

ST-Segment Level and Slope in Exercise-Induced Myocardial Ischemia Evaluated With Body Surface Potential Mapping

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Body surface potential mapping (BSPM) is superior to 12-lead electrocardiography for detection of acute and old myocardial infarctions (MIs). We used BSPM to examine electrocardiographic criteria for acute reversible myocardial ischemia. BSPM with 123 channels was performed in 45 patients with coronary artery disease (CAD) and 25 healthy controls during supine bicycle exercise testing. Of the 45 patients, 18 patients had anterior, 14 had posterior, and 13 had inferior ischemia documented by coronary angiography and thallium scintigraphy. The ST amplitude was measured 60 ms after the J-point and the ST slope calculated by fitting a regression line from the J-point on to 60 ms after it. The optimal locations for detecting ST depression and ST-slope decrease were identified. In the pooled CAD patient group, the optimal location for ST depression was 5 cm below standard lead V₅ (CAD group: $-70 \pm 70 \mu\text{V}$; controls: $70 \pm 80 \mu\text{V}$, $p < 0.001$). Using a cut-off value of $-10 \mu\text{V}$, the ST depression separated the patients

with CAD from controls with a sensitivity of 84% and a specificity of 96%. The ST slope became more horizontal in the patient group than in the control group. The optimal location for ST-slope decrease was over the left side (CAD group: $20 \pm 20 \mu\text{V/s}$; controls: $720 \pm 320 \mu\text{V/s}$, $p < 0.001$). Using a cut-off value of $320 \mu\text{V/s}$, the ST slope separated patients with CAD from controls with a sensitivity of 93% and a specificity level of 88%. The area under the receiver operating characteristic curve of ST slope tended to be higher than the one of ST depression (97% vs 93%; $p = 0.097$). In conclusion, regions sensitive for ST depression and for ST-slope decrease could be identified in BSPM, despite variation in the location of ischemia and the presence or absence of a history of MI. ST slope is a sensitive and specific marker of transient myocardial ischemia, and might perform even better than ST depression. ©2001 by Excerpta Medica, Inc.

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The diagnostic power of 12-lead electrocardiography (ECG) in acute ischemia and myocardial infarction (MI) might not be optimal because coverage of the standard precordial leads over the thorax is limited.¹ Right precordial leads have improved the sensitivity of ischemia detection in patients with right coronary artery stenosis.² Body surface potential mapping (BSPM), by sampling ECG over the whole thorax, allows extensive spatial analysis of ECG for detection of ischemia. BSPM is superior to 12-lead ECG for detection of transient myocardial ischemia³⁻⁵ and acute and old MIs.⁶⁻¹⁰ In patients with non-Q-wave MI, minor potential losses during QRS complex can be identified in BSPM; these losses are undetectable in 12-lead ECG.¹¹ BSPM can also localize MIs^{7,8} and exercise-induced ischemia in patients with single-vessel disease who do not have a history of MI.⁵ The capability of BSPM to detect acute ischemia in patients with prior ischemic myocardial damage is not

known. We used BSPM to evaluate electrocardiographic criteria for ischemia in stress testing. Particular emphasis was given to the diagnostic performance despite variation in the ischemic vessel branch and the presence of single or multivessel disease or old MIs.

METHODS

Patients and controls: The study population consisted of 70 subjects: 45 patients with coronary artery disease (CAD) and 25 age-matched healthy volunteers (Table 1). Of the 45 patients with CAD, 27 had no history of MI and had single-vessel disease and 18 patients had a history of ≥ 1 MIs and multivessel disease. The entire patient population was divided into 3 groups based on the ischemia location: anterior (left anterior descending [LAD] artery), posterior (left circumflex [LC] artery), or inferior (right coronary artery); these groups included all patients with and without history of MI.

The 27 non-MI patients had single-vessel disease ($>50\%$ luminal diameter stenosis in 1 of the main coronary arteries as seen on coronary angiography). At inclusion, they were required to have anginal pain and 12-lead electrocardiographic documented evidence of ischemia with ≥ 0.1 mV ST-segment depression at symptom-limited upright bicycle ergometry. The inclusion criteria required that they did not have

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Group	Number	Age (yrs)	Men/ Women	LVEF (%)	Stenosis (%)
All CAD	45	59 ± 9	32/13	57 ± 14	87 ± 13
No MI	27	57 ± 10	16/11	64 ± 8	86 ± 12
Post-MI	18	61 ± 8	16/2	47 ± 15	88 ± 13
LAD ischemic area	18	59 ± 9	12/6	56 ± 13	81 ± 14
LAD no MI	13	57 ± 10	7/6	63 ± 6	81 ± 14
LC ischemic area	14	60 ± 7	14/4	57 ± 19	92 ± 11
LC no MI	6	59 ± 7	3/3	70 ± 9	90 ± 13
Right ischemic area	13	58 ± 11	10/3	59 ± 11	92 ± 8
Right no MI	8	57 ± 12	6/2	60 ± 7	92 ± 5
Controls	25	55 ± 7	19/6	66 ± 7	—

Number of study subjects or mean ± SD.
LVEF = left ventricular ejection fraction; Stenosis = the degree of coronary artery stenosis as the percentage luminal narrowing of vessel diameter.

abnormal Q-waves or bundle branch block at 12-lead ECG, or wall motion abnormalities or left ventricular hypertrophy in echocardiography at rest.

The 18 post-MI patients had triple-vessel CAD. They underwent thallium perfusion single-photon emission computed tomographic stress imaging with redistribution imaging at 4 hours, and coronary angiography for definition of the main ischemia region and the culprit vessel. Classification was based on a reversible thallium perfusion defect supplied by the stenotic ($\geq 70\%$ luminal diameter) coronary artery. Two investigators independently classified the patients into 3 groups according to the main ischemia region.

All patients were clinically stable and receiving appropriate medication: 41 patients were on β blockers, 11 patients on calcium antagonists, 36 patients on long-acting nitrates, and 9 patients on angiotensin-converting enzyme inhibitors. The healthy controls did not have a history of hypertension, smoking, or heart disease in the family, and had normal findings on echocardiography as well as in bicycle ergometry. Before inclusion, all patients and controls gave informed consent.

Body surface potential mapping: In the BSPM measurements, unipolar potentials were recorded at 120 locations covering the whole thorax.¹² In addition, 3 limb leads were recorded with electrodes on the right and left shoulder and on the left hip. A Wilson central terminal was used as the reference for the unipolar leads. The electrodes were mounted on 18 strips with an interelectrode distance of 5 cm. The strips were vertically placed on the subject's thorax; the dimensions of the upper body determined horizontal spacing. The highest electrode density was on the left anterior chest. After band-pass filtering from 0.16 to 300 Hz, the signals were digitized with the sampling rate of 1,000 Hz.

First, the signals were recorded at baseline for 5 minutes. Then, the subjects performed a supine bicycle exercise test while the workload was increased and blood pressure measured every 2 minutes. Cessation criteria were severe fatigue or dyspnea, severe chest pain, progressive decrease or abnormal elevation of

systolic blood pressure, or repetitive ventricular arrhythmias. BSPM was continuously recorded during exercise and up to 10 minutes in the recovery phase.

The study was performed according to the Declaration of Helsinki, and approved by the local Ethics Committee.

Signal processing: The signals were averaged as previously described in detail.¹³ All leads judged invalid in visual observation were excluded and replaced by data interpolated from other leads.

Three phases of the exercise test were analyzed: (1) baseline, (2) before cessation of exercise, and (3)

immediately after cessation of exercise. The time period after cessation of exercise performed better than the exercise period, probably due to lower noise level. Therefore, the main results are presented from the immediate recovery period.

ST amplitude and ST slope were measured in each lead. ST amplitude was measured 60 ms after the J-point.¹⁴ ST slope (in microvolts per second) was calculated by fitting a regression line to the signal from the J-point on to 60 ms after the J-point. The J-point was defined manually from the left precordial leads equivalent to leads V_1 to V_6 in 12-lead ECG.

Discriminant index: To find the most useful recording sites irrespective of the localisation of ischemia in each patient subgroup, the group mean ST-segment isopotential and isoslope maps were calculated. A discriminant index, suggested by Kornreich et al,⁸ indicated the ability of each sensor site to separate a patient subgroup from other patients and controls. The discriminant index was calculated for each subgroup in each recording location. First, the mean ST amplitude or slope of the control group was subtracted from the corresponding mean of the patient subgroup. The difference was then divided by the SD of ST amplitudes or slopes in all subjects at the same sensor site. The analysis was performed for ST amplitude and ST slope data during the last exercise period and immediately after stress.

The highest negative discriminant indexes indicate the optimal locations for the ST depression and ST-slope decrease and the highest positive discriminant indexes the optimal locations for the reciprocal ST elevation and ST-slope increase. To illustrate the spatial distribution, discriminant index maps were formed for pooled CAD patients and for patient subgroups.

Statistical analysis: The Mann-Whitney U test was used for the statistical analysis of parameters. A 2-tailed p value < 0.05 was considered statistically significant.

RESULTS

ST segment immediately after cessation of stress: ST AMPLITUDE In the pooled CAD patient group and in the single-vessel CAD subgroup the optimal location

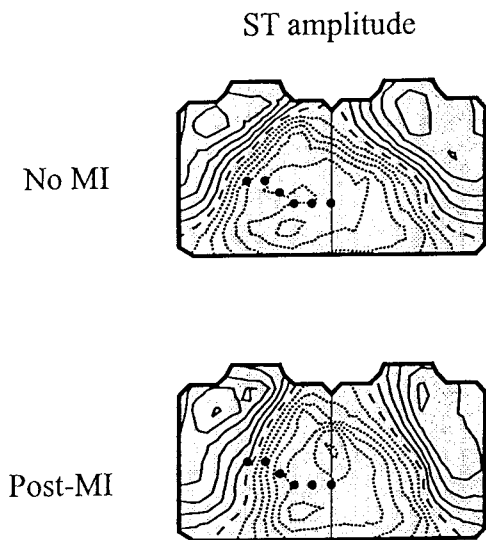


FIGURE 1. The discriminant index maps of the ST-segment amplitude for patients with single-vessel CAD and no MI (top) and post-MI patients with multivessel CAD (bottom) directly after cessation of stress. The optimal sites for ST depression are roughly the same in both groups. Torso silhouettes represent the discriminant index over the anterior chest (left) and over the back (right). The step between 2 isocontour lines is 0.25. Solid lines, positive values; dotted lines, negative values. Dashed line, 0 value of discriminant index. Black dots, the positions of the V_1 to V_6 electrodes in standard 12-lead ECG.

for ST depression was 5 cm below the standard lead V_5 (Figures 1 and 2, Table 2). In the LAD and LC patient subgroups the optimal location for ST depression was on the left anterior thorax 5 cm above the standard lead V_5 , and in the right subgroup 5 cm below lead V_6 . Reciprocal ST elevation was found over the right shoulder (Figures 2 and 3).

Using cut-off value of $-10 \mu V$, the ST depression separated patients with CAD from controls with a sensitivity of 84% and a specificity of 96%.

ST SLOPE: The optimal location for ST-slope decrease was over the left side posteriorly to standard lead V_6 in all patient subgroups (Figure 2, Table 2). The ST slope was more horizontal in all patient groups than in the control group (Figure 3). Reciprocal increase in ST slope was found over the right shoulder (Figures 2 and 3).

Using a cut-off value of $320 \mu V/s$, the ST slope separated patients with CAD from controls with a sensitivity of 93% and a specificity level of 88%.

The best sites for ST-slope decrease were not exactly the same as for ST depression. The spatial variation in between patient subgroups in the optimal location for ST slope was less extensive than for ST depression (Figure 2). The standard left precordial leads cover the regions of relatively good discriminant indexes for both ST amplitude and ST slope.

ST segment at maximum stress: The optimal locations for ST depression and ST-slope decrease were roughly the same at maximum stress as immediately after cessation of stress. The immediate recovery period performed better than the last exercise period in

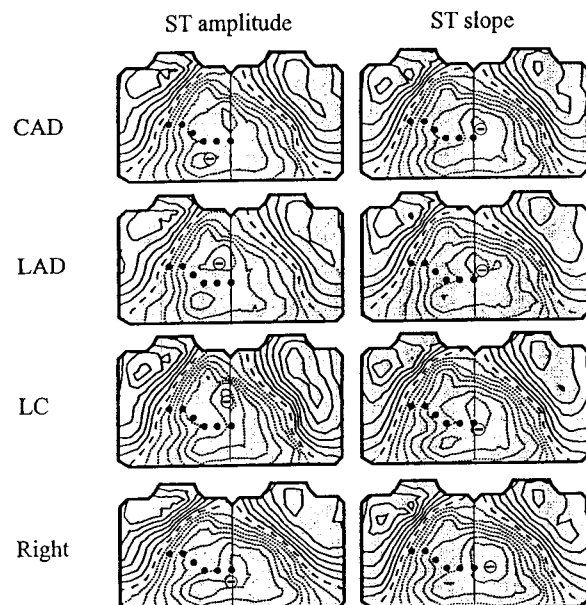


FIGURE 2. The discriminant index maps of the ST-segment amplitude and ST slope directly after cessation of stress. From top to bottom: patients with CAD, patients with anterior (LAD), posterior (LC), and inferior (right) ischemia. The channels having the highest (most positive) or lowest (most negative) value of discriminant index are the optimal ones to detect the presence of ischemia. The optimal site for ST depression was on the left anterior thorax above lead V_5 both in anterior and in posterior ischemia and below lead V_6 on the left midaxillary line in inferior ischemia. The optimal sites for ST slope decrease were not the same as the ones for ST depression. Despite the variation in the best sites in patient subgroups, the optimal locations for the pooled CAD group also performed well in patient subgroups, demonstrated by almost as good index values in the maps. The reciprocal ST elevation and ST slope increase were found over the right shoulder. Torso silhouettes represent the discriminant index over the anterior chest (left) and over the back (right). The step between 2 isocontour lines is 0.25. Solid lines, positive values; dotted lines, negative values. Dashed line, 0 value of discriminant index. Black dots, the positions of the V_1 to V_6 electrodes in standard 12-lead ECG. The optimal lead location for ST depression or ST-slope decrease is marked with a minus sign inside the white circle.

ischemia detection (discriminant index of ST depression for CAD: -1.40 vs -1.17 ; discriminant index of ST slope for CAD: -1.62 vs -1.44) (Table 3). It is interesting to that the ST slope performed better than ST depression also during the last exercise period.

Comparison between the isopotential and discriminant index maps: The maximal differences of the ST amplitude and ST slope between the patients and controls did not coincide with the optimal locations indicated by the discriminant index (Figures 2 and 3); the locations of the largest ST amplitude and slope changes evolving during stress were also not identical with the optimal sites.

Receiver operating characteristic curves: At cessation of stress ST slope had a slightly higher area under the receiver operating characteristic curve than ST depression (97% vs 93%) but the difference was not statistically significant (Table 3). Also, at maximum stress the ST slope performed slightly better than ST

TABLE 2 The ST Amplitudes and ST Slopes at Cessation of Stress in the Optimal Lead for ST Depression and ST-slope Decrease in the Pooled Coronary Artery Disease Patient Groups

Group	All CAD Patients	LAD Ischemic Area	LC Ischemic Area	Right Ischemic Area
ST amplitude				
Discriminant index	-1.40	-1.28	-1.54	-1.76
Patients (μV)	$-70 \pm 70^*$	$-60 \pm 90^*$	$-90 \pm 90^*$	$-100 \pm 70^*$
Controls (μV)	70 ± 80	80 ± 90	80 ± 90	40 ± 70
ST slope				
Discriminant index	-1.62	-1.42	-1.69	-1.89
Patients ($\mu\text{V/s}$)	$20 \pm 240^*$	$110 \pm 290^*$	$20 \pm 170^*$	$-100 \pm 220^*$
Controls ($\mu\text{V/s}$)	720 ± 320	720 ± 320	900 ± 430	720 ± 320

*p <0.001 comparing the patient group with the control group; Mann-Whitney U test. Mean \pm SD.

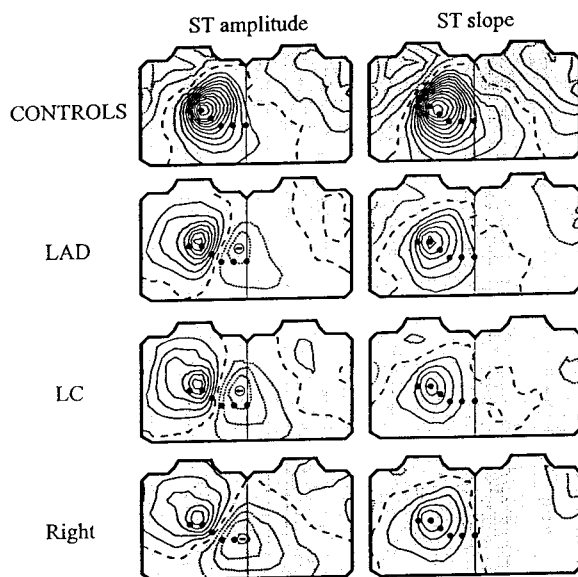


FIGURE 3. The group mean maps of the ST amplitude and ST slope directly after cessation of stress. From top to bottom: healthy controls, patients with anterior (LAD), patients with posterior (LC), and patients with inferior (Right) ischemia. Healthy controls have a large maximum potential over the anterior thorax. In anterior and posterior ischemia the maximal ST depression is found on the adjacent locations on the left side of the thorax, whereas in inferior ischemia the maximal ST depression is further down over the abdominal area. The reciprocal ischemic ST elevation is found over the right shoulder, where the healthy controls have negative ST amplitude. An ascending ST slope is found over the left precordium both in patients and in controls. The ST slope is more horizontal in patients with CAD than in controls. Torso silhouettes represent the potential and slope over the anterior chest (left) and over the back (right). The step between 2 isocontour lines is $25 \mu\text{V}$ in amplitude maps and $300 \mu\text{V/s}$ in ST slope maps. Solid lines, positive values; dotted lines, negative values. Dashed line, 0 line. Black dots, positions of the V_1 to V_6 electrodes in standard 12-lead ECG. The location of maximal ST depression is marked with a minus sign inside the white circle.

depression (area under curve 92% vs 86%). Overall, in the pooled CAD group and in all coronary vessel subgroups ST slope had a trend toward better performance than ST depression (Table 3).

Other parameters: The maximum ST-segment depression at cessation of stress was an average of -120

$\pm 90 \mu\text{V}$ in the pooled CAD patient group, $-100 \pm 100 \mu\text{V}$ in the LAD group, $-140 \pm 90 \mu\text{V}$ in the LC group, $-130 \pm 70 \mu\text{V}$ in the right group, and $-80 \pm 40 \mu\text{V}$ in the control group.

DISCUSSION

The present study shows that not only ST depression but also ST slope detects transient myocardial ischemia in BSPM. Despite variation in the location of ischemia and the presence or absence of a history of MI, 2 nearby regions, 1 sensitive for ST depression and the other for ST slope decrease, could be identified. The

morphology of the ST segment, reflected by the ST slope, appeared to be a sensitive and specific marker of transient myocardial ischemia in the tested heterogeneous CAD population. The left precordial leads of standard ECG are located in the region where the ability to discriminate myocardial ischemia is good.

ST slope: Even in the heterogeneous CAD population studied, which was chosen to represent the patients with CAD in general, a single optimal location for ST-slope decrease was identified. This location identified ischemia well not only in the pooled CAD group but also in the subgroups of different ischemia regions. The ST-slope decrease performed best among the studied parameters, and seemed to perform slightly better than conventional ST depression.

In a study by Ribisl et al,¹⁵ the maximal ST slope in lead V_5 of standard ECG was a sensitive marker of myocardial ischemia. The maximal ST slope both during maximal stress and at recovery performed as well as ST depression in ischemia detection. Of note is that their criteria of $<300 \mu\text{V/s}$ for horizontal ST slope was close to our optimal cut-off value for ST slope during recovery ($320 \mu\text{V/s}$).

ST depression: In the present study the optimal location for detecting ST depression was the same for ischemia in anterior and posterior regions but different for ischemia in the inferior wall. In a previous study, the optimal sites for ST depression were different for each culprit vessel in single-vessel disease.⁵ Our post-MI patients with multivessel CAD had less spatial variation in the best sites for ST depression, possibly due to existing ischemia also in other regions than the most severe one identified. The spatial variation of optimal location in different patient groups was more extensive for ST depression than for ST slope. ST slope and ST depression performed better immediately after stress than during maximal stress, probably due to a better signal quality. Although the most informative sites for the ST parameters are outside the coverage area of 12-lead ECG, the left precordial leads are located in the sites of good discriminant indexes.

Montague et al³ compared 14 patients with LAD disease with 8 normal subjects during stress BSPM. The group mean isointegral maps of the LAD patients

TABLE 3 The Areas Under the Receiver Operating Characteristic Curves for ST Depression and ST-slope Decrease in All Patient Groups

Group	Last Exercise Period		At Cessation of Stress	
	ST Depression	ST Slope	ST Depression	ST Slope
CAD	86%	92%	93%	97%
No MI	83%	91%	93%	95%
Post MI	90%	94%	94%	99%
LAD	82%	91%	94%	94%
LC	88%	95%	92%	99%
Right	88%	90%	94%	99%

showed ST depression, persisting up to 5 minutes after exercise even when the 12-lead electrocardiographic ischemia criteria were not fulfilled. The variation in the location of the ischemic changes in combined ST-T integral maps has been shown to depend on the ischemic region.¹⁶⁻¹⁸

Our patient population was selected to represent patients with CAD in general by including subsets of patients with ischemia in any of the main coronary artery branch regions and also healed MI. Therefore, the performance of the ST-segment parameters could be evaluated with a relatively small number of study subjects, and was found not to depend markedly on the ischemia location. The optimal recording locations identified transient ischemia in the pooled CAD group with similar accuracy as in separate vessel subgroups. The sensitivity and specificity values were calculated to compare the performance of the ST amplitude and ST slope. The numbers strongly depend on the patient population examined, and cannot be directly transferred to clinical practice. The interpretation of stress ECG is rather independent of the ischemia location and the presence or absence of previous MI. The ST-segment slope is a sensitive marker of transient ischemia and may assist in diagnosis. The standard precordial leads cover areas of high discriminant indexes and therefore serve well in ischemia detection.

Study limitations: Determining the most severely ischemic myocardial region is difficult in patients with multivessel CAD. However, in multivessel CAD, both thallium single-photon emission tomography and coronary angiography in each patient were used to determine the ischemic region, requiring concordance. However, the number of patients with multivessel

CAD in this study was small, and therefore, only preliminary conclusions can be made.

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