteria by EKG predicted mortality.28 An echo substudy from the SOLVD trials found that LV mass and end-systolic dimension were significant predictors of mortality in addition to NYHA class, age, and ejection fraction.29

Diastolic predictors

Aurigemma et al studied echocardiographic pa-
rameters as predictors of incident CHF in a large cohort and found subclinical contractile dysfunc-
tion measured by diastolic filling abnormalities such as high and low E/A ratios are predictive of subsequent CHF.30 Similarly, our studies showed that diastolic echocardiographic measures of mitral inflow E wave >1.5 m/sec predicted cardio-
vascular outcomes including stroke and myocardial infarction ($p = 0.05$). Data from participants of the Strong Heart Study showed an E/A ratio <0.6 and E/A >1.5, in patients with LVEF <40%, correlated with 25% and 35% cardiac mortality compared to 10% in those with normal E/A.31 In our patients with diastolic dysfunction graded as 2 or higher, the cardiac event rate at follow up was 76% event

![Figure 1](http://ehjcimaging.oxfordjournals.org/) The average percent decrease in ejection fraction between initial echo and follow-up echo in those with and without event outcomes.

![Figure 2](http://ehjcimaging.oxfordjournals.org/) Comparison of changes in mitral valve E/A ratio in those with and without follow-up events.
rate versus an event rate of 17% in those with normal diastolic function.

The PRAISE-2 echocardiographic study demonstrated that in patients with non-ischemic cardiomyopathy and severe heart failure, baseline echo measurements including restrictive diastolic LV filling pattern were predictive of death.32 We confirmed this finding by showing an event rate of 44% in those with restrictive diastolic filling patterns defined as E/A ratio >1.5 and e′ < 0.8 in our study. Identifying these patients with restrictive filling and treating them appropriately has been proven to reduce overall morbidity and mortality.33,34

Serial predictors

Although risk stratification of patients may be based on systolic and diastolic echocardiographic indices, little attention has been placed on the predictive value of serial changes in these indices. In this study group, patients with an event had an average decrease in ejection fraction of 17% versus 1% in those without an event. Moller et al. discussed baseline and subsequent echo changes in the setting of acute MI and found patients with a persistently abnormal or deteriorating LV filling pattern (compared to improvement or normal filling pressures) was associated with increased risk of cardiac death and hospital readmission secondary to heart failure.15

This study demonstrates that in comparison to baseline echocardiographic measurements, serial changes in these functional indices provide additional prognostic information, augmenting the clinical utility of echocardiography in the management of patients with compromised systolic and diastolic function.

Limitations

Secondary to the retrospective study design, there was variability in the time between serial echocardiographic examinations among patients. Although interobserver variability is difficult to control in a retrospective study, variability was reduced with one experienced observer performing the echocardiographic measurements. Mitral inflow was not corrected for age in this study, however only 2% of patients were over the age of seventy.35

Future suggestions

These data indicate that a variety of echocardiographic measures including both systolic and diastolic function aid in risk stratifying patients. The use of serial echocardiographic information may be important in treatment and secondary prevention of future events. Since beta-blockade and ACE inhibitors slow the progression and decrease mortality in those with reduced LVEF, it is of interest to correlate serial changes in systolic and diastolic echocardiographic indices with use of and adherence to these therapies and further track outcome data in these patients.

References


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