Left Atrial Volume
A Powerful Predictor of Survival After Acute Myocardial Infarction

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Background—After acute myocardial infarction (AMI), diastolic function assessed by Doppler echocardiography provides important prognostic information that is incremental to systolic function. However, Doppler variables are affected by multiple factors and may change rapidly. In contrast, left atrial (LA) volume is less influenced by acute changes and reflects subacute or chronic diastolic function. This may be of importance when one assesses risk in patients with AMI.

Methods and Results—Three hundred fourteen patients with AMI who had a transthoracic echocardiogram with assessment of left ventricular (LV) systolic and diastolic function and measurement of LA volume during admission were identified. The LA volume was corrected for body surface area, and the population was divided according to LA volume index of 32 mL/m² (2 SDs above normal). LA volume index was >32 mL/m² in 142 (45%). The primary study end point was all-cause mortality. During follow-up of 15 (range 0 to 33) months, 46 patients (15%) died. LA volume index was a powerful predictor of mortality and remained an independent predictor (hazard ratio 1.05 per 1-mL/m² change, 95% CI 1.03 to 1.06, \( P < 0.001 \)) after adjustment for clinical factors, LV systolic function, and Doppler-derived parameters of diastolic function.

Conclusions—Increased LA volume index is a powerful predictor of mortality after AMI and provides prognostic information incremental to clinical data and conventional measures of LV systolic and diastolic function. (Circulation. 2003;107:2207-2212.)

Key Words: atrium ■ myocardial infarction ■ echocardiography ■ diastole

Multiple Doppler echocardiographic variables may be used to assess left ventricular (LV) diastolic function. However, these variables reflect the beat-to-beat interaction of LV filling pressures and ventricular compliance, making them sensitive to rapid alternations in ventricular preload and afterload. Because of opposing effects of preload and compliance on transmitral velocities, the mitral inflow pattern may appear normal (pseudonormal) despite abnormal filling pressures. Despite these limitations, Doppler indices of diastolic function have been shown to predict morbidity and mortality in patients with acute myocardial infarction (AMI). In particular, a restrictive diastolic filling pattern, characterized by an abbreviated mitral E-wave deceleration time, predicts a poor outcome.

During ventricular diastole, the left atrium (LA) is directly exposed to LV pressures through the open mitral valve. LA size is therefore largely determined by the same factors that influence diastolic LV filling. It is, however, a more stable indicator, reflecting the duration and severity of diastolic dysfunction. For this reason, we hypothesized that LA volume would predict long-term outcome after AMI and might be superior in this respect to conventional Doppler indices of diastolic function. To address this, we performed a retrospective study of patients who had comprehensive assessment of LV systolic and diastolic function, including assessment of LA volume, early after AMI.

Methods

Patient Selection
From October 1999 to July 2001, 314 unselected patients admitted to St Mary’s Hospital, Rochester, Minn, with AMI had a transthoracic echocardiogram with assessment of LA volume performed during their hospitalization. Myocardial infarction was defined by the European Society of Cardiology/American College of Cardiology guidelines. Patients with prosthetic mitral valves and mitral stenosis were excluded. The Institutional Review Board of the Mayo Clinic, Rochester, Minn, approved the study.

Echocardiography
Echocardiography was performed a median of 1 day (range 0 to 4 days) after admission. All studies were performed by experienced sonographers and reviewed by staff cardiologists with advanced training in echocardiography. LV systolic function was assessed semiquantitatively with a visually estimated ejection fraction and wall-motion score index. We have previously demonstrated an excellent agreement between sub-
jective interpretation of ejection fraction and volumetric assessment (95% limits of agreement −6% to 7%), with low interobserver variability (95% limits of agreement −5% to 10%). Each of 16 LV segments was assigned a score (1 to 5) based on myocardial thickening. A wall-motion score index was calculated by dividing the sum of scores by the number of segments visualized. Mitral regurgitation was graded with color flow imaging.

Mitrail inflow was assessed with pulsed-wave Doppler echocardiography from the apical 4-chamber view. The Doppler beam was aligned parallel to the direction of flow, and a 1- to 2-mm sample volume was placed between the tips of mitral leaflets during diastole. From the mitral inflow profile, the E- and A-wave velocity, E-deceleration time, and E/A velocity ratio were measured. Pulmonary venous flow was recorded with pulsed-wave Doppler with a sample volume placed ~1 cm into the right upper pulmonary vein. The flow velocities were recorded, and the ratio of systolic to diastolic forward flow (S/D ratio) was calculated. In a subgroup of 188 patients, Doppler tissue imaging of the mitral annulus was also obtained. From the apical 4-chamber view, a 1- to 2-mm sample volume was placed in the septal mitral annulus.

Diastolic filling was categorized as normal (grade 0), impaired relaxation (grade 1), or restrictive (grade 3) by a combination of transmitral and pulmonary flow patterns as validated previously. In addition, patients were categorized based on E-deceleration time alone, which has been shown to be an effective prognostic indicator in this setting. In these analyses, a deceleration time of >140 but

### TABLE 1. Clinical Characteristics and In-Hospital Management of Myocardial Infarction

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>LAVI ≤32 mL/m² (n=172)</th>
<th>LAVI &gt; 32 mL/m² (n=142)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>65 (53–75)</td>
<td>76 (67–82)</td>
<td>0.001</td>
</tr>
<tr>
<td>Risk factors and medical history</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male gender</td>
<td>114 (66)</td>
<td>83 (59)</td>
<td>0.15</td>
</tr>
<tr>
<td>Current smoker</td>
<td>46 (27)</td>
<td>23 (16)</td>
<td>0.03</td>
</tr>
<tr>
<td>Hypertension</td>
<td>84 (49)</td>
<td>91 (64)</td>
<td>0.007</td>
</tr>
<tr>
<td>Diabetes</td>
<td>28 (16)</td>
<td>37 (26)</td>
<td>0.03</td>
</tr>
<tr>
<td>Prior AMI</td>
<td>34 (20)</td>
<td>38 (27)</td>
<td>0.14</td>
</tr>
<tr>
<td>Prior revascularization</td>
<td>27 (16)</td>
<td>44 (31)</td>
<td>0.001</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>72 (42)</td>
<td>66 (47)</td>
<td>0.41</td>
</tr>
<tr>
<td>Anterior AMI</td>
<td>66 (38)</td>
<td>58 (41)</td>
<td>0.62</td>
</tr>
<tr>
<td>ST-elevation AMI</td>
<td>96 (56)</td>
<td>50 (35)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Thrombolytic therapy</td>
<td>32 (19)</td>
<td>17 (12)</td>
<td>0.11</td>
</tr>
<tr>
<td>In-hospital revascularization</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCI</td>
<td>115 (67)</td>
<td>73 (51)</td>
<td>0.004</td>
</tr>
<tr>
<td>CABG</td>
<td>14 (8)</td>
<td>12 (9)</td>
<td>0.92</td>
</tr>
<tr>
<td>Multivessel disease*</td>
<td>77 (50)</td>
<td>70 (63)</td>
<td>0.04</td>
</tr>
<tr>
<td>In-hospital therapy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heparin</td>
<td>163 (95)</td>
<td>134 (94)</td>
<td>0.53</td>
</tr>
<tr>
<td>Intravenous nitroglycerin</td>
<td>117 (68)</td>
<td>80 (56)</td>
<td>0.02</td>
</tr>
<tr>
<td>Inotropic therapy</td>
<td>14 (8)</td>
<td>13 (9)</td>
<td>0.78</td>
</tr>
<tr>
<td>IABP</td>
<td>21 (12)</td>
<td>21 (15)</td>
<td>0.53</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>3 (2)</td>
<td>14 (10)</td>
<td>0.002</td>
</tr>
<tr>
<td>Killip class ≥II on admission</td>
<td>52 (30)</td>
<td>74 (52)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

### TABLE 2. Echocardiographic Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>LAVI ≤32 mL/m² (n=172)</th>
<th>LAVI &gt; 32 mL/m² (n=142)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV ejection fraction, %</td>
<td>50 (43–60)</td>
<td>44 (35–57)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV end-systolic dimension, mm</td>
<td>34 (30–38)</td>
<td>37 (33–45)</td>
<td>0.001</td>
</tr>
<tr>
<td>LV end-diastolic dimension, mm</td>
<td>50 (46–54)</td>
<td>52 (50–57)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Wall-motion score index</td>
<td>1.7 (1.4–2.1)</td>
<td>1.5 (1.2–1.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peak E-wave velocity, m/s</td>
<td>0.8 (0.6–0.9)</td>
<td>0.9 (0.7–1.0)</td>
<td>0.003</td>
</tr>
<tr>
<td>Peak A-wave velocity, m/s</td>
<td>0.8 (0.6–0.9)</td>
<td>0.7 (0.6–0.9)</td>
<td>0.93</td>
</tr>
<tr>
<td>E/A ratio</td>
<td>1.0 (0.8–1.3)</td>
<td>1.1 (0.8–1.5)</td>
<td>0.32</td>
</tr>
<tr>
<td>Pulmonary vein S velocity, m/s</td>
<td>0.5 (0.4–0.6)</td>
<td>0.5 (0.4–0.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>Pulmonary vein D velocity, m/s</td>
<td>0.5 (0.3–0.5)</td>
<td>0.5 (0.4–0.6)</td>
<td>0.003</td>
</tr>
<tr>
<td>Pulmonary vein S/D ratio</td>
<td>1.3 (1.0–1.7)</td>
<td>1.0 (0.6–1.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diastolic function*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>65 (43%)</td>
<td>28 (21%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Grade 1</td>
<td>40 (26%)</td>
<td>39 (28%)</td>
<td>0.65</td>
</tr>
<tr>
<td>Grade 2</td>
<td>31 (20%)</td>
<td>37 (27%)</td>
<td>0.17</td>
</tr>
<tr>
<td>Grade 3</td>
<td>16 (11%)</td>
<td>32 (24%)</td>
<td>0.003</td>
</tr>
<tr>
<td>E-deceleration time, ms</td>
<td>192 (175–222)</td>
<td>190 (160–237)</td>
<td>0.62</td>
</tr>
<tr>
<td>&gt;240 ms</td>
<td>32 (19%)</td>
<td>32 (22%)</td>
<td>0.65</td>
</tr>
<tr>
<td>≤140 ms</td>
<td>7 (4%)</td>
<td>25 (17%)</td>
<td>0.001</td>
</tr>
<tr>
<td>DTI e', m/s†</td>
<td>7 (5–8)</td>
<td>6 (4–7)</td>
<td>0.001</td>
</tr>
<tr>
<td>Ratio E/e'†</td>
<td>11 (9–12)</td>
<td>13 (10–18)</td>
<td>0.001</td>
</tr>
<tr>
<td>LA dimension, mm</td>
<td>41 (38–45)</td>
<td>48 (43–53)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LA volume, mL</td>
<td>46 (38–55)</td>
<td>77 (67–93)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LA volume index, mL/m²</td>
<td>24 (20–27)</td>
<td>42 (36–49)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Moderate or severe MR</td>
<td>12 (7)</td>
<td>38 (27)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

LAVI indicates LA volume index; MR, mitral regurgitation. Data are median (interquartile range) or number (percentage).
* Doppler assessment of diastolic function was possible in 288 (92%) patients; see text for definitions.
† Data available in 188 patients.

<240 ms was regarded as normal, ≥240 ms as abnormally prolonged, and ≤140 ms as abnormally abbreviated.

LA volume was assessed by the biplane area-length method from apical 4- and 2-chamber views. Measurements were obtained in end systole from the frame preceding mitral valve opening, and the

![Figure 1](http://circ.ahajournals.org/content/109/3/1720/F1.large.jpg)

**Figure 1.** Unadjusted 2-year mortality rates in 10 equal groups of patients according to LA volume index. Increase in mortality with increasing LA volume appeared exponential (solid line).
volume was indexed for body surface area. The normal value of indexed LA volume has been reported to be $20\pm 6 \, \text{mL/m}^2$. Patients were therefore divided according to the mean value plus 2 SDs, corresponding to $32 \, \text{mL/m}^2$.

Follow-Up

Follow-up was performed between January and April 2002 by mailed questionnaires, by review of medical records, and through the Social Security Agency Death Index. The end point was death due to all causes.

Statistical Analysis

Continuous data are expressed as medians with interquartile range unless otherwise specified. Rank sum tests were used for comparisons of continuous variables, and the $\chi^2$ test was used for categorical variables.

Mortality was plotted according to the Kaplan-Meier method, and death rates were compared by the log-rank test. Further estimation of risk was performed with Cox proportional hazard models. Variables considered as potential predictors for multivariate modeling were selected by univariate analyses and subsequently selected in a stepwise forward conditional manner with entry and retention in the model set at a significance level of 0.05. The power of the final Cox model was based on calculation of the risk score, defined as the linear combination created by the model. The score was used to divide patients into quartiles, and Kaplan-Meier survival estimates were calculated for each quartile. The stability of the Cox proportional hazards model was assessed by a bootstrap resampling technique. This was used to estimate the likelihood that each of the final model variables would have been selected in repeated samples. The incremental value of LA volume index was assessed in 4 modeling steps. The first step consisted of fitting a multivariate model of clinical parameters. LV systolic and diastolic data were then added sequentially. Finally, LA volume index was included. The change in overall log likelihood ratio $\chi^2$ was used to assess the increment of predictive power at each step. SPSS version 10.0 (SPSS Inc) was used for calculations.

Results

Clinical Characteristics

The study included 314 patients with a median age of 70 (range 32 to 94) years. LA volume index was $>32 \, \text{mL/m}^2$ in 142 (45%). Compared with patients with LA volume index $\leq 32 \, \text{mL/m}^2$, these patients were older; had a greater prevalence of hypertension, diabetes, and previous revascularization; presented more frequently with non-ST elevation AMI; and were less likely to undergo percutaneous coronary intervention (Table 1). At hospital discharge, there was no difference in the use of aspirin (166/171 versus 134/137, $P=0.74$), $\beta$-adrenergic blocking agents (150/171 versus 114/137, $P=0.26$), or lipid-lowering drugs (136/171 versus 101/137, $P=0.23$) in patients with LA volume index $\leq 32 \, \text{mL/m}^2$ or $>32 \, \text{mL/m}^2$. However, patients with LA volume index

### Table 3. Univariate Predictors of Mortality

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Surviving Patients (n=268)</th>
<th>Deceased Patients (n=46)</th>
<th>Hazard Ratio (95% CI)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>69 (58–78)</td>
<td>79 (69–84)</td>
<td>1.06 (1.03–1.10)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male gender</td>
<td>172 (64)</td>
<td>25 (54)</td>
<td>0.69 (0.38–1.2)</td>
<td>0.20</td>
</tr>
<tr>
<td>Anterior AMI</td>
<td>108 (40)</td>
<td>16 (35)</td>
<td>0.75 (0.41–1.4)</td>
<td>0.36</td>
</tr>
<tr>
<td>ST-elevation AMI</td>
<td>133 (50)</td>
<td>13 (28)</td>
<td>0.44 (0.23–0.84)</td>
<td>0.01</td>
</tr>
<tr>
<td>Multivessel disease</td>
<td>127 (54)</td>
<td>20 (69)</td>
<td>1.9 (0.85–4.1)</td>
<td>0.12</td>
</tr>
<tr>
<td>PCI or CABG during admission</td>
<td>196 (73)</td>
<td>16 (38)</td>
<td>0.22 (0.13–0.42)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Killip class $\geq$II on admission</td>
<td>95 (35)</td>
<td>31 (67)</td>
<td>3.7 (1.9–6.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>55 (21)</td>
<td>10 (22)</td>
<td>1.1 (0.5–2.1)</td>
<td>0.86</td>
</tr>
<tr>
<td>Prior AMI</td>
<td>58 (22)</td>
<td>14 (30)</td>
<td>1.5 (0.8–2.8)</td>
<td>0.20</td>
</tr>
<tr>
<td>Hypertension</td>
<td>145 (54)</td>
<td>30 (65)</td>
<td>1.6 (0.8–2.9)</td>
<td>0.15</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>9 (3)</td>
<td>8 (17)</td>
<td>4.1 (1.9–8.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV ejection fraction</td>
<td>50 (40–59)</td>
<td>40 (29–49)</td>
<td>1.5 (1.2–1.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Wall-motion score index</td>
<td>1.6 (1.2–1.9)</td>
<td>1.9 (1.5–2.2)</td>
<td>1.1 (1.1–1.2)‡</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diastolic dysfunction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 1</td>
<td>65 (27)</td>
<td>14 (30)</td>
<td>4.4 (1.5–13.4)‡</td>
<td>0.009</td>
</tr>
<tr>
<td>Grade 2</td>
<td>56 (23)</td>
<td>12 (27)</td>
<td>4.4 (1.4–13.5)‡</td>
<td>0.01</td>
</tr>
<tr>
<td>Grade 3</td>
<td>32 (13)</td>
<td>16 (35)</td>
<td>9.2 (3.1–27.6)‡</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>E-deceleration time</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\geq$240 ms</td>
<td>52 (19)</td>
<td>12 (26)</td>
<td>2.1 (1.1–4.3)</td>
<td>0.04</td>
</tr>
<tr>
<td>$\leq$140 ms</td>
<td>18 (7)</td>
<td>14 (30)</td>
<td>6.0 (3.0–11.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LA volume index $&gt;$32 mL/m²</td>
<td>104 (39)</td>
<td>38 (83)</td>
<td>6.1 (2.8–13.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Moderate or severe MR</td>
<td>35 (14)</td>
<td>15 (33)</td>
<td>2.9 (1.5–5.4)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

PCI indicates percutaneous coronary intervention; MR, mitral regurgitation.
Data are expressed as median (interquartile range) or number (percentage) of patients.
*Hazard ratio calculated for a 10% decrease in ejection fraction.
†Hazard ratio calculated for a 0.1 increase in wall-motion score index.
‡Hazard ratio versus normal diastolic function (see text for definitions).
32 mL/m² were more often receiving ACE inhibitors (100/137 versus 106/171, P=0.04) and diuretics (47/137 versus 30/171, P=0.001).

Echocardiographic Characteristics

The relationship between LA volume index and other echocardiographic parameters is shown in Table 2. LA volume index was greater in patients with moderate or severe mitral regurgitation (42 [33 to 53] mL/m² versus 29 [23 to 38] mL/m², P<0.001) and in patients with chronic atrial fibrillation (45 [34 to 58] mL/m² versus 30 [23 to 39] mL/m², P<0.001). Among 244 patients with no or trivial mitral regurgitation and sinus rhythm, LA volume index >32 mL/m² was found in 94 patients (39%). Among patients in whom Doppler tissue imaging was performed, a modest correlation was found between the E/e' ratio and LA volume index (r=0.30, P<0.001).

Predictors of Outcome

During follow-up of a median of 15 (range 0 to 33) months, 46 patients (15%) died. Patients were divided in 10 equal groups according to LA volume index and unadjusted 2-year mortality rate assessed for each group. The mortality rate increased with LA volume index (Figure 1).

Univariate associations with all-cause mortality are shown in Table 3 and multivariate associations in Table 4. In the final model, LA volume index was associated with a hazard ratio of 1.05 for a 1-mL/m² increase (95% CI 1.02 to 1.06, P<0.0001). Ejection fraction was not a significant predictor of mortality when LA volume index was included in the model (P=0.56). There was no significant interaction effect of moderate or severe mitral regurgitation (P=0.60) or atrial fibrillation (P=0.26) with LA volume index, which indicates comparable risk stratification for these subgroups. The power of the model was assessed from the final multivariate Cox model and is shown in Figure 2. To assess the stability of the final Cox proportional hazards model, a bootstrap resampling technique of 1000 samples was performed with the 12 candidates listed in Table 4. The most frequently selected variables were those of the final model. Importantly, LA volume index was more frequently selected than any other variable (Figure 3).

The incremental value of LA volume index assessed in 4 modeling steps is shown in Figure 4. Addition of LA volume index increased the χ² of a model containing clinical, LV systolic, and LV diastolic variables from 63.3 to 83.7 (P<0.001 for change in χ²).

Discussion

To the best of our knowledge, this is the first study to demonstrate that LA volume index is a predictor of survival after AMI. Furthermore, LA volume index provides prognostic information incremental to clinical data and standard echocardiographic predictors of outcome, including LV systolic function and Doppler assessment of diastolic function.

### Table 4. Predictors of Mortality by Forward Conditional Cox Proportional Hazards Analysis

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
<th>Wald χ²</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>LA volume index (per 1 mL/m²)</td>
<td>1.05</td>
<td>1.02–1.06</td>
<td>32.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Killip class*</td>
<td>1.71</td>
<td>1.26–2.33</td>
<td>11.7</td>
<td>0.001</td>
</tr>
<tr>
<td>E-deceleration time</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤140 ms</td>
<td>2.74</td>
<td>1.38–5.40</td>
<td>8.4</td>
<td>0.004</td>
</tr>
<tr>
<td>≥240 ms</td>
<td>2.9</td>
<td></td>
<td>0.08</td>
<td></td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>3.7</td>
<td></td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>3.6</td>
<td></td>
<td>0.07</td>
<td></td>
</tr>
<tr>
<td>Primary angioplasty/thrombolysis</td>
<td>1.9</td>
<td></td>
<td>0.17</td>
<td></td>
</tr>
<tr>
<td>Wall-motion score index</td>
<td>1.3</td>
<td></td>
<td>0.25</td>
<td></td>
</tr>
<tr>
<td>Diastolic dysfunction</td>
<td>2.5</td>
<td></td>
<td>0.11</td>
<td></td>
</tr>
<tr>
<td>ST-elevation MI</td>
<td>0.4</td>
<td></td>
<td>0.50</td>
<td></td>
</tr>
<tr>
<td>LV ejection fraction</td>
<td>0.3</td>
<td></td>
<td>0.56</td>
<td></td>
</tr>
<tr>
<td>Moderate or severe MR</td>
<td>0.2</td>
<td></td>
<td>0.66</td>
<td></td>
</tr>
</tbody>
</table>

MR indicates mitral regurgitation.

*Hazard ratio calculated for a 1-class increase in Killip class.
†Calculated for an increase of 1 grade in diastolic dysfunction (see text for definition of diastolic function).

>32 mL/m² were more often receiving ACE inhibitors (100/137 versus 106/171, P=0.04) and diuretics (47/137 versus 30/171, P=0.001).

Figure 2. Kaplan-Meier plot demonstrating survival in patients based on final Cox multivariate model containing LA volume index, Killip class, and mitral deceleration time ≤140 ms. Patients were divided into quartiles based on this score.

Figure 3. Bootstrap investigation of stability of Cox proportional hazards model. One thousand bootstrap samples were generated based on 12 variables listed in Table 4. For each sample, forward conditional Cox analysis with entry and retention level set at 0.05 was done to identify significant predictors of mortality. Proportion of models containing listed variables are given as percentages. DT indicates deceleration time; WMSI, wall-motion score index; A-fib, atrial fibrillation; MR, moderate or severe mitral regurgitation; Revas, acute angioplasty or thrombolysis; EF, ejection fraction; and ST, ST-elevation myocardial infarction.
Diastolic Function and Survival

Deteriorating diastolic function is associated with increased LV diastolic pressure, dyspnea, fatigue, and reduced exercise tolerance.1,2,18 Furthermore, LV pressure overload causes myocyte stretch and reduced myocardial energy production, eventually leading to ventricular remodeling, neurohormonal activation, and elevated pulmonary venous pressure.19–21 All of these factors would be expected to adversely affect outcome. In agreement with this, the present and several previous studies demonstrate that advanced diastolic dysfunction, characterized by an increased E/A ratio and shortening of the E-deceleration time, is strongly associated with increased mortality.7–9

Added Value of LA Volume Index

LA volume index was a predictor of mortality after AMI, even after adjustment for conventional indices of systolic and diastolic function. There are several possible explanations. First, LA volume reflects the duration and severity of increased LA pressure.12 In contrast, Doppler assessment provides an instantaneous assessment of diastolic function. Therefore, the combination of parameters representing acute (abbreviated E-deceleration time) and chronic (LA volume index) diastolic dysfunction provided the best prognostic power. Second, apparently normal filling patterns may be associated with significant elevation of LV filling pressures.1–3 These “pseudonormal” filling patterns have been associated with increased mortality after AMI13 but may be difficult to identify with standard Doppler techniques. In contrast, LA volume index may better differentiate such patients.10,11 Furthermore, in adaptation to decreased ventricular compliance, LA pressure rises, increasing LA wall tension and stretching the atrial myocardium. LA stretch and LV pressure overload are the main stimuli for secretion of cardiac peptides,22 levels of which correlate strongly with survival after AMI.20 Neurohormonal activation may be more pronounced if LA enlargement is present.

In agreement with previous studies, we found that LV ejection fraction was not an independent predictor of outcome when assessment of diastolic function was available.7–9 Furthermore, we found that among 27 patients with an ejection fraction <40% but LA volume index <32 mL/m², only 1 patient died compared with 22 of 55 patients with increased LA volume index and ejection fraction <40%. If LA volume index is normal, outcome is good, even if systolic function is depressed. This suggests that more favorable hemodynamics before infarction may enable these patients to withstand an acute decrease in myocardial contractility.

Study Limitations

The entry criterion for the study was measurement of LA volume index. This may have introduced a selection bias. Although it appears unlikely that this could have affected the observed results, it may reduce their applicability to a more general population. Conversely, measurements of LA volume were obtained by multiple observers working in a clinical environment, which suggests that the findings can be widely applied.

Doppler assessment may have resulted in the misclassification of diastolic function in several cases, highlighting the limitations of such measurements. In particular, some patients with normal Doppler parameters had LA enlargement and vice versa. Assessment of mitral annulus motion appears to be particularly useful for assessment of diastolic function. Unlike other Doppler parameters of diastolic function, it appears to be relatively independent of preload and recently has been shown to be the most accurate noninvasive predictor of elevated LV filling pressure. However, the role of Doppler tissue imaging in the prediction of outcome after AMI remains to be defined. Although Doppler tissue imaging may have provided further prognostic information and reduced misclassification, this was assessed in only 60% of patients in whom 18 deaths occurred. Thus, multivariate survival analyses were not feasible in this subgroup.

Conclusions

The present study demonstrates that LA enlargement implies a poor prognosis in patients with AMI. The prognostic usefulness of LA volume persisted after adjustment for clinical predictors of outcome and conventional echocardiographic indices of LV systolic and diastolic function. If confirmed in prospective studies, measurement of LA volume could emerge as a simple and important tool for risk stratification and as a guide for future surveillance and therapy in patients with AMI.

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References

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