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

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The precordial ST depression associated with transmural posterolateral AMI is generally more pronounced in left-
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 lead V1, V2, V3, V4, V5, and V6.

**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.

The primary analysis examined the relationship between ST elevation in lead V1 on the baseline ECG and 30-day mortality. Exploratory analysis was performed stratified according to clinically relevant ST depression cut points in lead V3 (V3 ST level at or above −0.5 mm, V3 ST level of −1.7 or −1.5 mm, V3 ST level of −2 mm or below).

Multivariable logistic regression analysis incorporated summed baseline ST-segment elevation (inferior leads II, III, and aVF and lateral leads V5, V6, I, and aVL) and other clinical prognostic factors in the HERO-2 cohort.11–16 These 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. The V1 ST level was explored both as a continuous variable per each step of 0.5-mm change from the isoelectric 0-mm level and as a dichotomous variable using clinically relevant ST level cut points of 0.5 or 1 mm. In the latter analyses, interaction terms between the dichotomously defined V1 ST elevation and V3 ST level were tested. Further analysis was performed among patients with V1 ST elevation to ascertain whether the persistence of V1 ST elevation in the first hour after fibrinolytic therapy was related to 30-day mortality.

**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 V2 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 ≥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.

#### V3 ST Depression and Mortality

Examination of lead V3 ST level in the whole cohort shows that those with ST depression of ≥1 mm had higher mortality than those without ST depression (7.9% versus 5.8%);
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 a 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.

Table 2. 30-Day Mortality According to V1 and V3 ST Levels

<table>
<thead>
<tr>
<th>Subgroups According to V3 ST Level</th>
<th>No V3 ST depression</th>
<th>V3 ST level ≤ 0.5 mm (Depression)</th>
<th>V3 ST ≤ 0.5 mm vs 0 mm</th>
<th>P for V3 ST ≤ 0.5 mm vs 0 mm</th>
<th>P for V1 ST Elevation (0.5 mm Step Increase in V1 ST Level in Patients With V1 ST Level &gt; 0 mm)</th>
<th>P for V1 ST Depression (0.5 mm Step Decrease in V1 ST Level in Patients With V1 ST Level &lt; 0 mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, n</td>
<td>932</td>
<td>1374</td>
<td>1367</td>
<td>6.5</td>
<td>4.3</td>
<td>6.7</td>
</tr>
<tr>
<td>30-d mortality, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.022</td>
<td>0.005</td>
</tr>
<tr>
<td>Lead V3 ST level of −1 or −1.5 mm</td>
<td>Patients, n</td>
<td>1044</td>
<td>507</td>
<td>284</td>
<td>5.8</td>
<td>5.3</td>
</tr>
<tr>
<td>30-d mortality, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.679</td>
<td>0.175</td>
</tr>
<tr>
<td>Lead V3 ST level of ≤−2 mm</td>
<td>Patients, n</td>
<td>1904</td>
<td>332</td>
<td>223</td>
<td>9.0</td>
<td>8.7</td>
</tr>
<tr>
<td>30-d mortality, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.885</td>
<td>0.146</td>
</tr>
<tr>
<td>V3 ST level ≤−1 mm</td>
<td>Patients, n</td>
<td>2948</td>
<td>839</td>
<td>507</td>
<td>7.9</td>
<td>6.8</td>
</tr>
<tr>
<td>30-d mortality, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.338</td>
<td>0.048</td>
</tr>
<tr>
<td>P for V3 ST level ≤−1 mm vs no V3 ST depression</td>
<td>0.201</td>
<td>0.014</td>
<td>0.030</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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 Interlateral ST Elevation*</th>
<th>Adjusted for Interlateral ST Elevation and Clinical Factors†</th>
<th>Unadjusted</th>
<th>Adjusted for Interlateral ST Elevation*</th>
<th>Adjusted for Interlateral 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 (0.96–1.5)</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 (0.85–1.13)</td>
<td>0.96 (0.82–1.12)</td>
</tr>
<tr>
<td>All patients with inferior infarction</td>
<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>
</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.
*Interlateral 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 was 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 V5 ST level (Tables 2 and 3), and the prognostic effect of V1 ST elevation was analyzed with V5 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 V5 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 therapy2,17,18 and in patients having primary percutaneous coronary intervention.19 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
ventricular infarction. Similarly, ST elevation in leads V2 through V3 adds significantly to precordial ST depression in aiding the diagnosis of posterolateral AMI. However, recording leads V4R and V5 through V6 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 V4R 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 V3 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 level. 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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10. Hirulog and Early Reperfusion or Occlusion (HERO)-2 Trial Investigators. Thrombin-specific anticoagulation with bivalirudin versus heparin.


**CLINICAL PERSPECTIVE**

The standard 12-lead ECG is a cornerstone in the diagnosis and stratification of patients with ST-elevation acute myocardial infarction. Concomitant right ventricular infarction (often manifested with V1 ST elevation) or posterolateral infarction (often manifested with V1 ST depression) can be associated with worse prognosis of patients with acute inferior myocardial infarction. In this study of 7967 patients with acute inferior myocardial infarction from the Hirulog and Early Reperfusion or Occlusion-2 (HERO-2) trial, ST elevation in V1 at baseline had incremental adverse prognostic significance that was independent of the adverse effect of any precordial V5 ST depression. Thirty-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 ≥1.5 mm; P for trend <0.0001). Each 0.5-mm-step increase in ST level above the isoelectric level was associated with ≈25% increase in 30-day mortality before and after adjustments. 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, 1.18 to 1.92) adjusted for V5 ST level, and 1.35 (95% confidence interval, 1.04 to 1.76) adjusted for ECG and clinical factors. Resolution of V1 ST elevation after fibrinolytic therapy was associated with lower 30-day mortality (5.5% versus 10.8%; P = 0.0012), lending further support to the independent prognostic value of this simple ECG parameter. Standard 12-lead ECGs are increasingly being performed before hospitalization to enable shorter times to fibrinolysis or to percutaneous coronary intervention. This study supports use of information from readily available V1 recordings in aiding risk stratification and prognostication.

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Prognostic Value of Lead V₁ ST Elevation During Acute Inferior Myocardial Infarction
Cheuk-Kit Wong, Wanzhen Gao, Ralph A. Stewart, John K. French, Philip E. Aylward, Jocelyne Benatar and Harvey D. White
on behalf of the Hirulog and Early Reperfusion or Occlusion-2 (HERO-2) Investigators

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