Prognostic Value of Lead aVR in Patients With a First Non–ST-Segment Elevation Acute Myocardial Infarction

José A. Barrabés, MD; Jaume Figueras, MD; Cristina Moure, MD; Josefa Cortadellas, MD; Jordi Soler-Soler, MD

Background—ST-segment elevation in lead aVR has been associated with severe coronary artery lesions in patients with acute coronary syndromes, but the prognostic significance of this finding is unknown.

Methods and Results—We analyzed the initial ECG in 775 consecutive patients admitted to our center with a first acute myocardial infarction without ST-segment elevation in leads other than aVR or V₁. The rates of in-hospital death in patients without (n=525) and with 0.05 to 0.1 mV (n=116) or ≥0.1 mV (n=134) of ST-segment elevation in lead aVR were 1.3%, 8.6%, and 19.4%, respectively (P<0.001). After adjustment for the baseline clinical predictors and for ST-segment depression on admission, the odds ratios for death in the last 2 groups were, respectively, 4.2 (95% CI, 1.5 to 12.2) and 6.6 (95% CI, 2.5 to 17.6). The rates of recurrent ischemic events and heart failure during hospital stay also increased in a stepwise fashion among the groups, whereas creatine kinase–MB levels were similar. Among the 437 patients that were catheterized within 6 months, the prevalence of left main or 3-vessel coronary artery disease in the 3 groups was 22.0%, 42.6%, and 66.3%, respectively (P<0.001).

Conclusions—Lead aVR contains important short-term prognostic information in patients with a first non–ST-segment elevation acute myocardial infarction. Because the poorer outcome predicted by ST-segment elevation in lead aVR seems to be related to a more severe coronary artery disease, an early invasive approach might be especially beneficial in patients presenting with this finding. (Circulation. 2003;108:814-819.)

Key Words: myocardial infarction ■ electrocardiography ■ prognosis ■ mortality

Because patients with non–ST-segment elevation acute myocardial infarction (AMI) are heterogeneous with respect to the pathophysiological mechanisms, the size of the infarction, and the amount of jeopardized myocardium, early risk stratification is a fundamental step in the management of this condition. The ECG has been extensively used for this purpose, and ST-segment depression on admission is now recognized as one of the strongest predictors of an adverse outcome. In these patients, ST-segment depression has also been related to the presence of extensive coronary artery disease and to a greater benefit of an early invasive therapeutic approach.

Lead aVR, whose positive pole is oriented to the right upper side of the heart, usually gives a mirror image of the leads oriented leftward, for which reason it is often ignored. ST-segment elevation in lead aVR, in combination with other repolarization changes, has been associated with severe coronary artery lesions in patients with unstable angina or ST-segment elevation AMI. However, the prognostic significance of this finding is unknown.

Accordingly, we aimed to investigate the short-term prognostic implications of ST-segment elevation in lead aVR on the initial ECG in a series of consecutive patients admitted to our center with a first AMI without other ST-segment elevation. Part of these patients had been included in a previous study assessing the significance of the extent and distribution of ST-segment depression, in which lead aVR was not considered.

Methods

Patients

All admissions to our coronary care unit between January 1984 and December 1999 were screened. Patients with a first AMI presenting within 24 hours after onset of symptoms without ST-segment elevation ≥0.1 mV in leads other than aVR or V₁ or left bundle branch block were selected. Diagnosis of AMI was based on the presence of anginal pain and a transient elevation of serum creatine kinase–MB (CK-MB) levels over the upper limit of normal (25 IU/L). CK-MB activity was measured at 4- to 6-hour intervals during the first 48 hours. Medical histories were reviewed, and patients with previous coronary artery bypass grafting or recent (<6 months) percutaneous coronary interventions were excluded. Among 856 patients suitable to enter the study, 46 were excluded because the medical charts were incomplete and 35 because of the presence of abnormal Q- or posterior R-waves on admission and 775 were finally included.
Electrocardiographic Evaluation

The initial 12-lead ECG obtained at the emergency room, or, occasionally, another tracing from the first hours showing more pronounced changes, was examined by one investigator blinded to the patients’ clinical outcome and to the results of coronary angiography. Left ventricular hypertrophy (LVH) was defined as a sum of R waves in leads V1 or V5 plus an S wave in lead V5 ≥3.5 mV. ST-segment shifts were measured at 80 ms after the J point for ST-segment depression and at 20 ms after this point for ST-segment elevation using the preceding TP-segment as a baseline. ST-segment depression was considered to be present if measured ≥0.1 mV in any lead, and its magnitude and extent were measured. Anterior, inferior, and lateral ST-segment depressions were defined as ST-segment depression ≥0.1 mV in ≥2 leads oriented anteriorly (V1 through V4), inferiorly (II, III, aVF), or leftward (I, aVL, V5, or V6), respectively. The presence of T-wave inversion was also determined.

Clinical Data Collection

Clinical data were recorded without knowledge of the electrocardiographic findings. Demographic data, risk factors for coronary heart disease, ongoing treatment with cardiovascular medications, and data from physical examination on admission were collected. Major in-hospital adverse events such as death, reinfarction, heart failure, and postinfarction angina were also recorded in all patients, along with the pharmacological treatment and the use of coronary revascularization procedures.

Cardiac Catheterization Data

A cardiac catheterization was performed within 6 months in 437 patients (56.4%). Of them, 405 (92.7%) were catheterized before hospital discharge. A stenosis ≥50% in the diameter of the left main coronary artery or a stenosis ≥70% in 1 or more of the major epicardial vessels or their main branches was considered significant. The culprit lesion was defined as the one with local thrombus or the most severe lesion. A contrast left ventriculogram was obtained in 355 patients.

Statistical Analysis

Categorical variables are described as frequencies and percentages and continuous variables as mean ± SD. Because magnitudes of ST-segment elevation in lead aVR as low as 0.05 mV have been related to the presence of proximal lesions in the left coronary tree,16,17 we aimed to characterize the prognostic implications of incremental levels of this ST-segment elevation. Therefore, patients were categorized into 3 groups, without and with minor (≥0.05 but <0.1 mV) or overt (≥0.1 mV) ST-segment elevation in lead aVR. Comparisons between these groups were performed with the use of the Mantel-Haenszel χ² test for proportions and by linear regression after assigning a value of 0, 1, or 2, respectively, to each of these categories for continuous variables. A multivariate logistic regression analysis using backward stepwise elimination was used to identify baseline clinical predictors of in-hospital death among the variables associated (P<0.2) with this outcome in univariate analysis. Subsequent analyses included the significant predictors, the presence, or, in a separate analysis, location, of ST-segment depression, and patient’s category according to ST-segment measurements in lead aVR. The goodness of fit of the model was assessed with the Hosmer-Lemeshow test.19 Finally, the association of ST-segment depression elsewhere with in-hospital complications was examined after patients had been stratified for ST-segment elevation in lead aVR.

Results

Baseline Characteristics

Of the 775 patients and with regard to lead aVR on admission, 525 (66.7%) did not have ST-segment elevation whereas 116 (15.0%) had 0.05 to 0.1 mV and 134 (17.3%) had ≥0.1 mV of ST-segment elevation. ST-segment elevation in lead aVR was associated with older age, a higher risk profile, and a higher prevalence of previous angina as well as with an increased heart rate and systolic blood pressure on admission and with a higher Killip class (Table 1).
Patients with ST-segment elevation in lead aVR had an increased prevalence of right bundle branch block, LVH, and ST-segment elevation in lead V₁, a more frequent and extensive ST-segment depression in other leads, and a lower frequency of T-wave inversion than the remaining patients (Table 2). ST-segment elevation in lead aVR was especially associated with downsloping ST-segment depression.

**In-Hospital Outcome**

Forty-three patients (5.5%) died before hospital discharge. Cardiogenic shock, preceded in 10 cases by reinfarction or severe angina, was the cause of death in 31 patients. In-hospital mortality increased in a stepwise fashion across increasing categories of ST-segment elevation in lead aVR (Table 3), and this was the only variable from the initial ECG that was retained as an independent predictor of death in the multivariate analysis (Table 4). The predictive value of this variable was maintained after adjusting for ST-segment elevation in lead V₁ or after excluding patients with LVH from the analysis.

ST-segment elevation in lead aVR was also strongly associated with the rates of in-hospital recurrent ischemic events and heart failure but not with total CK or CK-MB levels. There were small between-group differences with respect to pharmacological treatment and the rates of percutaneous revascularization procedures were similar, but patients with ST-segment elevation in lead aVR required a coronary artery bypass grafting operation more often than the...
rest. Although ST-segment depression was associated with all major adverse events, this association was no longer present after patients had been stratified for ST-segment elevation in lead aVR (Figure). Among patients without this ST-segment elevation, the presence of ST-segment depression elsewhere was associated only with a moderate increase in the incidence of heart failure, probably because patients in this subgroup showed the highest CK-MB levels (169±130 IU/L, \(P=0.001\) with respect to the subgroups without ST-segment changes [101±70 IU/L] or with ST-segment elevation in lead aVR [128±102 and 119±95 IU/L]).

**Cardiac Catheterization Data**

Cardiac catheterization was performed in 52.8%, 58.6%, and 68.7% of patients among the 3 categories with increasing ST-segment elevation in lead aVR, respectively (\(P=0.001\)). Compared with the remaining patients, those with ST-segment elevation in lead aVR were more likely to have multiple wall motion abnormalities and had a lower left ventricular ejection fraction and a more severe coronary artery disease (Table 5). Prevalence of left main or 3-vessel disease in the 3 groups was 22.0%, 42.6%, and 66.3%, respectively (\(P<0.001\)). Among patients with left anterior descending coronary artery disease but without left main disease, those with ST-segment elevation ≥0.05 mV in lead aVR tended to have a more frequent involvement of the proximal segment than the rest (37% versus 27%, respectively, \(P=0.14\)). ST-segment elevation in lead aVR was inversely associated with the frequency of left circumflex-related infarctions, although the culprit vessel was not identified in a high proportion of patients with this finding.

**Discussion**

This study shows that lead aVR on the admission ECG contains valuable short-term prognostic information among patients with a first non–ST-segment elevation AMI. ST-segment elevation in lead aVR was closely associated with the rates of in-hospital death, recurrent ischemic events, and heart failure and was more efficient than ST-segment depression elsewhere in predicting these complications.

Previous studies have found analysis of lead aVR to be useful in estimating the likelihood or the location of coronary artery disease using exercise stress testing,20,21 in the classification of inferior and lateral AMI, 22 or in the prediction of left ventricular dysfunction after anterior AMI. 23 ST-segment elevation in lead aVR has been also related to the presence of severe coronary artery lesions among patients with unstable angina or AMI.15–17 Although attempts have been made to improve the usefulness of the ECG in predicting the clinical outcome in patients with non–ST-segment elevation acute coronary syndromes by considering the extent or the distribution of ST-segment depression,2,5,7,11 the prognostic information provided by lead aVR had not previously been explored.

In our study, patients with ST-segment elevation in lead aVR were older and had a higher baseline risk profile than the remaining patients, but the association of this variable with

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>(P) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Killip class ≥2</td>
<td>6.11</td>
<td>2.73 to 13.67</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ST-segment elevation in lead aVR</td>
<td>4.24</td>
<td>1.47 to 12.25</td>
<td>(P=0.001)</td>
</tr>
<tr>
<td>0.05 to 0.1 mV</td>
<td>6.61</td>
<td>2.49 to 17.56</td>
<td></td>
</tr>
<tr>
<td>≥0.1 mV</td>
<td>1.16</td>
<td>1.04 to 1.30</td>
<td>0.006</td>
</tr>
<tr>
<td>Systolic arterial pressure, 10-mm Hg decrease</td>
<td>2.76</td>
<td>1.29 to 5.91</td>
<td>0.010</td>
</tr>
<tr>
<td>Peripheral artery disease</td>
<td>1.04</td>
<td>1.00 to 1.09</td>
<td>0.045</td>
</tr>
<tr>
<td>Age, 1-year increment</td>
<td>1.04</td>
<td>1.00 to 1.09</td>
<td>0.045</td>
</tr>
</tbody>
</table>

Neither the presence nor the location of ST-segment depression retained an independent association with death. The fit of the model was good (Hosmer-Lemeshow test \(P=0.90\)).

**TABLE 4. Multivariate Predictors of In-Hospital Death**
mortality was independent of baseline clinical predictors. Not surprisingly, ST-segment elevation in lead aVR was also related to ST-segment depression in other leads, a finding with well-known adverse prognostic implications.2–11 Because lead aVR points at ~150 degrees in the frontal plane (or inverted lead aVR at ~30 degrees), ST-segment elevation in this lead was especially associated with lateral or to a minor extent inferior ST-segment depression. However, ST-segment elevation in lead aVR was superior to ST-segment depression elsewhere in predicting the risk of death even after adjusting for the location of ST-segment depression, which had incremental prognostic value in our previous study.7 The particular orientation of inverted lead aVR falling between leads I and II and not matching exactly the lateral or the inferior leads may help explain these results.

The lack of association between ST-segment elevation in lead aVR and peak CK-MB levels makes it unlikely that its adverse prognostic significance was dependent on a larger infarct size. In contrast, and in agreement with existing observations,15–17 this finding was related to the presence of a severe coronary artery disease, another determinant of the clinical outcome in patients with acute coronary syndromes.24,25

The fact that coronary angiography was not always performed in the acute phase and the high prevalence of multivessel disease among patients with ST-segment elevation in lead aVR likely accounted for the difficulties in identifying the culprit vessel in these patients (50% of those in whom this occurred had 3-vessel disease). The trend toward a more frequent proximal versus mid/distal involvement of the left anterior descending artery in patients with ST-segment elevation in lead aVR and the inverse relation between this finding and the frequency of left circumflex artery-related infarctions concur with previous observations in patients with ST-segment elevation AMI.16,26 It is possible that a significant proportion of the patients without ST-segment elevation in lead aVR but with ST-segment depression in other leads, a subset with low complication rates despite having the highest CK-MB peak, had posterior infarctions.27 In a recent study of patients with non–ST-segment elevation acute coronary syndromes, those with the highest elevations of biochemical markers for myocardial necrosis frequently had an occlusion of the left circumflex artery and were at lower risk of suffering a reinfarction than those with intermediate elevations.28

Several limitations must be acknowledged in relation to the present study. Our series was drawn from a single center throughout a prolonged period of time. Although most patients received standard antithrombotic therapy, the results cannot be extrapolated to patients treated with the more contemporary aggressive approach. The fact that coronary anatomy was not documented in all patients and that a coronary angiography was performed more often in those with ST-segment elevation in lead aVR constitutes an additional limitation. Finally, interpretation of coronary angiograms by our laboratory staff could have been influenced in some cases by the knowledge of the electrocardiographic findings. However, it seems unlikely that awareness of ST-segment status in lead aVR had had a major impact on the description of coronary lesions.

<table>
<thead>
<tr>
<th>TABLE 5. Cardiac Catheterization Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>ST-Segment Elevation in Lead aVR</td>
</tr>
<tr>
<td>None (n=277) 0.05 to 0.1 mV (n=68) ≥0.1 mV (n=92) P Value for Trend</td>
</tr>
<tr>
<td>Wall motion abnormalities*</td>
</tr>
<tr>
<td>None 107 (45) 22 (39) 22 (36) 0.1</td>
</tr>
<tr>
<td>Anterior 45 (19) 12 (21) 12 (19) 0.9</td>
</tr>
<tr>
<td>Posteroinferior 75 (32) 18 (32) 18 (29) 0.7</td>
</tr>
<tr>
<td>Multiple segments 9 (4) 5 (9) 10 (16) 0.001</td>
</tr>
<tr>
<td>Left ventricular ejection fraction,* % 66±12 63±11 59±16 &lt;0.001</td>
</tr>
<tr>
<td>No. of diseased vessels</td>
</tr>
<tr>
<td>None 18 (6) 1 (2) 3 (3) 0.1</td>
</tr>
<tr>
<td>One 121 (44) 20 (29) 12 (13) &lt;0.001</td>
</tr>
<tr>
<td>Two 77 (28) 18 (26) 16 (17) 0.06</td>
</tr>
<tr>
<td>Three 52 (19) 22 (32) 44 (48) &lt;0.001</td>
</tr>
<tr>
<td>Left main 9 (3) 7 (10) 17 (18) &lt;0.001</td>
</tr>
<tr>
<td>Infarct-related artery</td>
</tr>
<tr>
<td>Left main 2 (1) 0 (0) 7 (8) &lt;0.001</td>
</tr>
<tr>
<td>Left anterior descending 58 (21) 13 (19) 18 (20) 0.7</td>
</tr>
<tr>
<td>Left circumflex 112 (40) 22 (32) 14 (15) &lt;0.001</td>
</tr>
<tr>
<td>Right 46 (17) 8 (12) 12 (13) 0.3</td>
</tr>
<tr>
<td>Not identified 59 (21) 25 (37) 41 (45) &lt;0.001</td>
</tr>
<tr>
<td>Data are mean±SD or No. (%) of patients. *Values from the 355 patients who had a left ventriculogram.</td>
</tr>
</tbody>
</table>

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Because a widespread use of an early invasive therapeutic strategy in the large and heterogeneous population of patients with non-ST-segment elevation AMI might be cost-ineffective or even harmful in those at the lowest risk, identification of the subsets likeliest to benefit from this strategy is a focus of continued attention.

Accordingly, and in view of its association with severe coronary artery disease, ST-segment elevation in lead aVR could be used, if the results of the present study are confirmed in the large databases now available, as a readily available tool for an early selection of patients for coronary angiography and revascularization.

References


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