

The effect of lead selection on traditional and heart rate-adjusted ST segment analysis in the detection of coronary artery disease during exercise testing

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Several methods of heart rate-adjusted ST segment (ST/HR) analysis have been suggested to improve the diagnostic accuracy of exercise electrocardiography in the identification of coronary artery disease compared with traditional ST segment analysis. However, no comprehensive comparison of these methods on a lead-by-lead basis in all 12 electrocardiographic leads has been reported. This article compares the diagnostic performance of ST/HR hysteresis, ST/HR index, ST segment depression 3 minutes after recovery from exercise, and ST segment depression at peak exercise in a study population of 128 patients with angiographically proved coronary artery disease and 189 patients with a low likelihood of the disease. The methods were determined in each lead of the Mason-Likar modification of the standard 12-lead exercise electrocardiogram for each patient. The ST/HR hysteresis, ST/HR index, ST segment depression 3 minutes after recovery from exercise, and ST segment depression at peak exercise achieved more than 85% area under the receiver-operating characteristic curve in nine, none, three, and one of the 12 standard leads, respectively. The diagnostic performance of ST/HR hysteresis was significantly superior in each lead, with the exception of leads aVL and V₁. Examination of individual leads in each study method revealed the high diagnostic performance of leads I and -aVR, indicating that the importance of these leads has been undervalued. In conclusion, the results indicate that when traditional ST segment analysis is used for the detection of coronary artery disease, more attention should be paid to the leads chosen for analysis, and lead-specific cut points should be applied. On the other hand, ST/HR hysteresis, which integrates the ST/HR depression of the exercise and recovery phases, seems to be relatively insensitive to the lead selection and significantly increases the diagnostic performance of exercise electrocardiography in the detection of coronary artery disease. (Am Heart J 1997;134:488-94.)

Traditional interpretation of exercise electrocardiography for the detection of coronary artery disease is based on a positive criterion of 0.10 mV ST segment depression at the end of exercise, irrespective of which electrocardiographic lead is observed.^{1,2} This type of fixed cut-point procedure does not account for the differences in the measurement sensitivity distribution between the leads. These differences were clinically observed in 1976 by Froelicher et al.,³ who suggested that different cut points should be applied for the different leads.

Several methods have been suggested to improve the

insufficient diagnostic accuracy of end-exercise ST segment depression. Inclusion of the recovery phase in the analysis has been shown to increase the diagnostic yield of the exercise test.^{4,5} During the past 15 years, new and improved algorithms for extracting the diagnostic variables relating to the magnitude of ST segment depression to heart rate during the exercise test have been developed. Heart rate-adjusted ST segment (ST/HR) slope, ST/HR index, and multivariate ST/HR analysis, which use only the exercise phase, have been shown to improve the diagnostic accuracy compared with ST segment depression.⁶⁻¹¹ Moreover, ST/HR hysteresis, which combines the ST/HR analysis of both the exercise and recovery phases, has been suggested to provide further improvements.^{12,13} In these studies the diagnostic variables have been determined as maximal values obtained from the 12-lead system or some specific subset of leads. Because the leads have dissimilar measurement sensitivities, this type of maximization reduces the information content and might distort detection of ischemia.

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The objective of this study was to compare the diagnostic performances of the individual electrocardiographic leads and the effect of the lead selection on the analyses of ST/HR and ST segment depression in the discrimination of patients with angiographically proved coronary artery disease and the patients with a low likelihood of the disease. Two different methods of ST segment depression and two different ST/HR methods were used as diagnostic variables.

Methods

Study population

Subjects were selected from a group of 1507 consecutive patients who underwent routine clinical exercise testing in Tampere University Hospital. Patients with either left or right bundle branch block and recent myocardial infarction (<8 weeks) and without electrocardiographic recording of at least 3 minutes during postexercise recovery were excluded.

Patients with catheterization-proved coronary artery disease. The maximum time between the exercise test and coronary angiography was set at 180 days. Those patients who were treated with coronary angioplasty or surgical operations within that time were excluded. After the above restrictions were applied, there were 128 patients with a stenosis of $\geq 50\%$ in at least one of the major coronary arteries who were included in the group with coronary artery disease (Table I). Of these patients, 49 had significant stenosis in all three major coronary arteries or the left main coronary artery. The patients with single-vessel disease and two-vessel disease were 46 and 33 years of age, respectively.

Reference group. The reference group consisted of 189 patients with a low likelihood of coronary artery disease (Table I). All patients have been referred for exercise testing at the University Hospital. There were no volunteer subjects in this group. All the reference patients had no history of any heart disease, had a normal resting electrocardiogram, and had no anginal-type chest pain or heart medication. In addition, all subjects were free of chest pain during bicycle exercise testing. With probabilistic assessment, the reference group can be assumed to have a low likelihood ($p < 0.05$) of coronary artery disease.¹⁴

Coronary angiography

Selective coronary angiography was performed according to the Judkins technique. In all cases each coronary artery was imaged in multiple views. The degree of stenosis was defined as the greatest percentage reduction of luminal diameter in any view compared with the nearest normal segment. Coronary artery disease was considered significant when $\geq 50\%$ luminal narrowing in the major coronary arteries was present.

Exercise electrocardiography

The exercise electrocardiographic test was performed on a bicycle ergometer according to a computerized recording system (SYSTEM II EXES; Siemens-Elma, Solna, Sweden). The

Table I. Clinical characteristics of the study population

	CAD group (n = 128)	Reference group (n = 189)
Age (yr)	55 \pm 8	47 \pm 12
Sex (M/F)	101/27	100/89
β -Blockers	105	0
Calcium antagonist	47	0
Digitalis	3	0
Nitrates	87	0
Maximum heart rate (beats/min)	126 \pm 21	164 \pm 19
Anginal type chest pain	61	0

Continuous data are mean \pm SD.

CAD, Coronary artery disease.

protocol followed a standard clinical routine with an initial workload of 40 W for women and 50 W for men and an increment of 40 and 50 W every 4 minutes for women and men, respectively. The lead system used was the Mason-Likar modification of the standard 12-lead system.¹⁵ Exercise tests were maximal, with recommended criteria used for termination.¹⁶

Computer-determined ST segment amplitudes, measured to the nearest 10 μ V at 60 msec after the J point with the end of the PR segment as a reference, were obtained in each lead after every minute of exercise, at the end of exercise, and after every minute during the first 3 consecutive minutes of postexercise recovery. The ST segment amplitude and heart rate data were stored for further processing and analysis.

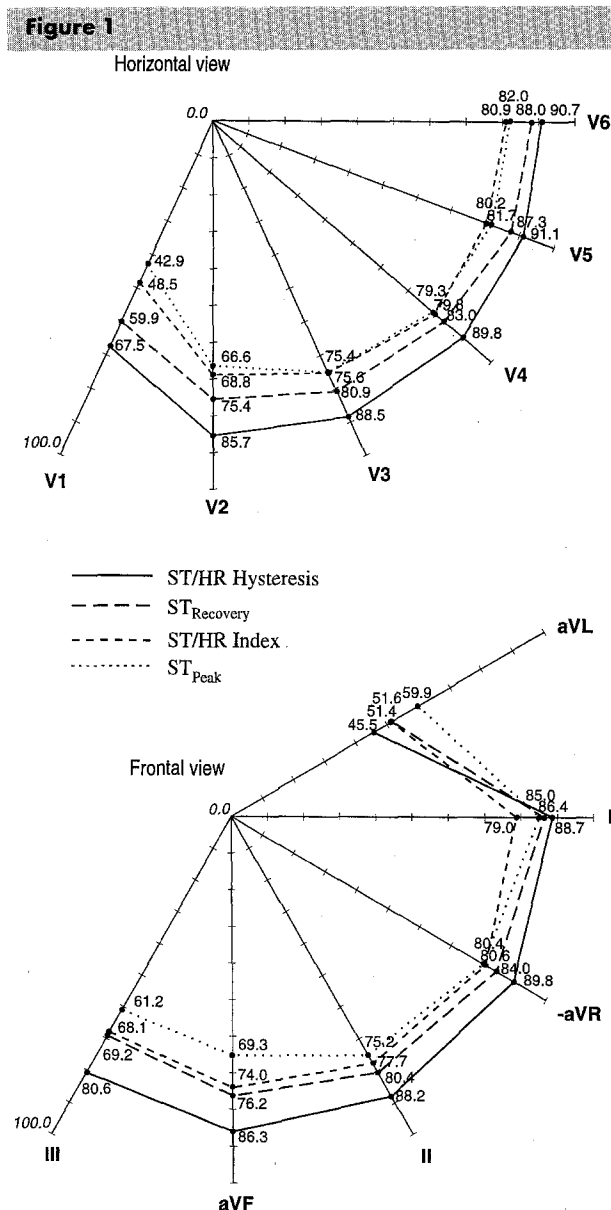
Diagnostic variables

The ST/HR hysteresis, ST/HR index, ST segment depression at 3 minutes of recovery (ST_{Recovery}), and ST segment depression at peak exercise (ST_{Peak}) were determined for each lead from the stored data with a computer program developed for comprehensive ST/HR analysis.¹⁷ ST segment depressions are expressed as positive values, whereas values of ST segment elevations have negative signs. The material was inappropriate for the calculation of the ST/HR slope for each lead.

Calculation of the ST/HR index was performed by dividing the overall ST segment deviation at end exercise by the exercise-induced change of heart rate.⁸ ST/HR hysteresis was calculated, as described by Lehtinen et al.,¹² by integrating the difference in ST segment depression between the exercise and recovery phases over the heart rate from the minimum heart rate of recovery to the maximum heart rate of the exercise test. The integral was divided by the difference in heart rate over the integration interval to normalize ST/HR hysteresis with respect to the decrement in heart rate during recovery. This variable represents the average difference of ST segment depression between the recovery phase and the exercise phase.

Statistics

Differences among study groups with respect to age, sex, and maximum heart rate were examined by the nonparametric Kruskal-Wallis test. Quantitative variables were analyzed



Values of area under receiver-operating characteristic curves in standard leads shown on scales (0% to 100%) in direction of lead. *Horizontal view* presents results for chest leads; *frontal view* shows results for limb leads. Values presented are percentages of total receiver-operating characteristic space.

with the Student's *t* test. The discriminative capacity of the study leads and methods were compared by means of receiver-operating characteristic analysis. Differences between the areas under the receiver-operating characteristic curves were compared by nonparametric analysis of correlated curves¹⁸ with a routine written by Vida (version 2.5).¹⁹

Results

Group characteristics

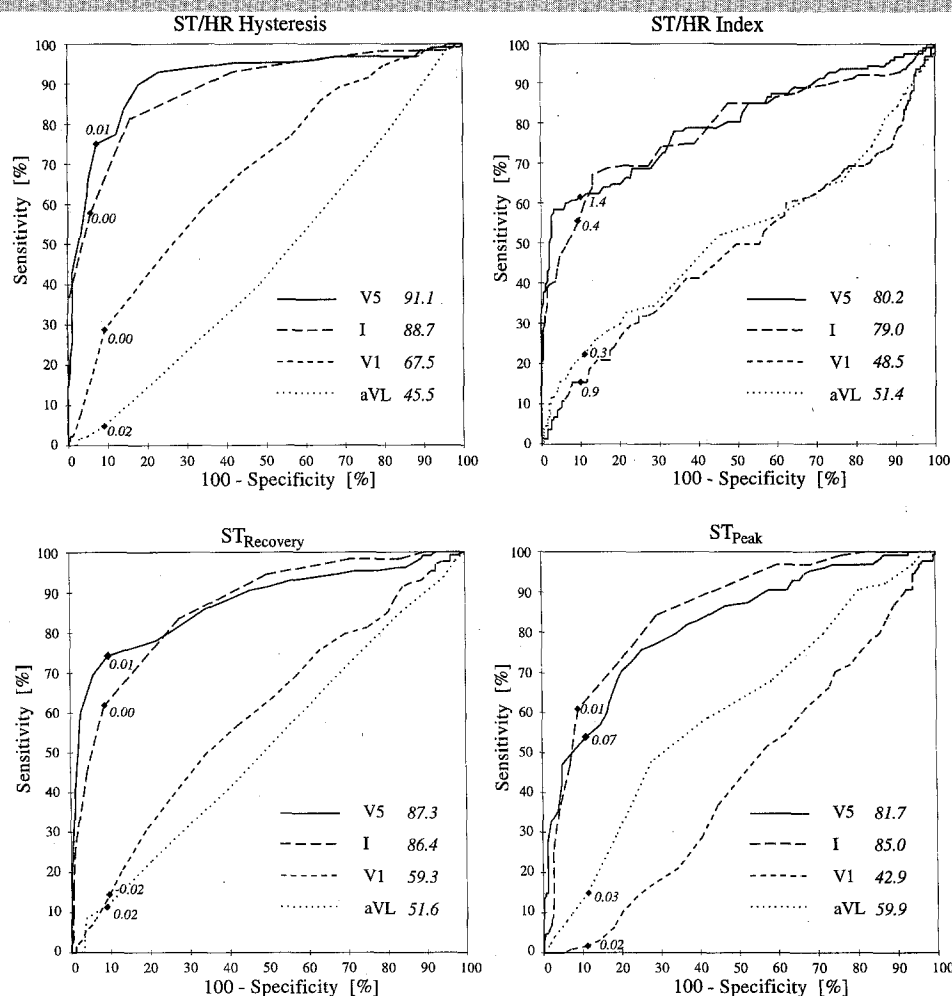
The characteristics of the study population are given in Table I. Because of the different exclusion criteria used in the selection of the groups, highly significant differences ($p < 0.0001$) between the groups were achieved with respect to age, sex, and maximum heart rate. Patients in the reference group were younger, more often women, and achieved higher maximum heart rates than did patients of the group with coronary artery disease.

Diagnostic variables

The means, standard deviations, and *p* values for ST/HR hysteresis, ST/HR index, ST_{Recovery}, and ST_{Peak} in each of the standard 12 leads grouped by status are given in Table II. The differences between the groups were statistically significant in almost each lead. It is noteworthy that lead aVL did not achieve significant differences at a level of $p < 0.0001$ in any of the methods used and lead V₁ attained a significant difference only in the case of ST/HR hysteresis. Furthermore, the ST/HR hysteresis has a minor spread of variables in both the group with coronary artery disease and the reference group and thus improves the discrimination of patients with and without coronary artery disease.

Fig. 1 presents areas under the receiver-operating characteristic curves in each lead for every method as a lead direction presentation; the axes have been aligned with the standard lead direction in the frontal and horizontal views. With receiver-operating characteristic analysis used for the identification of coronary artery disease, ST/HR hysteresis, ST/HR index, ST_{Recovery}, and ST_{Peak} methods achieved more than 85% area under the receiver-operating characteristic curves in nine, none, three, and one of the 12 leads, respectively. An important characteristic of the ST/HR hysteresis method was the uniformity of the receiver-operating characteristic areas in each lead, except aVL and V₁. Moreover, it is important to appreciate the performance of limb leads I and -aVR, which are used less often in the conventional diagnosis of coronary artery disease. The excellent diagnostic performances of chest leads V₅ and V₆ are apparently irrespective of the analytic method employed. These leads generally yield the best areas under the receiver-operating characteristic curves. However, in statistical comparison between leads I, -aVR, V₅, and V₆, there was a signifi-

Figure 2



Receiver-operating characteristic curves for chest leads V_5 and V_1 and limb leads I and aVL in each study method. Cut points presented in curves indicate variable values that yield specificity of 90% (in millivolts for ST/HR hysteresis and ST segment depressions and in microvolts per beat per minute for ST/HR index). Numbers after marking of lead express area under receiver-operating characteristic curves as percentages. Differences between area under receiver-operating characteristic curves of leads V_5 or I and V_1 or aVL were significant in each method. Statistically significant differences were not observed between leads V_5 and I with any of these methods. Total number of patients is 317 (128 with coronary artery disease and 189 normal patients) in each analysis.

cant difference only in the case of the $ST_{Recovery}$ method between leads $-aVR$ and V_6 ($p = 0.0043$).

Fig. 2 presents the receiver-operating characteristic curves of leads V_5 , I , V_1 , and aVL for the ST/HR hysteresis, ST/HR index, $ST_{Recovery}$, and ST_{Peak} methods. The cut points that yield nearest to the specificity of 90% are shown in Fig. 2. Corresponding sensitivity values have considerable variation. In each method the areas under the receiver-operating characteristic curves for leads V_5 or I were significantly higher than for leads V_1 or aVL (p

< 0.0001). Comparison between the methods also revealed some differences: For example in lead V_5 the area under the receiver-operating characteristic curve for ST/HR hysteresis was significantly higher than that for $ST_{Recovery}$ ($p = 0.0269$), ST/HR index ($p < 0.0001$), and ST_{Peak} ($p < 0.0001$). Furthermore, in lead V_5 there were significant differences between $ST_{Recovery}$ and ST_{Peak} ($p = 0.0011$), as well as between $ST_{Recovery}$ and ST/HR index ($p = 0.0025$), whereas no significant difference was obtained between ST_{Peak} and ST/HR index ($p = 0.3967$).

Table II. Mean values and standard deviations of the study methods in the standard leads grouped according to status

	I	II	III	-aVR	aVL
ST/HR hysteresis (mV)					
CAD group (n = 128)	0.01 ± 0.02	0.01 ± 0.03	0.00 ± 0.02	0.01 ± 0.02	0.00 ± 0.01
Reference group (n = 189)	-0.02 ± 0.02	-0.05 ± 0.05	-0.03 ± 0.04	-0.04 ± 0.03	0.01 ± 0.02
p Value	*	*	*	*	0.2103
ST/HR index (μV/beat/min)					
CAD group (n = 128)	0.51 ± 0.65	1.14 ± 1.28	0.64 ± 1.02	0.82 ± 0.87	-0.06 ± 0.57
Reference group (n = 189)	-0.08 ± 0.38	0.03 ± 0.86	0.11 ± 0.73	-0.03 ± 0.54	-0.09 ± 0.41
p Value	*	*	*	*	0.6167
ST _{recovery} (mV)					
CAD group (n = 128)	0.01 ± 0.02	0.02 ± 0.05	0.01 ± 0.04	0.02 ± 0.04	0.00 ± 0.02
Reference group (n = 189)	-0.02 ± 0.02	-0.04 ± 0.06	-0.02 ± 0.05	-0.03 ± 0.04	0.00 ± 0.02
p Value	*	*	*	*	0.8155
ST _{peak} (mV)					
CAD group (n = 128)	0.02 ± 0.03	0.05 ± 0.07	0.02 ± 0.06	0.04 ± 0.04	0.00 ± 0.03
Reference group (n = 189)	-0.02 ± 0.04	-0.03 ± 0.09	0.00 ± 0.07	-0.02 ± 0.06	-0.01 ± 0.03
p Value	*	*	0.0002	*	0.007

CAD, Coronary artery disease.

**p* < 0.0001.

Discussion

Although the sensitivity distributions of the individual electrocardiographic leads are different, conventional analysis of ST segment depression employs the same fixed cut point for every lead. Froelicher et al.³ have concluded in their study that lead-specific criteria should be used, especially for computerized analysis. The results of this study support their finding of differences between the cut-point values of the individual leads employing the end-exercise ST segment depression and demonstrate the dissimilar diagnostic performances of the individual leads. The results also indicate that these interlead differences are reduced considerably with the ST/HR hysteresis method in the detection of coronary artery disease.

Performances of individual leads

For each method the highest diagnostic performances according to receiver-operating characteristic analysis were in chest leads V₄, V₅, and V₆ and limb leads I and -aVR (Fig. 1). Statistical comparison between the leads of the 12-lead electrocardiography suggested the exclusion of leads aVL and V₁ from the analysis; the areas under the receiver-operating characteristic curves were the smallest, and the statistical significances between these leads and leads I or V₅ in each case were at a level of *p* < 0.0001 (Fig. 2). These findings support previous studies, in which these leads have been routinely excluded.^{9-13,20,21} Furthermore, in these studies lead aVR is also rejected, but the apparent reason is that the researchers have not used aVR as inverted. The low

diagnostic performance of leads aVL and V₁ might arise from the sensitivity of the leads to interindividual differences in position and rotation of the heart,^{22,23} as well as the direction of the main injury current.¹

The comparison of discriminative capacities between the chest leads in this study were in concordance with the medical literature; the highest capacities were obtained in leads V₅ or V₆, whereas in the case of limb leads the very high discriminative capacities of lead I and inverted lead aVR were unexpected. For each diagnostic method the areas under the receiver-operating characteristic curves in leads I and -aVR were practically equal to those of the best chest leads. The apparent reason why the high diagnostic performances of leads I and -aVR have not been observed earlier is the relatively low signal (Table II), which hampers the manual analysis in these leads.

Comparison of the methods

Interlead differences were noticed for each method of analysis (Table II; Fig. 1). However, the smallest variation was obtained with ST/HR hysteresis. This result indicates that ST/HR hysteresis is not as sensitive to the lead selection as the other methods. The results of this study regarding the use of the ST_{peak} (Table II; Fig. 2) support the previous studies,^{3,24,25} in which it has been suggested that more detailed, lead-specific criteria should be defined and applied. The improved diagnostic performance and greater reliability of ST/HR hysteresis may be explained because the method integrates the diagnostic information of both the exercise and recov-

aVF	V ₁	V ₂	V ₃	V ₄	V ₅	V ₆
0.01 ± 0.03 -0.04 ± 0.04 *	-0.02 ± 0.04 -0.04 ± 0.05 *	-0.02 ± 0.09 -0.16 ± 0.12 *	0.00 ± 0.09 -0.16 ± 0.12 *	0.01 ± 0.08 -0.14 ± 0.11 *	0.02 ± 0.07 -0.10 ± 0.09 *	0.02 ± 0.05 -0.07 ± 0.06 *
0.89 ± 1.11 0.07 ± 0.76 *	-0.23 ± 1.25 -0.16 ± 1.00 0.58	0.37 ± 2.86 -1.33 ± 2.31 *	0.92 ± 3.11 -1.58 ± 2.62 *	1.69 ± 3.08 -1.21 ± 2.49 *	1.98 ± 2.51 -0.48 ± 1.84 *	1.81 ± 1.92 -0.08 ± 1.25 *
0.01 ± 0.04 -0.03 ± 0.05 *	-0.07 ± 0.06 -0.09 ± 0.07 0.0105	-0.10 ± 0.12 -0.22 ± 0.17 *	-0.04 ± 0.13 -0.20 ± 0.17 *	0.02 ± 0.12 -0.13 ± 0.15 *	0.05 ± 0.09 -0.07 ± 0.10 *	0.05 ± 0.06 -0.04 ± 0.07 *
0.04 ± 0.06 -0.01 ± 0.08 *	-0.09 ± 0.09 -0.07 ± 0.10 0.0274	-0.13 ± 0.17 -0.26 ± 0.24 *	-0.07 ± 0.18 -0.27 ± 0.25 *	0.02 ± 0.17 -0.20 ± 0.23 *	0.08 ± 0.13 -0.10 ± 0.17 *	0.09 ± 0.10 -0.05 ± 0.12 *

ery phases of the exercise test: the method examines the relationship between ST segment changes in the exercise and recovery phases at the same heart rate and moreover proportions the exercise and recovery values to each other and thus the dependence on the observed lead is reduced.

In general, ST/HR hysteresis provided the best diagnostic performance, whereas the ST_{Peak} analysis gave the poorest results. The superior ability of ST/HR hysteresis was clearly demonstrated by the large areas under the receiver-operating characteristic curves in each lead (Fig. 1). Statistical comparison of the receiver-operating characteristic curves revealed significant differences between ST/HR hysteresis and other study methods in more leads. ST/HR hysteresis had the most uniform areas under the receiver-operating characteristic curves over all 12 leads. This makes it possible to use ST/HR hysteresis with more efficiency and more versatility than the other methods. In the detection of coronary artery disease, another interesting observation was the capacity of the ST segment depression method during the recovery phase. The ST_{Recovery} method gave higher diagnostic performances than ST_{Peak} in each lead, and the areas under the receiver-operating characteristic curves for ST_{Recovery} were even higher than the corresponding areas of the ST/HR index method, indicating the high information content of the recovery phase.

Study limitations

There were several limitations in this study. The patients with coronary artery disease had angiographi-

cally proved coronary artery disease, but the reference patients were defined only by clinical history. In an ideal study the entire study population would have been examined by angiography. This is of course an unreasonable procedure for patients without symptoms. The group with coronary artery disease was heavily weighted toward men. Therefore the conclusions of the study regarding sensitivity in women may be limited. Heart medication (the majority of the patients with coronary artery disease used β -blockers), the type of exercise test, and the protocol used influenced the results. However, these influences can be assumed identical for each lead and thus the comparison of the leads is regardless of the medication, exercise modality, or protocol. Conversely, the comparison of the ST and ST/HR analyses might be more susceptible to these factors. The reason for the exclusion of the ST/HR slope method from the study has arisen from the exercise protocol used (illustrated in the previous study¹¹); the acceptable number of ST/HR slope values for each lead was too small.

The comparison of the leads has been made by analysis of the receiver-operating characteristic curve. Certainly in this type of study population the specificity should be high without decrease of sensitivity. Thus the most important characteristics of the lead are easy to recognize by observing the receiver-operating characteristic curve over 90% specificity (Fig. 2). However, for the overall comparison of the diagnostic performance of the different leads or methods, the entire receiver-

operating characteristic curve should be employed. This approach is reasonable, because there is no need to determine any fixed cut point (i.e., fixed sensitivity and specificity). Thus the effect of referral bias on the results is minimized and the results are more reliable and can be extended more easily to the different populations.

Conclusions

The results of this study suggest that the use of a fixed cut point for each lead is inappropriate. More detailed, lead-specific criteria should be defined, especially for the traditional analysis of ST segment depression. On the other hand, the use of ST/HR hysteresis decreases the differences between the individual leads. In addition to leads V_5 and V_6 , leads I and $-aVR$ have a significant diagnostic performance in the detection of coronary artery disease, whereas the diagnostic performances of leads aVL and V_1 are insufficient. According to this study, ST/HR hysteresis seems to be relatively insensitive to the selection of the leads and also significantly increases the diagnostic performance of the exercise electrocardiogram in the detection of coronary artery disease.

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