Prognostic value of maximum ST-vector magnitude during the first 24 h of vectorcardiographic monitoring in patients with unstable angina pectoris

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Aims To assess the prognostic importance of alternate ways of quantifying myocardial ischaemia by continuous ST analysis, the maximum ST vector magnitude and the area under the ST vector magnitude trend curve during the first 24 h of continuous ST monitoring.

Methods and Results During a 22-month period from 1991 to 1993, 195 patients admitted to our CCU with suspected unstable angina pectoris, were included in the study. During the first 24 h the patients were monitored for ischaemic episodes with computerized vectorcardiography, using a MIDA 1000 system. Twenty seven (14%) of the 195 patients died or had a non-fatal myocardial infarction within 1 year and the maximum ST vector magnitude among those patients was, on average, 201 \( \mu V \) compared with 118 \( \mu V \) in patients who survived 1 year free of myocardial infarction (\( P<0.01 \)). The area under the ST vector magnitude trend curve was, on average, 1598 \( \mu Vmin \) compared with 164 \( \mu Vmin \) (\( P<0.01 \)). By multivariate analysis, the maximum ST vector magnitude emerged as a superior predictor of death or myocardial infarction, compared with the area under the ST vector magnitude trend curve and the number of ST vector magnitude and ST change vector magnitude episodes. The maximum ST vector magnitude and age were independent predictors of death or non-fatal myocardial infarction within 1 year.

Conclusion Maximum ST vector magnitude during the first 24 h of vectorcardiographic monitoring seems to be a strong predictor of subsequent death or non-fatal myocardial infarction.

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Key Words: Unstable angina pectoris, prognosis, vectorcardiography.

Introduction

Patients with unstable angina pectoris run a high risk for subsequent death or non-fatal myocardial infarction. Patients with medically or surgically treated unstable angina suffer a 3% to 5% in-hospital mortality and up to 10% mortality within 2 years and the risk for non-fatal myocardial infarction is about 10% within the first 2 weeks and about 12% within 2 years\(^4-3\). In more recent studies where heparin treatment has been introduced among patients with unstable angina or non-Q wave myocardial infarction, the rate of death or myocardial infarction at 2 weeks is 5% to 6% and at 5 months about 15%\(^4-5\). Different indicators for identifying patients at high risk have been described. Clinical risk evaluation\(^6-7,8-10\), admission ECG\(^11,12\) and predischarge exercise test\(^10,11,13\) have limited prognostic value. Recently, promising results have been demonstrated from biochemical markers (i.e. creatine kinase-MB, Troponin T and Troponin I)\(^14-17\). The value of transient ischaemic episodes found on Holter monitoring in patients with unstable angina pectoris, or non-Q wave infarction, is documented in numerous previous reports. Ischaemic episodes are detected as transient ST-segment elevations or depressions, or T-wave alterations regardless of accompanying symptoms. The presence of ischaemic episodes on Holter is a strong indicator of adverse outcome in the short- as well as in the long-term\(^18-24\). Furthermore, it is documented that Holter monitoring is superior to clinical characteristics, admission ECG and predischarge exercise test in identifying patients at high risk of subsequently dying, or developing a non-fatal myocardial infarction after an episode of unstable angina or a non-Q wave myocardial infarction\(^18-21\).
Andersen *et al.* found that the presence of at least one episode of ST change during the first 24 h of vectorcardiographic ST monitoring was a strong predictor of death or non-fatal myocardial infarction within 1 year. It was superior to clinical risk evaluation, ST depression on admission ECG, predischarge exercise test and creatine kinase-MB elevation[32]. In addition to its major advantage of providing on-line prognostic information, vectorcardiography may possibly be more sensitive than Holter monitoring in detecting high risk patients[30].

Previous reports on the prognostic value of ST-segment monitoring in unstable coronary syndromes have focused on the number and duration of ischaemic episodes in the acute phase. However, less attention has been paid to the degree of ST-segment deviation. Studies of patients with ST elevation and Q wave infarction indicate that considerable ST-segment deviation on the admission ECG is associated with a worse outcome[27–30]. A correlation between the magnitude of ST-segment deviation and the amount of myocardium at risk has been demonstrated in an animal experiment model[31]. In man, however, no such correlation is proven, but rather a correlation between the magnitude of ST-segment changes and the severity of ischaemia[32]. On the other hand, the role that quantified ischaemia plays over time, in the prediction of adverse outcome in patients with unstable angina is demonstrated in previous Holter studies. The longer the duration of ischaemia during the initial 24–48 h after hospitalization for unstable angina detected on Holter, the higher the incidence of cardiac morbidity and mortality in the short- as well as the long-term[33,34].

The aim of the present study was to assess whether the risk of subsequent death or non-fatal myocardial infarction, after an episode of unstable angina pectoris or a non-Q wave myocardial infarction, was associated with the peak magnitude of the ST change or to the accumulated ischaemia over time, measured as the area under the ST trend curve during the first 24 h of continuous on-line vectorcardiographic monitoring.

### Methods

The study was performed over a 22 month period during 1991 to 1993, and patients admitted to the coronary care unit of Östra Hospital with suspected unstable angina pectoris were included. The patients should have had at least one episode of chest pain within the last 24 h and at least one of the following criteria: (1) new effort-related chest pain of increasing severity within the last 6 weeks, (2) a clear worsening of a previously stable pattern of angina pectoris, or (3) chest pain at rest or at minimal effort. Patients were excluded if there was a strong suspicion of ongoing myocardial infarction, pacemaker or a complete bundle branch block, or if the patient had previously been included. Informed consent was obtained from all patients. Every 6 h for 48 h creatine kinase-MB mass (Boeringer Mannheim, Germany) was measured. An exercise test was performed before discharge from hospital in all capable patients.

During the first 24 h the patients were monitored with computerized on-line vectorcardiography, using a MIDA 1000 system (Oritius Medical, Täby, Sweden). The technique of continuous computerized vectorcardiographic monitoring has been described previously[35]. Using the Frank lead system[36] via eight body surface electrodes, electrocardiographic signals from three orthogonal leads (X, Y and Z) were collected. The QRS vector difference was defined as the difference of the area of the current QRS complex and the reference complex (QRS-vd=√(areaX+areaY+areaZ)). The ST vector magnitude was defined as the sum of the ST-segment deviation 20 ms after the J-point (ST-vector magnitude=√(X^2+Y^2+Z^2)). The ST change vector magnitude represented the ST vector change from the reference ST vector. The averaging period was 30 s. An ST vector magnitude or ST change vector magnitude increase of at least 50 μV from the baseline for at least 1 min was considered an ischaemic episode. The maximum ST vector magnitude was defined at the peak level of ST vector magnitude during the 24 h registration, and the area under the ST vector magnitude trend curve was defined as the accumulated area between curve and baseline during ischaemic episodes. All vectorcardiographic registrations were analysed by two independent observers, blinded to clinical data and outcome, and whenever there were different opinions, the definite interpretation was made in consensus.

The patients were followed-up for 1 year regarding revascularizing procedures, occurrence of myocardial infarction, hospitalization for unstable angina and death. No patient was lost from follow-up. The primary end-point was death or myocardial infarction within 1 year; however, follow-up was terminated in cases of revascularization after discharge. The index event leading to inclusion in the study was not used as an end-point. The diagnosis of myocardial infarction was based upon an increase in cardiac enzymes (creatine kinase-MB mass >15 μg·l⁻¹) on two separate occasions, and on at least one of the following: (1) typical chest pain of at least 15 min duration or (2) typical ECG changes with transient ST elevation in at least two leads (at least 0·1 mV in limb leads and 0·2 mV in precordial leads) or evolution of a significant Q wave (duration >0·04 s and amplitude >25% of the R wave).

Coronary angiography in hospital or during follow-up was performed in 73 patients, and the angiograms were examined by a specially trained cardiologist who was blinded to all other information concerning each patient. Decisions for revascularization were made in consensus by the responsible cardiologist, a surgeon and a cardiologist with special training in transluminal coronary angioplasty. Forty-five patients (23%) underwent a revascularization procedure after discharge and before reaching the end-point of myocardial infarction or death, follow-up was terminated among these patients. The vectorcardiographic pattern was not used for making the decision whether or not a patient should...
undergo a coronary angiogram or a revascularization procedure. These decisions were based on symptoms and other clinical data.

Statistics

For the statistical analyses we used SPSS software\textsuperscript{37}. The prognostic value of demographic data, previous morbidity, biochemical markers and exercise test were invested univariately using the log rank test for proportions and the Mann–Whitney U test for comparing means. The vectorcardiographic parameters' number of ST vector magnitude episodes or the maximum ST vector magnitude level and the area under the ST vector magnitude trend curve, were analysed univariately by the Mann–Whitney U test, and a separate Cox’ backward conditional test was used to compare them with each other. The vectorcardiographic parameter which was most important for outcome was compared with the demographics, previous morbidity, and biochemical and exercise test data that were significant in the univariate analysis using a Cox’ backward conditional analysis. When revascularization procedures and readmission for unstable angina pectoris were added to the combined end-point of death and myocardial infarction, a backward conditional logistic regression model was used. A receiver operating curve was employed in order to find an optimal cut-off value for the ST vector magnitude maximum; specificity and sensitivity were considered equally important.

Results

One hundred and ninety-five patients were included. The overall results have been described by Andersen et al.\textsuperscript{38} At discharge, 99 patients were diagnosed as having unstable angina, 29 chest pain, 25 non-Q wave infarction, 19 angina pectoris, 14 Q wave infarction and 10 other diagnoses. Seventy-three patients underwent coronary angiography and 41 of these patients had three vessel disease, 16 two-vessel disease, 10 one-vessel disease and six no significant coronary stenoses. No correlation between angiographic findings and the number of ST vector magnitude episodes or the maximum ST vector magnitude level was found among these patients. Forty-five patients underwent revascularization procedures after discharge and their follow-up was therefore terminated. Twenty-seven patients (13.8%) died or had a non-fatal myocardial infarction within 1 year. Among demographic data, only female sex and age indicated an increased risk for subsequent death or myocardial infarction. Hypertension, prior revascularization, diabetes mellitus, a history of angina pectoris or prior myocardial infarctions were not associated with a higher risk of death or non-fatal myocardial infarction.

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The previously documented vectorcardiographic parameters, number of ST vector magnitude episodes and ST change vector magnitude episodes, as well as the maximum ST vector magnitude level and the area under the ST vector magnitude trend curve, ST depression on the admission electrocardiogram, creatine kinase-MB maximum, and inability to perform an exercise test all indicated an increased risk of subsequent death or myocardial infarction within 1 year (Table 1).

### Table 3 Vectorcardiographic risk indicators by multivariate analysis (Cox’ backward conditional test)

<table>
<thead>
<tr>
<th>Risk Indicator</th>
<th>Relative Risk</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>ST-VM maximum (risk per 10 μV increase)</td>
<td>1.059</td>
<td>1.035–1.086</td>
</tr>
<tr>
<td>ST-VM episodes (risk per one episode)</td>
<td>1.015</td>
<td>0.93–1.11</td>
</tr>
<tr>
<td>STC-VM episodes (risk per one episode)</td>
<td>0.99</td>
<td>0.95–1.04</td>
</tr>
<tr>
<td>ST-VM area under the curve (risk per 10 μVmin increase)</td>
<td>0.999</td>
<td>0.998–1.0008</td>
</tr>
</tbody>
</table>

ST-VM=ST vector magnitude; STC-VM=ST change vector magnitude.

### Table 4 Multivariate analysis of risk markers and demographic data. Cox regression backward conditional

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Relative Risk</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (risk per 10 years increase)</td>
<td>1.91</td>
<td>1.23–2.97</td>
</tr>
<tr>
<td>Female sex</td>
<td>2.06</td>
<td>0.92–4.58</td>
</tr>
<tr>
<td>ST-VM maximum (risk per 10 μV increase)</td>
<td>1.05</td>
<td>1.03–1.08</td>
</tr>
<tr>
<td>≥1 mm ST depression on admission ECG</td>
<td>1.50</td>
<td>0.59–3.85</td>
</tr>
<tr>
<td>CK-MB max (risk per one μg/l increase)</td>
<td>0.9992</td>
<td>0.99–1.006</td>
</tr>
<tr>
<td>Exercise test not performed</td>
<td>1.06</td>
<td>0.39–2.92</td>
</tr>
</tbody>
</table>

MI=myocardial infarction; ST-VM=St vector magnitude; CK-MB max=creatinekinase myocardial/brain mass maximum concentration during 48 h serial measurements.

### Table 5 Patients with an infarct diagnosis are excluded. Risk factors and demographic data by Cox regression backward conditional test

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Relative Risk</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (risk per 10 year increase)</td>
<td>1.70</td>
<td>1.08–2.66</td>
</tr>
<tr>
<td>Female sex</td>
<td>1.35</td>
<td>0.53–3.44</td>
</tr>
<tr>
<td>ST-VM maximum (per 10 μV increase)</td>
<td>1.06</td>
<td>1.022–1.11</td>
</tr>
<tr>
<td>≥1 mm ST depression on admission ECG</td>
<td>0.58</td>
<td>0.12–2.93</td>
</tr>
<tr>
<td>CK-MB max (risk per one μg/l increase)</td>
<td>0.97</td>
<td>0.97–1.22</td>
</tr>
<tr>
<td>Exercise test not performed</td>
<td>1.66</td>
<td>0.56–4.92</td>
</tr>
</tbody>
</table>

MI=myocardial infarction; ST-VM=ST vector magnitude; CK-MB max=creatinekinase myocardial/brain mass maximum concentration during 48 h serial measurements.
infarction, all patients with a myocardial infarction were excluded in a second multivariate analysis. However, the ST vector magnitude maximum emerged as an independent predictor of death or non-fatal myocardial infarction within 1 year (Table 5).

Eighty-two patients (42%) reached the combined end-point of death, myocardial infarction, unstable angina or revascularization (PTCA or CABG) within 1 year. Only age and ST vector magnitude maximum were independent risk indicators for this combined end-point (Table 6). The risk of death or myocardial infarction within 1 year increased as levels of ST vector magnitude maximum increased and the increase was more pronounced in the highest quintile (Fig. 1). In order to find a cut-off value for the maximum ST vector magnitude level that would identify high and low risk patients, a receiver operating curve was employed. With a cut-off value of 144 μV the sensitivity for predicting death or myocardial infarction within 1 year was 59% and the specificity 80% (Fig. 2).

Patients with an ST vector magnitude ≥144 μV had a higher risk for death or non-fatal myocardial infarction within 1 year regardless of whether they had any ischaemic episodes, as previously described[26] (Fig. 3).

For further evaluation of the prognostic value of the area under the ST vector magnitude trend curve, a cut-off value was determined by a receiver operating curve. With a cut-off value of 162 μVmin the sensitivity for predicting death or myocardial infarction was 42% and the specificity 90% (Fig. 4).

Discussion

The present study aimed at looking beyond the mere detection of ischaemic episodes, by investigating other vectorcardiographic parameters. Based on previous documentation we focused on the maximum ST vector magnitude level and the area under the ST vector magnitude trend curve during ST monitoring.[31–34]

ST vector magnitude maximum

Previous studies on vectorcardiography and prognosis in patients with unstable angina or non-Q wave infarction have focused on the number of ST vector magnitude and

Table 6 Multivariate analysis of risk markers and demographic data. Logistic regression backward conditional

<table>
<thead>
<tr>
<th>Relative risk of death, MI, UAP or revascularization procedures within 1 year</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (risk per 10 year increase)</td>
<td>1·37</td>
</tr>
<tr>
<td>Female sex</td>
<td>0·84</td>
</tr>
<tr>
<td>ST-VM maximum (per 10 μV increase)</td>
<td>1·06</td>
</tr>
<tr>
<td>≥1 mm ST depression on admission ECG</td>
<td>1·49</td>
</tr>
<tr>
<td>CK-MB max (risk per one μg·L⁻¹ increase)</td>
<td>1·00</td>
</tr>
<tr>
<td>Exercise test not performed</td>
<td>1·03</td>
</tr>
</tbody>
</table>

MI=myocardial infarction; ST-VM=ST vector magnitude; CK-MB max=creatine kinase myocardial/brain mass maximum concentration during 48 h serial measurements. UAP=unstable angina pectoris.
results from our study indicate that the magnitude of ST changes carries important and independent prognostic information. The main result of the present study was that the maximum ST vector magnitude level during 24 h of vectorcardiographic monitoring was a stronger predictor of adverse long-term outcome than the previously documented vectorcardiographic risk indicators and that the ST vector magnitude maximum carries important independent prognostic information in addition to other clinical and demographic data (Tables 3–6).

Increasing levels of ST vector magnitude maximum were associated with an increasing risk of death or myocardial infarction at 1 year and the risk increased markedly in the quintile of patients with the highest ST vector magnitude levels (Fig. 1). Previously it was seen that at least one ST vector magnitude episode was the best cut-off value for separating high and low risk patients [25]. For the ST vector magnitude maximum the optimal cut-off value was 144 μV, provided that a high sensitivity and a high specificity were considered equally important (Fig. 2). Patients in our population who had ST vector magnitude episodes and patients who had high ST vector magnitude maximum levels were, to a large extent, overlapping, which explains why the previous variable did not have any predictive value, other than the latter in the multivariate analysis (Table 3). However, the patients who fulfilled the criteria of at least one ST vector magnitude episode, but did not reach the maximum ST vector magnitude of 144 μV (n=16) had a better outcome than the patients who had a ST vector magnitude maximum at least 144 μV (n=40). Thus it seems that small ST vector magnitude episodes do not indicate a
high risk of adverse outcome; however, high peak ST vector magnitude levels, even though not fulfilling the criteria of an ST vector magnitude episode, do. It is not clear from the present data in what way the ST vector magnitude maximum data should be interpreted best: as a cut-off value above which the risk increases markedly or as a discrete variable of which each step of increase corresponds to a proportional increase of risk? In a clinical setting our findings could suggest that the risk for death or myocardial infarction is predictable directly from the ST vector magnitude maximum value, as described by the example in Fig. 5, provided that they are reproducible in other populations.

Index infarction and ST vector magnitude maximum

Thirty-nine patients were discharged with a diagnosis of acute myocardial infarction, the majority as an index event. Thus the prognostic value of the maximum ST vector magnitude may reflect detection of index infarctions. Therefore, the value of maximum ST vector magnitude was assessed after excluding patients with a discharge diagnosis of acute myocardial infarction. The prognostic power of the ST vector magnitude maximum remained evident even after excluding patients with an index myocardial infarction (Table 4).

Area under the ST vector magnitude curve

The area under the ST vector magnitude trend curve may quantify accumulated ischaemia over time. In the TIBET trial, other methods for quantifying accumulated ischaemia were used[40]. In the present study, a larger area under the ST vector magnitude trend curve was associated with a higher risk for death or myocardial infarction during the follow-up period (Table 2). A cut-off value of 162 µVmin resulted in a 42% sensitivity and a 90% specificity. However, comparing the area under the ST vector magnitude trend curve directly to the maximum ST vector magnitude did not yield any independent prognostic value (Table 3).

Angiographic pattern

Whether the degree of ST-segment change reflects the extent of coronary artery disease is not clear. Severi et al. found that pathological outcome on exercise test and signs of ischaemia on the admission ECG were associated with a more severe degree of coronary artery disease on coronary angiograms in a population of patients with unstable angina pectoris[11]. In contrast, Langer et al. could not demonstrate that ischaemic episodes on Holter monitoring in the early post myocardial infarct phase were associated with a larger number of vessels with stenoses[39]. Only 73 patients in our study underwent coronary angiography, and in this highly selected subpopulation there was no linkage between the number of ST vector magnitude episodes or the ST vector magnitude maximum and the number of affected vessels.

Exercise test

Only 103 patients in the present study were considered to be able to perform an exercise test and it was
performed at the discretion of the responsible cardiologist. Therefore the outcome of an exercise test in this study is difficult to interpret. Inability to perform an exercise test was indicative of worse outcome; however, it did not add any prognostic information to that of continuous ST-segment monitoring (Tables 2 and 3).

Limitations

The present study is limited by the small number of patients investigated. Furthermore the study used two new concepts of continuous ST-segment monitoring for predicting outcome. The cut-off values for the ST vector magnitude maximum and the area under the ST-trend curve that was drawn from receiver operating curve curves in the present study must be validated in other populations.

Conclusion

In patients with unstable angina pectoris, the maximum ST vector magnitude during the first 24 h of ST-segment monitoring, which may reflect the amount of myocardium at risk or the severity of ischaemia, seems to be a strong indicator of risk for subsequent death or myocardial infarction. A larger area under the ST vector magnitude trend curve is associated with a higher risk of subsequent death or myocardial infarction; however, it did not add any prognostic information to that of the ST vector magnitude maximum. The prognostic importance of the maximum ST vector magnitude and the area under the ST vector magnitude trend curve need confirmation in prospective studies.

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References


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[37] SPSS Inc. NMA, Chicago, IL 60611.

