Frequency, characteristics, and clinical significance of transient ST segment elevation in patients with acute coronary syndromes

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Background  Prior investigations of transient myocardial ischaemia have focused on ST depression events. Therefore, the purpose of this analysis was to determine the frequency, characteristics, and clinical significance of transient ST segment elevation in patients with acute coronary syndromes.

Methods  A secondary analysis from two prospective studies utilizing 12-lead ST segment monitoring was used to compare ST elevation vs ST depression events.

Results  Of 868 patients, 177 (20%) had 574 events (242, ST elevation; 332, ST depression). Patients with ST elevation were more likely to have single vessel coronary artery disease, whereas patients with ST depression were more likely to have triple vessel coronary artery disease. ST elevation events were of shorter duration, more often associated with chest pain, and had greater ST changes than ST depression events. There was no difference in clinical outcome between patients with ST elevation vs depression; however, those with ST events were more likely to have adverse hospital outcomes (OR, 3·67) or death (OR, 2·03) than patients without ST events. After controlling for clinical prognostic factors, transient ST events observed with continuous ST monitoring predicted hospital death independently from signs of ischaemia on the initial standard 12-lead ECG.

Conclusions  Transient ST elevation is nearly as prevalent as transient ST depression in patients with acute coronary syndromes. Since the vast majority of ST events are brief and otherwise clinically silent, ST segment monitoring is more efficacious in detecting ischaemic events and in predicting adverse clinical outcomes than patients’ symptoms or the initial standard 12-lead ECG.


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Key Words: Electrocardiogram, ST segments, myocardial ischaemia, myocardial infarction, physiological monitoring, coronary heart disease.

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Introduction

Acute ST segment elevation is generally understood to indicate a primary reduction in coronary blood flow producing severe myocardial ischaemia that is typically associated with chest pain. Although ST elevation is known to occur transiently in vasospastic, or ‘variant’ angina[1], and, on rare occasions, during exercise testing[2], it is more commonly encountered as the more persistent ‘injury’ pattern associated with evolving acute myocardial infarction. However, in the recently published guidelines for the management of acute coronary syndromes without persistent ST segment elevation, experts agreed that transient ST elevation does occur in patients with acute coronary syndromes apart from a vasospastic mechanism[3]. These experts propose that the underlying pathophysiology of transient ST segment elevation in acute coronary syndromes is related to platelet aggregation and subsequent mural thrombus formation which can lead to transient complete coronary occlusion.

While undertaking a study to determine the value of continuous 12-lead ST segment monitoring of patients hospitalized with acute coronary syndromes, we were impressed by how often we were seeing brief episodes of major ST segment elevation (Fig. 1). Therefore, the purpose of this analysis was to determine: (1) how often...
transient ST elevation events occur in this population, (2) how ST elevation events compare to ST depression events in terms of (a) changes in heart rate, (b) duration, (c) chest pain, (d) magnitude of ST deviations, (e) time of day, (f) clinical outcome, and (3) whether ST events observed with continuous ST segment monitoring adds additional prognostic information above and beyond the initial standard 12-lead ECG.

**Methods**

**Sample and setting**

A secondary analysis was conducted on data from two prospective clinical trials conducted at the University of California, San Francisco Medical Center: (1) the ST Analysis Trial (STAT) study and, (2) the ST Analysis and Monitoring of Patients and Evaluation of a Derived Electrocardiogram (STAMPEDE) study. Patients enrolled in these studies included those with acute myocardial infarction, unstable angina, and patients with more stable coronary artery disease admitted for diagnostic cardiac catheterization and possible percutaneous coronary intervention. As much as possible, all consenting, consecutive patients with acute coronary syndromes were enrolled over a 39-month period; however, there were short periods of no enrollment at holiday periods (about 2 weeks/year) when the research nurses were unavailable. Because the aims of the parent studies were to evaluate various multi-lead ECG configurations to detect acute ischaemia, specially-trained research nurses were required to initiate and maintain 12-lead ST monitoring in all patients to ensure accurate lead placement and uninterrupted monitoring. In the STAT study (1993–1996), ST monitoring was initiated upon the patient’s admission to the coronary care unit and was maintained in the cardiac catheterization laboratory during catheter-based interventions. In the STAMPEDE study (1996–1999), ST monitoring was initiated in the emergency department and continued in the cardiac catheterization laboratory, coronary care unit, and 'step-down' telemetry unit.

**ST segment monitoring**

In both studies, continuous 12-lead ST segment monitoring was performed with Mortara ELI 100 STM monitors (Milwaukee, WI, U.S.A.). The Mortara ST monitor is a portable, programmable, microprocessor-based device that samples electrical potentials from all 12 ECG leads at 4 ms intervals over a 10 s period to identify a noise-free median beat from which ST segment deviation relative to the PR segment is measured. The monitor stores all ECGs with a change of ST amplitude of ≥50 μV in one lead. In addition, the monitor was programmed to automatically store an ECG every 1 min in the emergency department, every 20 s in the cardiac catheterization laboratory, and every 10 min in the coronary care unit and telemetry unit.

At the end of the monitoring period, all stored ECGs were down-loaded to the Mortara ST Review Station for off-line analysis of ST segment trends and amplitudes. The investigators who analysed the ST data were blinded from patients’ clinical information and outcomes. The Review Station also allowed for printing any of the stored 12-lead ECGs in the standard format for confirmation of ischaemic events by the investigators. When a potential ischaemic event was identified on the ST graphic trend, three 12-lead ECGs were printed out: (1) a baseline ECG obtained prior to the ST changes, (2) an ‘event’ ECG obtained during the ST changes, and (3) a return to baseline ECG obtained after the event.
Diagnosis of transient myocardial ischaemia

A transient ischaemic event was defined as a change in the ST segment level from baseline to event (delta, or ΔST) of ≥200 μV in ≥1 lead or ≥100 μV in ≥2 leads lasting at least 1 min but less than 120 min. ST amplitudes were measured at J+80 ms (STAT study) or J+60 ms (STAMPEDE study). Because spontaneous transient myocardial ischaemia was the event of interest in this analysis, the initial ST deviation observed in acute myocardial infarction patients was not counted as an event. Only if acute myocardial infarction patients had recurrent ST events were they counted as having transient myocardial ischaemia. The time period for the initial ST deviation was defined for each myocardial infarction patient by observing the point at which ST segments returned to a normal or near-normal steady state on the graphic ST segment trend.

Analysis of initial standard 12-lead ECG

The initial ECG was defined as the first standard 12-lead ECG recording taken in the hospital and almost all of them were recorded in the emergency department with Marquette MAC 15 ECG machines (GE Medical Systems, Milwaukee, WI, U.S.A.). Criteria used for analysis of initial ECGs were those recently defined by the European Society of Cardiology and American College of Cardiology Committee for the redefinition of myocardial infarction[6]. Using these criteria, the initial ECG was rated as showing evidence of ischaemia if any of the following were present: (1) ST segment elevation at the J point in two or more contiguous leads with the cut-off points of ≥0·2 mV in leads V1, V2, or V3 and ≥0·1 mV in other leads (contiguity in the frontal plane was defined as the lead sequence aVL, I, inverted aVR, II, aVF, III); (2) new or presumed new ST segment depression in two or more contiguous leads, or (3) new or presumed new T wave inversion ≥1 mm in two or more contiguous leads. If there was no previous ECG available for comparison, the ST/T wave abnormalities were presumed to be new and the ECG was rated as showing evidence of acute ischaemia.

Statistical analysis

ST elevation vs ST depression events were compared using independent t-tests for quantitative variables (e.g. event duration), and chi-square tests for categorical variables (e.g. pain). Chi-square analysis was used to test for differences in outcomes in three subgroups: (1) patients with ST elevation events, (2) patients with ST depression events, and (3) patients with no ST events. Patients who had both ST elevation and depression events were eliminated from this analysis because there were too few patients in this group to have adequate statistical power to detect differences in outcomes between the groups.

A Norris Coronary Prognostic Index score[7] was calculated for each patient. The Norris coronary prognostic value combines readily available clinical data including age, X-ray evidence of heart failure, and history of prior myocardial infarction into a score which has been shown to predict adverse outcomes in patients with acute coronary syndromes. To determine whether ST events observed with continuous ST segment monitoring predicted adverse coronary events independently from the initial standard 12-lead ECG or other clinical variables, multiple logistic regression analyses were performed, entering three predictor variables: (1) Norris coronary prognostic value, (2) presence/absence of ischaemia on the initial standard 12-lead ECG, and (3) presence/absence of ST events during ST monitoring.

Results

Sample characteristics

A total of 1165 patients underwent 12-lead ST segment monitoring. Of these, 155 were excluded from the analysis because they were discharged from the emergency department or hospital with a non-cardiac diagnosis. An additional 142 patients were excluded because they had been enrolled in the study previously. Thus, a total of 868 patients hospitalized with acute coronary syndromes were included in the analysis; 517 who had a final diagnosis of stable/unstable angina (60%), and 351 with acute myocardial infarction (40%).

Sample characteristics included a mean age of 67 years (±13 years; range 28 to 97 years), 65% male, and ethnicity reflective of the demographics of San Francisco (Hispanic, 9%; African American, 9%; Asian, 18%; Caucasian, 63%; and Native American, 1%). Mean ST segment monitoring time was not different between patients with ST elevation events compared to patients with ST depression events (59 vs 58 h, P=ns).

Frequency and comparison of ST elevation vs ST depression events

Of the 868 patients, 177 (20%) had a total of 574 ST events (Fig. 2). The breakdown of events were as follows: ST elevation events, 79 patients with 200 events; ST depression events, 87 patients with 301 events; and both ST elevation and depression events, 11 patients with 73 events (42, ST elevation; 31, ST depression). Seven patients who had ‘fixed’ ST depression due to a left ventricular hypertrophy ‘strain’ pattern or bundle branch block exhibited a total of 11 events in which the ST level shifted in a positive direction of ≥200 μV in one lead or ≥100 μV in two leads but the final ST level did not exceed +100 μV. These ST events were considered pseudo-normalization of the ST/T wave, and were counted as ST elevation events[8].
Compared to ST depression events, ST elevation events were of shorter duration (30 vs 36 min) and more often associated with chest pain (29% vs 19%); however, the majority of both types of ST events were silent (Table 1). ST elevation events also had greater ST segment changes than ST depression events (average maximal lead $\Delta ST$ with ST elevation = 250 $\mu$V vs 194 $\mu$V with ST depression). Likewise, the sum of $\Delta ST$ values across the 12 leads was greater in ST elevation events (mean, 843 $\mu$V) than in ST depression events (mean, 567 $\mu$V). Neither ST elevation nor ST depression events were associated with an increase in heart rate nor morning hour occurrence.

**Clinical significance of ST elevation vs ST depression events**

The group with transient ST elevation did not differ from the group with transient ST depression on a number of factors predictive of patient outcome including age, female sex, coronary risk factors, prior myocardial infarction, acute myocardial infarction diagnosis, or the Norris coronary prognostic value (Table 2). However, the two groups differed in terms of angiographic evidence of coronary artery disease in that patients with transient ST elevation were more likely to have single vessel disease whereas patients with transient ST depression were more likely to have triple vessel coronary artery disease. For example, the proportions of patients with single vessel coronary artery disease were 46% in the ST elevation group compared to 22% in the ST depression group ($P<0.001$). The proportions of patients with triple vessel coronary artery disease were 31% in the ST elevation group compared to 56% in the ST depression group ($P<0.001$).

Adverse clinical outcomes were defined as the development of cardiogenic shock, acute pulmonary oedema, acute myocardial infarction after hospitalization, or death. There were no differences in the incidence of adverse outcomes in patients with ST elevation vs ST depression events (44% vs 38%; $P=ns$) (Fig. 3). However, both ST event groups had more adverse outcomes compared to the group without events ($P<0.0001$).

**Initial standard 12-lead ECG**

Of the total of 868 patients, 296 (34%) had evidence of acute ischaemia on their initial standard 12-lead ECG (137 with ST elevation; 159 with ST depression and/or T wave inversion). The breakdown of the remaining 572 patients (66%) whose ECGs were classified as ‘non-ischaemic/non-diagnostic’ were as follows: (1) 160 patients (18%) had ST/T wave abnormalities secondary to left ventricular hypertrophy, bundle branch block, or

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**Figure 2** Summary of ST events in the sample.

**Table 1** Comparison of ST elevation vs ST depression events

<table>
<thead>
<tr>
<th>ST direction</th>
<th>Patients (%)</th>
<th>Events (%)</th>
<th>Duration (mean)</th>
<th>Pain Max $\Delta ST$ (mean)</th>
<th>12-lead sum $\Delta ST$ (mean)</th>
<th>Heart rate ↑ (&gt;10 beats . min$^{-1}$)</th>
<th>Morning hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>ST ↑ events</td>
<td>79 (45%)</td>
<td>200 (35%)</td>
<td>30 min</td>
<td>29%</td>
<td>843 $\mu$V</td>
<td>38%</td>
<td>29%</td>
</tr>
<tr>
<td>ST ↓ events</td>
<td>87 (49%)</td>
<td>301 (52%)</td>
<td>36 min</td>
<td>19%</td>
<td>567 $\mu$V</td>
<td>40%</td>
<td>27%</td>
</tr>
<tr>
<td>$P$ value</td>
<td></td>
<td></td>
<td>0.0019</td>
<td>0.0000</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Max $\Delta ST$ = measured in the ECG lead showing maximal ST deviation; sum $\Delta ST$ = sum of the absolute $\Delta ST$s across 12 ECG leads.
Table 2  Comparison of patients with ST elevation vs ST depression events

<table>
<thead>
<tr>
<th></th>
<th>ST ↑ &lt;br&gt;n=79</th>
<th>ST ↓ &lt;br&gt;n=87</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years, mean)</td>
<td>67 ± 13</td>
<td>70 ± 13</td>
<td>ns</td>
</tr>
<tr>
<td>Female sex</td>
<td>23 (29%)</td>
<td>28 (32%)</td>
<td>ns</td>
</tr>
<tr>
<td>Hypertension</td>
<td>50 (63%)</td>
<td>64 (74%)</td>
<td>ns</td>
</tr>
<tr>
<td>Diabetes</td>
<td>22 (28%)</td>
<td>22 (25%)</td>
<td>ns</td>
</tr>
<tr>
<td>Smoker</td>
<td>25 (32%)</td>
<td>19 (22%)</td>
<td>ns</td>
</tr>
<tr>
<td>Prior MI</td>
<td>35 (44%)</td>
<td>41 (47%)</td>
<td>ns</td>
</tr>
<tr>
<td>Acute MI</td>
<td>52 (66%)</td>
<td>49 (56%)</td>
<td>ns</td>
</tr>
<tr>
<td>Norris CPI (mean)</td>
<td>6.6</td>
<td>7.2</td>
<td>ns</td>
</tr>
<tr>
<td>Single vessel CAD</td>
<td>46%</td>
<td>22%</td>
<td>0·0007</td>
</tr>
<tr>
<td>Triple vessel CAD</td>
<td>31%</td>
<td>56%</td>
<td>0·0007</td>
</tr>
</tbody>
</table>

Note: This analysis excludes the 11 patients who had both ST elevation and depression events.
Norris Coronary Prognostic Index=sco rated system that combines age, X-ray evidence of heart failure and prior infarction to predict adverse outcomes in acute coronary syndromes. The higher the score, the worse the prognosis.
MI=myocardial infarction; CAD=coronary artery disease; cardiac catheterization diagnosis of ≥70% stenosis in ≥1 vessel(s).

![Proportion of patients with an adverse hospital outcome in the ST elevation, ST depression, and no ST event groups. Analysis excludes 11 patients with both ST↑ and ST↓. Adverse outcome=shock, pulmonary oedema, myocardial infarction after admission, death.](image)

![Prognostic value of ST monitoring vs initial standard 12-lead ECG](image)

The total number of hospital deaths in the group as a whole was 44 (5%). Mortality was not statistically different between patients with transient ST elevation vs ST depression. Multiple logistic regression analyses revealed that ST events observed with continuous ST segment monitoring provided prognostic information independent from the Norris coronary prognostic value score or the initial standard 12-lead ECG (Table 3). Patients with one or more ST events with ST segment monitoring were 3·67 times more likely to suffer an adverse hospital outcome, 2·83 times more likely to die or develop an acute myocardial infarction after admission and, 2·03 times more likely to die in the hospital.

**Discussion**

In this study, transient ST segment elevation occurred almost as frequently as transient ST depression in

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Table 3  Multiple logistic regression analyses on predictors of adverse outcomes in acute coronary syndromes (n=868)

<table>
<thead>
<tr>
<th>Predictor variables</th>
<th>$P$ value</th>
<th>Odds ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dependent variable — adverse hospital outcome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Norris CPI Score</td>
<td>0.000</td>
<td>1.18</td>
<td>1.12–1.24</td>
</tr>
<tr>
<td>Acute ischaemia on initial 12-lead ECG</td>
<td>0.000</td>
<td>1.90</td>
<td>1.31–2.77</td>
</tr>
<tr>
<td>ST event with ST segment monitoring</td>
<td>0.000</td>
<td>3.67</td>
<td>2.47–5.44</td>
</tr>
<tr>
<td>Dependent variable — MI after admission or hospital death</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Norris CPI Score</td>
<td>0.000</td>
<td>1.17</td>
<td>1.09–1.24</td>
</tr>
<tr>
<td>Acute ischaemia on initial 12-lead ECG</td>
<td>NS</td>
<td>1.55</td>
<td>0.95–2.53</td>
</tr>
<tr>
<td>ST event with ST segment monitoring</td>
<td>0.000</td>
<td>2.83</td>
<td>1.72–4.68</td>
</tr>
<tr>
<td>Dependent variable — hospital death</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Norris CPI Score</td>
<td>0.000</td>
<td>1.26</td>
<td>1.16–1.37</td>
</tr>
<tr>
<td>Acute ischaemia on initial 12-lead ECG</td>
<td>0.009</td>
<td>2.45</td>
<td>1.26–4.79</td>
</tr>
<tr>
<td>ST event with ST segment monitoring</td>
<td>0.039</td>
<td>2.03</td>
<td>1.04–3.97</td>
</tr>
</tbody>
</table>

MI=myocardial infarction.
Adverse outcome=cardiogenic shock, pulmonary oedema, myocardial infarction after admission, or death.

Many of our patients were hospitalized with acute coronary syndromes. In contrast to ST depression events, ST elevation events were of shorter duration, had greater ST amplitude changes, and were often associated with chest pain. Nonetheless, a major proportion (71%) of ST elevation events were also asymptomatic.

In contrast to the findings of Araki et al., who observed that transient ST elevation in patients with variant angina frequently occurred in the morning hours, there were no diurnal trends observed in our patients with ST elevation events. This lack of similarity to variant angina provides evidence that the mechanism of transient ST elevation in patients with acute coronary syndromes may not include a major vasospastic component.

Our observations are different from multiple investigations of patients with stable coronary artery disease using Holter monitor techniques, indicating that transient ST shifts are due to an increase in myocardial oxygen demand, as evidenced by an increased heart rate prior to an event. Rather, our findings are more similar to those of MacDonald et al., who found that both transient ST elevation and depression could be due to a primary reduction of blood supply, with collateral flow being an important determinant of the direction of ST deviation. Using the angioplasty balloon inflation model of acute coronary occlusion, MacDonald et al., showed that patients with ST depression had more extensive coronary artery disease and a greater prevalence of visible collateral vessels compared to patients with ST elevation. Of importance in MacDonald’s investigation, objective measures were used to determine the presence/absence of collateral circulation. MacDonald found less evidence of collateral circulation in patients with ST elevation compared to patients with ST depression including lower distal coronary pressure, lower great cardiac vein flow, and higher calculated coronary collateral resistance.

Most of our patients were on bed rest during ST monitoring and were treated with beta-blockers, resulting in heart rates in the 50–60 beats·min$^{-1}$ range. Moreover, we observed little difference in heart rate in most patients, whether they had an ST elevation or an ST depression event. Thus, it is reasonable to hypothesize that the mechanism of transient ischaemia in many of our patients may have been a primary reduction in coronary flow, rather than an increase in myocardial oxygen demand. In theory, such an hypothesis is plausible because patients with acute coronary syndromes presumably have disruption of an atherosclerotic plaque which would be expected to cause ‘supply-related’ rather than ‘demand-related’ ischaemia. In addition, the direction of ST deviation in our patients may have been related to the presence of collateral flow. Absence of collateral flow would be expected to cause more severe ischaemia, and we did observe greater ST deviation amplitudes in our patients with ST elevation, compared to our patients with ST depression. In contrast to patients with transient ST elevation, our patients with ST depression had more extensive coronary artery disease and lower ST deviation amplitudes during transient myocardial ischaemia, suggesting the presence of functional collateral circulation. Such an hypothesis is also in agreement with the findings of Guazzi et al., that the dynamic impairment in left and right heart haemodynamics during spontaneous angina is more severe in patients with ST elevation than in patients with ST depression.

Our findings are in agreement with multiple investigations that have linked transient ischaemia during ST monitoring to adverse outcomes in patients with acute coronary syndromes. Compared to patients without transient myocardial ischaemia, our patients who had one or more ST events were 3·67 times more likely to experience an adverse hospital outcome and 2·03 times more likely to die in the hospital, even after controlling for high risk clinical variables such as advanced age, prior myocardial infarction, and X-ray evidence of heart failure.

To our knowledge, this is the first study to report that the observation of ST events with continuous 12-lead ST
segment monitoring adds independent prognostic information above and beyond the initial standard 12-lead ECG in patients with acute coronary syndromes. Patel and co-workers\cite{16} reported that transient episodes of ST segment depression during 48 h of dual-lead Holter monitoring were a predictor of adverse hospital outcomes and had independent prognostic value beyond the clinical and ECG characteristics at presentation. However, a limitation of their study was that they included urgent revascularization, which is a subjective end point, in their definition of adverse hospital outcomes. In contrast to our findings, Patel et al.\cite{20}, did not report observing any transient ST elevation events; however, it is probable that the two ECG leads they used (lead locations were not reported) were less likely to show ST elevation, which is often localized to two to three leads, than the full 12-lead configuration used in our study.

We found that nearly one-half of the patients who had ST events with ST monitoring had no evidence of ischaemia in their initial 12-lead ECG. This is not surprising since ST segment changes are often dynamic in patients with acute coronary syndromes and a single ‘snap-shot’ ECG, which depicts a brief 10 s of ECG information, may not capture such dynamic ST changes, especially if the patient is asymptomatic at the time of the recording. According to the task force for the management of acute coronary syndromes without persistent ST segment elevation\cite{3}, the standard ECG at rest does not adequately reflect the dynamic nature of coronary thrombosis and myocardial ischaemia in acute coronary syndromes. Furthermore, these experts state that Holter monitoring of the ST segment is also insufficient because it is limited to two to three monitored leads and off-line analysis, providing the results several hours or days after the recording. The findings of our study support the task force’s recommendation to establish real-time multi-lead ST segment monitoring in order to detect recurrent ST episodes, the majority of which are otherwise clinically silent. However, future studies are needed to determine whether clinical decision-making regarding more aggressive pharmacological regimens or early angiography and revascularization based upon ST segment monitoring data results in better patient outcomes than a symptom-based approach.

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References


