Prognostic Value of Lead V1 ST Elevation During Acute Inferior Myocardial Infarction

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Background—Lead V1 directly faces the right ventricle and may exhibit ST elevation during an acute inferior myocardial infarction when the right ventricle is also involved. Leads V1 and V3 indirectly face the posterolateral left ventricle, and ST depression (“mirror-image” ST elevation) in V1 through V3 may reflect concomitant posterolateral infarction. The prognostic significance of V1 ST elevation during an acute inferior myocardial infarction may therefore be dependent on V3 ST changes.

Methods and Results—In 7967 patients with acute inferior myocardial infarction in the Hirulog and Early Reperfusion or Occlusion-2 (HERO-2) trial, V1 ST levels were analyzed with adjustment for lead V3 ST level for predicting 30-day mortality. V1 ST elevation at baseline, analyzed as a continuous variable, was associated with higher mortality. Unadjusted, each 0.5-mm-step increase in ST level above the isoelectric level was associated with ≈25% increase in 30-day mortality; this was true whether V3 ST depression was present or not. The odds ratio for mortality was 1.21 (95% confidence interval, 1.07 to 1.37) after adjustment for inferolateral ST elevation and clinical factors and 1.24 (95% confidence interval, 1.09 to 1.40) if also adjusted for V3 ST level. In contrast, lead V1 ST depression was not associated with mortality after adjustment for V3 ST level. V1 ST elevation ≥1 mm, analyzed dichotomously in all patients, was associated with higher mortality. The odds ratio was 1.28 (95% confidence interval, 1.01 to 1.61) unadjusted, 1.51 (95% confidence interval, 1.19 to 1.92) adjusted for V3 ST level, and 1.35 (95% confidence interval, 1.04 to 1.76) adjusted for ECG and clinical factors. Persistence of V1 ST elevation ≥1 mm 60 minutes after fibrinolysis was associated with higher mortality (10.8% versus 5.5%, P=0.001).

Conclusion—V1 ST elevation identifies patients with acute inferior myocardial infarction who are at higher risk. (Circulation. 2010;122:463-469.)

Key Words: mortality • myocardial infarction • ST segment elevation • electrocardiography • fibrinolysis

The concept of ST elevation acute myocardial infarction (AMI) originated from animal studies, with ST-segment elevation on the epicardial leads correlating with ST elevation on body surface ECG leads.1 Lead V1 directly faces the right ventricle and during an inferior AMI may exhibit ST elevation with concomitant right ventricular infarction. Lead V1 also faces the endocardial surface of the posterolateral left ventricle, and ST depression may reflect concomitant posterolateral infarction (as the “mirror image” of ST elevation involving posterolateral epicardial leads). Both right ventricular infarction and posterolateral infarction worsen the prognosis of an inferior AMI.2–4

Clinical Perspective on p 469

The precordial ST depression associated with transmural posterolateral AMI is generally more pronounced in left-sided chest leads V2 and V3 than in the right-sided chest lead V1. Because lead V3 does not directly face the right ventricle, ST changes in V3 reflect predominantly left rather than right ventricular pathologies. In lead V1, however, ST elevation from right ventricular AMI may potentially cancel out the ST depression from posterolateral AMI to give an isoelectric ST level. Diagnosis of right ventricular infarction during an inferior AMI may therefore be aided by evaluating both V1 and V3 ST levels. The prognostic meaning of V1 ST elevation and its serial changes after fibrinolysis is not well defined despite the otherwise wealth of literature on ST resolution in AMI.5–9

Therefore, we evaluated the prognostic value of V1 ST elevation in patients with inferior AMI from the Hirulog and Early Reperfusion or Occlusion-2 (HERO-2) trial, which included 17,073 patients with ST-elevation AMI. Patients...
were randomized within 6 hours of symptom onset to receive bivalirudin or heparin in addition to streptokinase and aspirin. The randomized treatments had no effect on the primary end point of 30-day mortality.10 The trial protocol specified recording serial ECGs at randomization and 60 minutes after streptokinase was begun.11–16

Methods
The protocol and results of the HERO-2 trial have been reported.10 Patients who presented with >30 minutes of ischemic chest pain and either ST-segment elevation or presumed new left bundle-branch block within 6 hours of symptom onset were randomized to receive bivalirudin or unfractionated heparin in addition to streptokinase and aspirin. All ECGs were sent to the core laboratory at Green Lane Hospital for analysis by 8 ECG technicians11–16 who were unaware of treatment assignment and patient outcomes.

ECG Analysis
The present analysis of ST changes in lead V1 was performed only in patients with inferior AMI showing normal intraventricular conduction at both randomization and the 60-minute time point. The amount of ST-segment change, for both elevation and depression, was measured to the nearest 0.5 mm at 60 milliseconds after the J point for all 12 standard leads on both ECGs by a team of 8 experienced technicians.11–16 Inferior AMI was diagnosed from ECG changes of 1-mm ST elevation in 2 adjacent inferior leads. Patients with concomitant ST elevation involving 2 adjacent leads in both the anterior territory and inferior territory were classified as having anterior AMI.

Statistical Analysis
On a normality test, the distributions of age, systolic and diastolic blood pressures, pulse rate, summed ST depression, and summed ST elevation were skewed. For consistency, all continuous variables are therefore reported as the median and 25th and 75th percentiles and compared by the Mann-Whitney U test or Kruskal-Wallis test when appropriate. Discrete variables are presented as percentages, and the χ² test was used for comparison.

Results
This analysis included 7967 patients with inferior AMI and normal intraventricular conduction at randomization and at 60 minutes as shown in the Figure. In lead V1, 1874 patients had ST elevation ≥0.5 mm (749 with 0.5 mm, 619 with 1 mm, and 506 with ≥1.5 mm), 2213 patients had isoelectric (0 mm) ST level, and 3880 had ST depression with ST level ≥0.5 mm.

Baseline Characteristics
Table 1 shows the baseline characteristics of all patients categorized according to V1 ST level as isoelectric (0 mm), elevation ≥0.5 mm, and depression ≥0.5 mm. Compared with patients with isoelectric ST level, patients with V1 ST elevation were younger (59 versus 61 years; P=0.005) and had more prior infarctions (17.7% versus 14.2%; P=0.02) and worse Killip class (P<0.001). They had similar magnitudes of summed
inferolateral (II, III, aVF, V5, V6, I, and aVL) ST elevation (5 versus 5 mm; \( P = 0.15 \)) but less summed V1 to V4 ST depression (0.5 versus 1.5 mm; \( P < 0.001 \)). At 30 days, mortality was higher in patients with V1 ST elevation compared with patients without V1 ST elevation (7.6% versus 5.2%; \( P = 0.002 \)). Compared with patients with isoelectric (0 mm) ST levels, patients with V1 ST depression also had worse baseline characteristics and higher 30-day mortality (7.6% versus 5.2%; \( P < 0.001 \)). Among patients with isoelectric or positive ST levels, 30-day mortality increased with increasing V1 ST elevation (5.2% with 0 mm, 6.4% with 0.5 mm, 6.8% with 1 mm, and 10.3% with \( \geq 1.5 \) mm; \( P \) for trend <0.0001).

**Relationship Between V1 ST Level and 30-Day Mortality**

Table 2 shows the relationship between V1 ST segment level (as elevation, isoelectric, or depression) and 30-day mortality in subgroups (columns) according to V3 ST depression stratified into 3 levels (rows). The lowest mortality of 4.3% was observed in the 1374 patients with V1 ST level of 0 mm and no V3 ST depression.

The majority of patients with ST depression in V1 also had ST depression in V3, and only 507 patients (6.4%) had V1 ST elevation concomitant with V3 ST depression of \( \geq 1 \) mm. In these 507 patients, 30-day mortality was 9.9% compared with 6.8% in the 839 patients who had a similar degree of V3 ST depression but an isoelectric (0 mm) V1 ST level (\( P = 0.048 \)).

**V3 ST Depression and Mortality**

Examination of lead V3 ST level in the whole cohort shows that those with ST depression of \( \geq 1 \) mm had higher mortality than those without ST depression (7.9% versus 5.8%);
Table 2. 30-Day Mortality According to V1 and V3 ST Levels

<table>
<thead>
<tr>
<th>Subgroups</th>
<th>No V3 ST depression</th>
<th>Lead V3 ST level of (-1) or (-1.5) mm</th>
<th>Lead V3 ST level of (-2) mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, n</td>
<td>932</td>
<td>1044</td>
<td>1904</td>
</tr>
<tr>
<td>30-d mortality, %</td>
<td>6.5</td>
<td>5.8</td>
<td>9.0</td>
</tr>
<tr>
<td>V1 ST level (\leq-0.5) mm (Depression)</td>
<td>1374</td>
<td>507</td>
<td>332</td>
</tr>
<tr>
<td>V1 ST level (\geq 0) mm (Elevation)</td>
<td>1367</td>
<td>284</td>
<td>223</td>
</tr>
</tbody>
</table>

P < 0.001). Table 2 shows the 30-day mortality according to V1 ST level subgroups (rows).

Significance of a 0.5-mm-Step ST Deviation From Isoelectric Level in Lead V1
V1 ST level was analyzed as a continuous variable per each step of 0.5 mm change from 0 mm stratified according to the 3 levels of V3 ST depression (Table 3). Unadjusted, each 0.5-mm-step increase in V1 ST level above 0 mm (ie, ST elevation) was associated with an ≈25% increase in 30-day mortality. This was true for all V3 level subgroups. In the whole cohort, the final odds ratio after adjustment for inferolateral ST elevation and clinical factors was 1.21 (95% confidence interval, 1.07 to 1.37) and 1.24 (95% confidence interval, 1.09 to 1.40) when adjusted also for V3 ST level. In contrast, each 0.5-mm-step decrease in V1 ST level below 0 mm was not significantly associated with 30-day mortality after adjustment for V3 ST level.

Significance of V1 ST Elevation Using Dichotomous Cut Points
V1 ST elevation \(\geq 1\) mm was significantly associated with higher 30-day mortality (28% higher unadjusted, 51% higher if adjusted for V3 ST level, 51% higher if adjusted for both V3 ST level and inferolateral ST elevation, and 35% higher after further adjustment for all clinical factors; Table 4). The C index of the full algorithm was 0.82. Findings were similar, albeit to a lesser extent, when the V1 ST elevation cut point of 0.5 mm was used (Table 4). The interaction term (V1 ST elevation times V3 ST level) was not significant in both analyses (P = 0.293 for 1-mm V1 ST cut point, P = 0.392 for 0.5-mm V1 ST cut point).

Table 3. Thirty-Day Mortality (Odds Ratios and 95% Confidence Intervals) According to Each Step of 0.5 mm Change in V1 ST Level

<table>
<thead>
<tr>
<th>Subgroups According to V3 ST Level</th>
<th>Unadjusted</th>
<th>Adjusted for Inferolateral ST Elevation*</th>
<th>Adjusted for Inferolateral ST Elevation and Clinical Factors†</th>
<th>Unadjusted</th>
<th>Adjusted for Inferolateral ST Elevation*</th>
<th>Adjusted for Inferolateral ST Elevation and Clinical Factors†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lead V3 ST level at or above (-0.5) mm</td>
<td>1.28 (1.11–1.47)</td>
<td>1.25 (1.08–1.44)</td>
<td>1.15 (0.99–1.35)</td>
<td>1.27 (1.07–1.52)</td>
<td>1.22 (1.0–1.51)</td>
<td>1.20 (0.96–1.50)</td>
</tr>
<tr>
<td>Lead V3 ST level of (-1) or (-1.5) mm</td>
<td>1.20 (0.91–1.57)</td>
<td>1.16 (0.89–1.53)</td>
<td>1.19 (0.88–1.61)</td>
<td>1.03 (0.85–1.26)</td>
<td>1.0 (0.81–1.25)</td>
<td>1.12 (0.88–1.42)</td>
</tr>
<tr>
<td>Lead V3 ST level of (-2) mm or below</td>
<td>1.29 (1.03–1.63)</td>
<td>1.29 (1.01–1.63)</td>
<td>1.56 (1.17–2.07)</td>
<td>0.98 (0.86–1.12)</td>
<td>0.98 (0.86–1.13)</td>
<td>0.96 (0.82–1.12)</td>
</tr>
<tr>
<td>All patients with inferior infarction</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any V3 ST level (ie, all V3 groups)</td>
<td>1.25 (1.12–1.39)</td>
<td>1.22 (1.09–1.36)</td>
<td>1.21 (1.07–1.37)</td>
<td>1.17 (1.08–1.27)</td>
<td>1.14 (1.04–1.25)</td>
<td>1.10 (0.99–1.22)</td>
</tr>
<tr>
<td>Any V3 ST level (ie, all V3 groups)†</td>
<td>1.25 (1.12–1.39)</td>
<td>1.24 (1.11–1.40)</td>
<td>1.24 (1.09–1.40)</td>
<td>1.17 (1.08–1.27)</td>
<td>1.05 (0.94–1.16)</td>
<td>1.06 (0.95–1.19)</td>
</tr>
</tbody>
</table>

OR indicates odds ratio; CI, confidence interval.
*Inferolateral ST elevation included summed baseline ST-segment elevation in the inferior (leads II, III, and aVF) and lateral (V5, V6, I, and aVL) leads.
†Clinical factors included age and sex, systolic blood pressure, Killip class, heart rate, history of previous AMI, diabetes mellitus, hypertension, prior angina, time from symptom onset to randomization, and geographic region of patient recruitment.
‡Adjusted also for V3 ST level.
Persistence of Lead V1 ST Elevation After Fibrinolysis

Among patients with V1 ST elevation, those with persistent elevation in lead V1 at 60 minutes after fibrinolysis started were associated with higher mortality than those who had V1 ST elevation resolved. This was true regardless of whether the ST cut point was 1 mm (10.8% versus 5.5%; \( P = 0.001 \)) or 0.5 mm (9.1% versus 4.4%; \( P < 0.001 \); Table 5).

Discussion

This study in 7967 patients with acute inferior AMI showed that lead V1 ST elevation is a marker of increased 30-day mortality independently of the extent of inferolateral ST elevation, V1 ST depression, and clinical parameters. In this cohort, 1874 patients (23.5%) had V1 ST elevation \( \geq 0.5 \) mm and 1125 (14.1%) had V1 ST elevation \( \geq 1 \) mm. Consistent with the finding that V1 ST elevation conferred a worse prognosis, there was a lower mortality among patients who had V1 ST elevation resolved than those with persistent V1 ST elevation at 60 minutes after administration of fibrinolytic therapy.

Patients with V1 ST depression also had higher mortality than those with isoelectric V1 ST level. This is consistent with the literature on the negative prognostic effects associated with precordial ST depression. Thus, V1 ST deviation in both directions was analyzed in subgroups according to V3 ST level (Tables 2 and 3), and the prognostic effect of V1 ST elevation was analyzed with V3 ST level as a cofactor in multivariable regression. The new finding was an association between a 0.5-mm-step increase in V1 ST elevation (referred to 0-mm ST level) and higher 30-day mortality that was independent of V3 ST level.

Further to the higher mortality found in patients with V3 ST depression compared with patients without V3 ST depression, the present study shows that most patients with V1 ST depression also have ST depression in lead V3. The odds ratio for 30-day mortality of a 0.5-mm-step increase in V1 ST depression below 0 mm was almost 1 when the analysis was adjusted for V3 ST segment level, suggesting that the prognostic information of V1 ST depression did not add further to V3 ST depression. This finding is consistent with the notion that ST depression from concomitant posterolateral infarction is often better seen in left-sided lead V3 than in right-sided lead V1.

In the entire 7967 patient cohort and with the use of dichotomous cut points, V1 ST elevation \( \geq 1 \) mm predicted a 28% higher unadjusted 30-day mortality and a 51% higher adjusted 30-day mortality when ECG factors were added. The serial adjustment process, as reported in Table 4, showed that the odds ratio increased after adjustment for V1 ST level.

The relative importance of right ventricular and posterolateral infarction to mortality with V1 ST elevation cannot be directly determined in this study because data on imaging of the right ventricle and LV were not available. The poor prognosis with right ventricular infarction has previously been reported, both in patients receiving fibrinolytic therapy and in patients having primary percutaneous coronary intervention. We speculate that because the normal right ventricle contains much less myocardial mass than the left ventricle, infarction of the majority of the right ventricular myocardium could significantly increase the mortality of patients with an acute inferior AMI with a relatively small increase in infarct mass. This contrasts with concomitant infarction of the posterolateral left ventricular wall, which significantly increases both total infarct mass and mortality. The present study shows the negative prognostic value of V1 ST elevation independently of and adding to the other negative prognostic ECG sign of V3 ST depression, which reflects posterolateral infarction.

The ECG diagnosis of right ventricular infarction is classically made by recording lead V4R. In an autopsy study of 43 patients, ST elevation in lead V4R had higher sensitivity and specificity than ST elevation in lead V1 in diagnosing right

Table 5. Serial ST Changes in Patients With Lead V1 ST Elevation Over 60 Minutes After Fibrinolysis

<table>
<thead>
<tr>
<th>Baseline V1 ST Elevation ( \geq 1 ) mm*</th>
<th>Baseline V1 ST Elevation ( \geq 0.5 ) mm†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent ST Increase ( \geq 1 ) mm</td>
<td>Persistent ST Increase ( \geq 0.5 ) mm</td>
</tr>
<tr>
<td>Resolution of ST Increase to &lt;1 mm</td>
<td>Resolution of ST Increase to &lt;0.5 mm</td>
</tr>
<tr>
<td>( P )</td>
<td>( P )</td>
</tr>
<tr>
<td>Patients, n</td>
<td>609</td>
</tr>
<tr>
<td>30-d mortality, %</td>
<td>10.8</td>
</tr>
<tr>
<td>512</td>
<td>587</td>
</tr>
<tr>
<td>5.5</td>
<td>4.4</td>
</tr>
<tr>
<td>0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Four and †7 patients had missing data for 60-minute ST level.
ventricular infarction. Similarly, ST elevation in leads V2 through V9 adds significantly to precordial ST depression in aiding the diagnosis of posterolateral AMI. However, recording leads V1R and V3 through V9 is an additional step in the performance of a standard 12-lead ECG and, although recommended, may not be routinely performed.

Recording lead V1 in the right parasternal position might capture the ST elevation from right ventricular infarction in more patients during the acute phase of AMI. Indeed, the prognostic role of V1R recordings relative to V1 recordings in patients receiving prompt reperfusion therapy needs to be studied. Standard 12-lead ECGs are increasingly being performed before hospitalization to enable shorter times to the administration of fibrinolytic therapy or to balloon inflation for primary percutaneous coronary intervention. The availability of pocket-size ECG machines capable of networking through cell phones will likely make this even more common. The present study supports the use of information from the readily available V1 recordings to aid risk stratification and prognostication.

Limitations
We have correlated 30-day mortality with V1 ST elevation, which we judged to be likely due to right ventricular infarction, but we acknowledge that there was no imaging confirmation. Despite careful adjustment of the V1 ST level, the possibility exists that in some patients, concomitant right ventricular and posterolateral infarctions might have ST elevation forces cancelling out ST depression forces over both precordial leads V1 and V3.

Statistical adjustment for multiple testing was not undertaken. However, the observation of consistent results with different ST segment cut levels and with different adjustments for other ECG and clinical variables in several exploratory analyses strengthens the conclusions of this article.

A number of factors other than myocardial ischemia and infarction influence V1 ST levels. High ST-segment takeoff in the V1 through V3 precordial chest leads occurs up to 1.5 mm in female and up to 2 mm in male patients. ST elevation is often more pronounced in V2 and V3 than in V1, causing diagnostic difficulties, particularly in patients with anterior AMI, and could be a confounding factor in assessing precordial ST levels in patients with inferior AMI. In the HERO-2 trial, most patients had cardiac biomarker elevation confirming the diagnosis of AMI. The present study did not include any patients with concomitant anterior ST elevation affecting >1 chest lead because they would not have been classified as having an inferior AMI.

Lead placement position can also affect ST level measurements, but leads V1 and V2, in the right and left parasternal positions, respectively, are the most reproducible of the 6 chest lead positions. Lead V1 can be regarded as lead V2R, and our analysis defines the prognostic meaning of right-sided ST elevation during inferior AMI in a large patient population database.

Conclusions
In this study of 7967 patients with inferior AMI, ST elevation in V1 at baseline had incremental adverse prognostic significance that was independent of the effect of precordial V3 ST depression. Resolution of V1 ST elevation after fibrinolysis was associated with improved 30-day survival, lending further support to the independent prognostic value of this simple ECG parameter. We speculate that the mechanistic link between V1 elevation and increased mortality is due to the occurrence of right ventricular infarction.

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