Prognostic Power of Dobutamine Echocardiography After Uncomplicated Acute Myocardial Infarction in the Elderly*

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Study objectives: To assess the prognostic value of dobutamine-atropine stress echocardiography (DSE) after uncomplicated acute myocardial infarction (AMI) in elderly patients.

Design: We analyzed 59 consecutive patients (42 men) aged ≥ 70 years (mean ± SD age, 75 ± 4 years) who underwent DSE within 10 days after uncomplicated AMI. DSE was carried out following the standard protocol. Five myocardial responses were considered: (1) negative, (2) sustained improvement of contractility, (3) biphasic response (initial improvement followed by worsening), (4) worsening of contractility in the infarcted area, and (5) worsening at a distance.

Results: Mean follow-up duration was 13 ± 8 months. Twenty-one patients had an event: cardiac death (n = 5), myocardial infarction (n = 1), heart failure (n = 1), unstable angina (n = 10), and revascularization (n = 4). Clinical and stress echocardiographic variables previously related to adverse prognosis were entered in Cox regression analysis, and the predictors of impaired outcome were inducible ischemia during DSE (hazard ratio [HR], 2.97; 95% confidence interval [CI], 1.77 to 4.99; p < 0.001) and resting wall motion score index (WMSI) > 1.6 (HR, 1.68; 95% CI, 1.02 to 2.77; p = 0.04). After excluding revascularization procedures and considering only spontaneous events, the following predictors were found: ischemia during DSE (HR, 2.95; 95% CI, 2.78 to 3.12; p < 0.001) and resting WMSI > 1.6 (HR, 2.53; 95% CI, 1.30 to 4.93; p = 0.006).

Conclusions: Inducible ischemia during DSE within 10 days after uncomplicated AMI predicts an impaired outcome in the elderly.

Key words: dobutamine echocardiography; elderly; myocardial infarction; risk stratification

Abbreviations: AMI = acute myocardial infarction; CAD = coronary artery disease; CI = confidence interval; DSE = dobutamine-atropine stress echocardiography; HR = hazard ratio; WMSI = wall motion score index

The prevalence and severity of coronary artery disease (CAD) increase with age, and CAD is the main cause of death in patients > 65 years old.1,2 Acute myocardial infarction (AMI) is a common presentation for CAD. In-hospital and subsequent mortality and complications after AMI are all increased in the elderly.3–5 On the other hand, aggressive management can improve the prognosis and the quality of life in these patients.6–8 Thus, risk stratification after AMI is mandatory in elderly patients. Physical limitations and cardiovascular changes related to aging often preclude conventional assessment. These facts make nuclear and echocardiographic stress tests particularly appealing. Dobutamine-atropine stress echocardiography (DSE) has been reported9–11 to be safe and well tolerated in elderly patients with CAD. It provides a useful tool to assess known prognostic characteristics like baseline left ventricular systolic function and inducible ischemia. Besides, viability can be detected at low dose. Nevertheless, previous investigations12–14 aimed at testing the role of DSE in the prognostic stratification after uncomplicated AMI have specifically excluded elderly patients. Our aim has been to assess the prognostic significance of DSE performed early after uncomplicated AMI in elderly patients.

Materials and Methods

Patients

From February 1996 to December 1998, 301 consecutive patients aged ≥ 70 years were admitted in the coronary care unit.
of our hospital for AMI. Of these 310 patients, there were 68 deaths during hospitalization. Patients with complicated AMI (Killip class ≥ III [n = 76] and severe ventricular arrhythmias [n = 16]) and those included in other protocols (n = 31) were excluded. Thus, 110 patients were admitted to the hospital for uncomplicated AMI. Twelve patients did not agree to participate in the study, and 30 patients underwent a revascularization procedure during hospitalization (percutaneous [n = 22] and surgical [n = 8]), while 9 patients had malignant or end-stage diseases.

We prospectively studied the remaining 59 patients (42 men; mean ± SD age, 75 ± 4 years) who underwent DSE within 10 days after uncomplicated AMI. The criteria for AMI consisted of a rise in serum creatinine kinase MB isoenzyme > 10% of the normal laboratory level combined with chest pain lasting at least 30 min and/or ST-segment upward or downward deviation of at least 0.2 mV in two contiguous leads. Thus, the results are widely generalizable, as the sample is a representative one of elderly people admitted to the hospital in everyday practice due to CAD. No age limit was imposed, and both non-Q-wave and Q-wave AMI and patients who did and did not receive thrombolysis were included. DSE results were not included in the decision-making process regarding the management of the patient.

**Dobutamine Infusion**

Dobutamine was IV administered with a pump in 3-min incremental stages at infusion rates of 5, 10, 20, and 30 μg/kg body weight per minute; then, dobutamine was administered at a dosage of 40 μg/kg/min during 6 min. In patients not achieving 85% of their maximal predicted heart rate or an end point, 1 mg of IV atropine was infused. A 12-lead ECG and BP were recorded at rest and every 3 min up to 10 min after finishing the infusion or recovery of contractility if the test result was positive.

The usual nonechocardiographic end points were considered: maximal predicted heart rate; severe chest pain; intolerable headache or tremor; symptomatic hypotension, systolic BP > 220 mm Hg, diastolic BP > 130 mm Hg; Mobitz type II or third-degree heart block; complex ventricular arrhythmias; and ST-segment downward deviation > 0.3 mV.

**Echocardiography**

An 11-segment model of the left ventricle was used to assess regional wall motion. The assessed segments were proximal anteroseptal, distal anteroseptal, proximal posteroseptal, distal posteroseptal, proximal anterolateral, distal anterolateral, apical, proximal posterolateral, distal posterolateral, posterobasal, and diaphragmatic.

Continuous two-dimensional echocardiography from parasternal (long-axis and short-axis) and apical (four-chamber, two-chamber, and three-chamber) views was performed throughout dobutamine infusion and up to 10 min after the end of the test. In those patients without adequate transthoracic view, transesophageal echocardiography was performed (n = 2).

Each segment was graded as follows: (1) normal and hyperkinetic, (2) mild hypokinetic, (3) severe hypokinetic, and (4) akinetic and dyskinetic. Wall motion score index (WMSI) was derived by dividing the sum of individual segment scores by the number of interpretable segments. It was evaluated at baseline, at low dose, and at peak stress. The difference between low-dose WMSI and baseline WMSI and the difference between peak-stress WMSI and baseline WMSI were used to estimate the extent of myocardium with contractile reserve and the extent of ischemic myocardium, respectively.

The following five myocardial responses were considered: (1) negative (improvement of contractility and thickening from a normal myocardium or no changes at all); (2) sustained improvement of contractility from a hypokinetic, akinetic, or dyskinetic segment; (3) biphase response (improvement of contractility from a hypokinetic, akinetic, or dyskinetic segment followed by worsening of contractility); (4) worsening of contractility in the infarcted zone (homozonal ischemia); and (5) worsening of contractility at a distance (heterozonal ischemia). Patients were separated into three groups according to the myocardial responses: negative group (response 1), viable and nonischemic group (response 2), and viable and ischemic group (responses 3, 4, and 5).

Image acquisition was gated with ECG signal and was digitized comparing four images of the same view at the different stages (basal, low dose, high dose, and atropine) in order to analyze them. The studies were also recorded on conventional videotape. Dobutamine tests were performed by the same echocardiographer with proven proficiency (> 500 studies done).

**Follow-up Data**

Follow-up data were obtained from regular outpatient clinic visits, phone interviews by medical personnel, and reviews of patient clinical files when needed. The worst adverse event was the only one taken into account. Adverse events considered were cardiac-related death, AMI, severe congestive heart failure (hard events), unstable angina, and revascularization (soft events). Death was assumed to be cardiac when it was sudden and/or noncardiac death was ruled out after detailed analysis of clinical and laboratory data obtained during hospital admission and/or pathology findings in necropsy. Noncardiac deaths were censored at follow-up. Nonfatal AMI was defined as a hospital admission for prolonged chest pain (> 30 min) and/or ECG changes and documented typical creatinine kinase MB curve. Severe congestive heart failure included pulmonary edema, New York Heart Association functional class IV/V, and that which needed hospital admission. Unstable angina was defined as that with an accelerated pattern or at rest requiring hospital admission.

**Statistical Analysis**

Prognosis after AMI depends strongly on aging: the older the patient, the more adverse the prognosis. During the first year after AMI, 40% of patients > 65 years old will have an adverse cardiovascular event. To predict at least 50% of those events (a 20% difference) with a type-1 error of 0.05 and a type-2 error of 0.10, and thinking that 5% of the patients could be unavailable for follow-up, the necessary sample was 58 patients. The statistical power was 90%. Numerical data are expressed as mean (SD). The results of categorical variables are given in percentages. Clinical variables (n = 11) and echocardiographic variables (n = 17) previously related with poor prognosis entered the univariate analysis. Continuous variables were compared by the unpaired two-sample t test and proportions by the χ² statistic; two-tailed Fisher’s Exact Test was used when appropriate. A p value < 0.05 was considered statistically significant. Prognostic indicators were obtained by Cox regression carried out using software (SPSS 9.0; SPSS; Chicago, IL). The Cox model met assumption of proportionality, and hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated for those variables with statistically significance. Kaplan-Meier curves were used to compare survival free of events using the log-rank test.
**Results**

**Events During Follow-up**

Of the 59 patients followed up for a mean duration of 13 ± 8 months, 21 patients had an event during follow-up and 38 patients remained free of events. Hard events were present in seven patients: cardiac deaths (n = 5), AMI (n = 1), and severe heart failure (n = 1). Soft events were unstable angina (n = 10) and percutaneous revascularization (n = 4).

Cardiac deaths were as follows: AMI, cardiogenic shock due to heart failure, sudden death, pulmonary edema, and cardiogenic shock due to refractory unstable angina. There were five noncardiac deaths, three caused by stroke (ischemic [n = 2] and hemorrhagic [n = 1]) and one by respiratory distress secondary to *Haemophilus influenzae* pneumonia, and one patient died after catheterization due to severe bleeding.

**Analysis of Clinical and Echocardiographic Variables**

The main clinical characteristics of patients with and without events are summarized in Table 1. Both groups were similar regarding most variables previously known to be related with poor prognosis, including risk factors and infarction characteristics, except for a significant higher prevalence of anterior infarction in the nonevent group. Of patients with an event, diabetes showed a trend to be more frequent.

DSE was well tolerated and minor symptoms appeared in a few patients (headache in three patients, and nausea and headache in one patient). Dobutamine infusion had to be discontinued in one patient due to nonsustained ventricular tachycardia. There were no other major complications. DSE response is shown in Table 2. Hemodynamic response during DSE was similar in patients with and without an event. Of patients with events, a moderate-to-severe resting left ventricular dysfunction (baseline WMSI > 1.6) showed a tendency to be more frequent. The event group had a higher rate of inducible ischemia or worsening of contractility (p < 0.001) and more extent of ischemic myocardium. However, a negative test result was more frequent in patients without events (p = 0.01), and only three patients without an event developed ischemia during DSE. The rate of patients with sustained improvement of contractility was similar in both groups, but the extent of contractile reserve was greater in patients without an event. Figure 1 summarizes DSE results and the different events.

Cox regression analysis showed that inducible ischemia was the best independent prognostic predictor (HR, 2.97; 95% CI, 1.77 to 4.99; p < 0.001). In addition to ischemia, baseline WMSI > 1.6 was a predictor of impaired outcome (HR, 1.68; 95% CI, 1.02 to 2.77; p = 0.039). After excluding the four patients who underwent revascularization (that is, taking into account only spontaneous events), similar prognostic predictors were obtained: ischemia during DSE (HR, 2.95; 95% CI, 2.78 to 3.12; p < 0.001), and baseline WMSI > 1.6 (HR, 2.53; 95% CI, 1.30 to 4.93; p = 0.005). The extent of myocardium with contractile reserve was not found to be related to prognosis. Figure 2 depicts the HRs and 95% CIs of the variables found to be predictors of events.

The event-free time related to the development of inducible ischemia is reported in Figure 3. Patients who had ischemia during DSE did worse during follow-up than patients with a negative response during DSE.

*Table 1—Clinical Characteristics* *

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Event Group (n = 21)</th>
<th>Nonevent Group (n = 38)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>75 ± 4</td>
<td>76 ± 5</td>
<td>0.30</td>
</tr>
<tr>
<td>Male patients</td>
<td>14 (67)</td>
<td>28 (76)</td>
<td>0.46</td>
</tr>
<tr>
<td>Diabetes</td>
<td>6 (29)</td>
<td>4 (11)</td>
<td>0.08</td>
</tr>
<tr>
<td>Hypertension</td>
<td>14 (67)</td>
<td>15 (49)</td>
<td>0.18</td>
</tr>
<tr>
<td>Dyslipemia</td>
<td>7 (33)</td>
<td>6 (16)</td>
<td>0.13</td>
</tr>
<tr>
<td>Smokers</td>
<td>3 (14)</td>
<td>7 (19)</td>
<td>0.65</td>
</tr>
<tr>
<td>Previous infarction</td>
<td>5 (24)</td>
<td>6 (16)</td>
<td>0.47</td>
</tr>
<tr>
<td>Q-wave infarction</td>
<td>14 (67)</td>
<td>29 (78)</td>
<td>0.32</td>
</tr>
<tr>
<td>Anterior infarction</td>
<td>2 (10)</td>
<td>15 (40)</td>
<td>0.03</td>
</tr>
<tr>
<td>Thrombolysis</td>
<td>4 (22)</td>
<td>14 (40)</td>
<td>0.39</td>
</tr>
<tr>
<td>Creatinine kinase-MB</td>
<td>1,476 ± 1,033</td>
<td>1,518 ± 1,476</td>
<td>0.73</td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SD or No. (%).
Our study is the first to assess the prognostic significance of DSE performed early after uncomplicated AMI in the elderly, and our results show that those patients aged ≥70 years who developed inducible ischemia during DSE are at higher risk of adverse cardiac events during follow-up and a negative response predicts a good outcome.

The prognostic value of DSE in patients with CAD with and without AMI has been extensively reported on.12–19 It is a safe technique in elderly patients.9–11 Furthermore, the usefulness of the test is not dependent on the physical ability of the patient. Although dipyridamole stress echocardiography has been used in the postinfarction period in the elderly,19 the choice of dobutamine instead of dipyridamole might be advantageous. At low dose, dobutamine is a recognized technique for detecting viability.20–22 Besides, dobutamine is safer in patients with COPD, whose prevalence is high among this subset of patients. The reduced myocardial response to β-adrenergic stimulation present in elderly individuals may impair the ability of dobutamine to induce ischemia.23,24 However, the addition of atropine avoids this potential drawback.10 Poldermans et al10 and Baudhuin et al11 assessed DSE in elderly patients. In their studies, DSE sensitivity, specificity, and predictive values were found to be high and similar to those in younger patients.

Previous investigations12–16 analyzed the prognostic value of DSE in the postinfarction period in the general population. Picano et al12 showed that the development of ischemia during DSE was the best predictor of cardiac death in patients with severe left ventricular dysfunction. In that study,12 viability was associated with a better outcome, and the higher the number of segments showing improvement of function, the better the impact on survival; however, patients >75 years old were excluded. Carlos et al15 found that the extent of infarction, global left ventricular function, lack of response to low-dose dobutamine (nonviability), and ischemia at a distance were powerful predictors of adverse spontaneous events. Although age was not among the exclusion criteria, the patients were younger than ours (the study population had a mean age of 58 ± 13 years). Previtali et al13 studied patients with a first AMI treated with thrombolysis and concluded that the presence and extent of ischemia were related to impaired prognosis, whereas viability was not. Again, older patients (≥70 years) were excluded. Finally, Sicari et al14 obtained somewhat different results in

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<th>Event Group (n = 21)</th>
<th>Nonevent Group (n = 38)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANGOR</td>
<td>4 (19)</td>
<td>4 (8)</td>
<td>0.22</td>
</tr>
<tr>
<td>ST-segment descent</td>
<td>13 (62)</td>
<td>14 (37)</td>
<td>0.08</td>
</tr>
<tr>
<td>Maximal pressure-rate product</td>
<td>14,906 ± 3,168</td>
<td>20,500 ± 2,505</td>
<td>0.29</td>
</tr>
<tr>
<td>Atropine</td>
<td>7 (33)</td>
<td>21 (55)</td>
<td>0.10</td>
</tr>
<tr>
<td>β-Blockers</td>
<td>10 (48)</td>
<td>14 (38)</td>
<td>0.46</td>
</tr>
<tr>
<td>Baseline WMSI &gt; 1.6</td>
<td>1.53 ± 0.34</td>
<td>1.60 ± 0.42</td>
<td>0.25</td>
</tr>
<tr>
<td>Low-dose WMSI</td>
<td>14 (67)</td>
<td>15 (41)</td>
<td>0.05</td>
</tr>
<tr>
<td>Low-dose minus baseline WMSI</td>
<td>1.48 ± 0.35</td>
<td>1.52 ± 0.46</td>
<td>0.29</td>
</tr>
<tr>
<td>Peak-stress minus baseline WMSI</td>
<td>1.60 ± 0.42</td>
<td>1.71 ± 0.48</td>
<td>0.33</td>
</tr>
<tr>
<td>Low-dose minus baseline WMSI</td>
<td>−0.05 ± 0.12</td>
<td>−0.16 ± 0.24</td>
<td>0.007</td>
</tr>
<tr>
<td>Negative results</td>
<td>7 (33)</td>
<td>25 (68)</td>
<td>0.01</td>
</tr>
<tr>
<td>Sustained improvement</td>
<td>2 (10)</td>
<td>9 (24)</td>
<td>0.16</td>
</tr>
<tr>
<td>Ischemia</td>
<td>12 (57)</td>
<td>3 (8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Biphasic response</td>
<td>6 (29)</td>
<td>1 (3)</td>
<td>0.003</td>
</tr>
<tr>
<td>Homozonal ischemia</td>
<td>10 (48)</td>
<td>1 (3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Heterozonal ischemia</td>
<td>4 (19)</td>
<td>2 (5)</td>
<td>0.10</td>
</tr>
</tbody>
</table>

*Data are presented as No. (%) or mean ± SD.

FIGURE 1. DSE results and the different events. PTCA = percutaneous transluminal coronary angioplasty.
patients with preserved left ventricular function: ischemia predicted hard events, and viability was associated with the appearance of unstable angina. Therefore, there is agreement that inducible ischemia marks an adverse outcome, but the meaning of viability remains controversial. Our results in the elderly are in agreement with those reported on in the general population and support the negative impact of ischemia on prognosis. Regarding viability, the extent of contractile reserve in the univariate analysis was greater in the nonevent group. Sustained improvement of contractility early after AMI occurs in stunned myocardium, which is likely to recover spontaneously with time. This recovery will improve left ventricular dysfunction and prognosis. However, this variable was related neither to better outcome nor to worse prognosis after stepwise Cox regression analysis. Finally, a moderate-to-severe left ventricular dysfunction (baseline WMSI > 1.6) was also found to predict poor outcome, and this fact has been previously shown to impair prognosis.

Limitations of This Study

It can be argued that revascularization is not an event, as it is a subjective decision. However, results did not differ after excluding the four patients with revascularization. In other words, DSE predicted both spontaneous and total events.

Regarding the extent of contractile reserve, a β-type error cannot be excluded due to the small number of patients. It would be necessary to undertake an analysis with enough patients to show its possible beneficial effect on prognosis.

DSE was performed by one echocardiographer. Although some may deem this improper, this echocardiographer has proven expertise by consistently interpreting large numbers of stress echocardiograms.
grams, and interinstitutional variability was avoided, making the results more homogeneous. Furthermore, it reflects the common clinical practice in a busy echocardiography laboratory of a major center. The lack of postdischarge management data is also a limitation of this study because a better long-term outcome has been shown with several drugs and certain lifestyle modifications.

**Conclusion**

Inducible worsening of contractility in the infarcted zone during DSE within 10 days after uncomplicated AMI is an independent predictor of impaired outcome in elderly patients. Therefore, DSE can be helpful in risk stratification after uncomplicated AMI in elderly patients.

**References**

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