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Detection of Coronary Artery Disease Using Maximum Value of ST/HR Hysteresis Over Different Number of Leads

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Abstract: We have studied the effect of the number and ordering of exercise electrocardiographic (ECG) leads when using the maximum value of the ST segment depression/heart rate (ST/HR) hysteresis over a different number of leads for the detection of coronary artery disease (CAD). The study population consisted of 127 patients with CAD and 220 patients with a low likelihood of the disease referred for an exercise test at Tampere University Hospital, Finland. The lead system used was the Mason-Likar modification of the standard 12-lead system, and exercise tests were performed on a bicycle ergometer. The number of leads was studied using lead sets consisting of first 2 leads, then 3 leads, and so on, up to all 12 leads. The criterion for the order of inclusion of the next lead in the new lead set was based on the maximized area under the receiver operating characteristic (ROC) curve for the new lead set. The importance of the number of leads was evaluated by means of three different approaches: ROC analysis; using a fixed partition criterion of 0.01 mV; and using a fixed specificity value of 80%. According to the results, the most powerful diagnostic capacity of an individual lead was in lead V_5, and the most deficient diagnostic capacities were in leads aVL and V_1. Using the maximum search procedure, it was possible to improve the diagnostic capacity of the ST/HR hysteresis by anything from 4 up to a maximum of 8 leads. After that it started to decrease rapidly. In conclusion, this study suggests that the diagnostic capacity of the ST/HR hysteresis could be improved by increasing the number of leads. However, the selection of leads is of major importance when using the maximum value of the ST/HR hysteresis over the leads in the detection of CAD. **Key words:** exercise ECG, coronary artery disease, ST/HR analysis, ECG leads.

The traditional interpretation of exercise electrocardiography (ECG) for diagnosing coronary artery disease (CAD) is based on the ST segment depression during an exercise test. However, the diagnostic accuracy of a positive criterion of 0.10-mV ST segment depression is only about 70% in the detection of CAD in clinical populations (1,2). The diagnostic variables, which relate the magnitude of ST segment depression to heart rate (HR) during an exercise test, for example, ST/HR slope (3) and ST/HR index (4), have been shown to improve the diagnostic accuracy compared with ST segment depression (5,6). Conventional ST/HR variables utilize only the exercise phase of the exercise ECG test.

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A new method, ST/HR hysteresis, which integrates the ST/HR analysis of the exercise and recovery phases, has recently been introduced, and the diagnostic capabilities of ST/HR hysteresis have been shown to be more competent than those of the other variables (7–11). The ST/HR hysteresis represents the average difference in ST segment depression between the recovery and exercise phases.

In the literature, the diagnostic performance of exercise ECG variables has been evaluated using maximal value obtained from the whole lead system or some specific subset of leads. The obvious target of the maximum search approach is to increase the sensitivity of the variable. It is apparent that the number of true positive responses increases when a specific fixed cut point is used universally with the increase in the number of leads. However, at the same time generally the number of false-positive responses tends also to increase, causing a decrement in specificity. Therefore, it is important to know how many leads and which leads should be included in the maximum search procedure when using the ST/HR hysteresis.

Materials and Methods

Study Population

The study population consisted of 347 patients, 127 patients with CAD and 220 references with a low likelihood of CAD, who underwent a bicycle ergometer stress test. All patients had been referred for exercise testing at Tampere University Hospital, Tampere, Finland. There were no patients with left/right bundle branch block or recent myocardial infarction (<8 weeks). All the CAD patients had ⩾50% luminal narrowing at least in one of the major epicardial coronary arteries according to the coronary angiography. The reference group consisted of 13 patients without CAD according to angiography, 18 patients without myocardial ischemia according to technetium-99m sestamibi single-photon emission computed tomography, and 189 patients who were clinically normal with respect to cardiac diseases. Group characteristics are shown in Table 1. Because of the different exclusion criteria used in the selection of the groups, the differences between the groups were marked in all characteristics.

Exercise ECG Test

The exercise test was performed on a bicycle ergometer using a computerized recording system (SYSTEM II EXES, Siemens-Elema, Solna, Sweden). The graded protocol performed with an initial workload of 40W for women and 50W for men and an increment of 40W and 50W every 4 min for women and men, respectively. The exercise tests were sign- and symptom-limited maximal tests using recommended criteria for termination. The lead system used was the Mason-Likar modification of the standard 12-lead system (12). Computer-determined ST segment amplitudes measured to the nearest 10 μV were obtained at a point 60 ms after the J-junction. The ST segment amplitude, HR, and workload data were stored for further processing and analysis. All individual leads were used separately in the detection of ischemic responses. Lead aVR was used in inverted form.

Table 1. Clinical Characteristics of Study Population

	CAD (n = 127)	Reference (n = 220)
Sex (male/female)	101/26	113/107
Age (years)	55 ± 8	48 ± 12
Maximal workload (W)	105 ± 36	143 ± 49
Maximum heart rate (bpm)	125 ± 21	162 ± 19
Anginal chest pain	60	3
Medication		
Beta blockers	104	4
Nitrate preparation	86	5
Calcium antagonist	46	4

Values for age, maximal workload, and maximum heart rate are mean ± standard deviation. CAD, coronary artery disease; W, watt; bpm, beats per minute.

ST/HR Hysteresis

The ST/HR hysteresis integrates the difference in ST segment depression between the exercise and recovery phases over the HR up to 3 min of the recovery phase. After the integration, the integral is divided by the HR difference (the maximum HR of the exercise test − the minimum HR of recovery) over the integration interval in order to normalize the ST/HR hysteresis with respect to the recovery HR decrement. The method examines the relationship between ST segment changes in the exercise and recovery phase at the same HR, and, moreover, it proportions the exercise and recovery values to each other. Thus, this variable represents the average difference in ST segment depression between the recovery phase and the exercise phase, and therefore the unit for the ST/HR hysteresis is mV. Determination of ST/HR hysteresis is illustrated in Fig. 1.

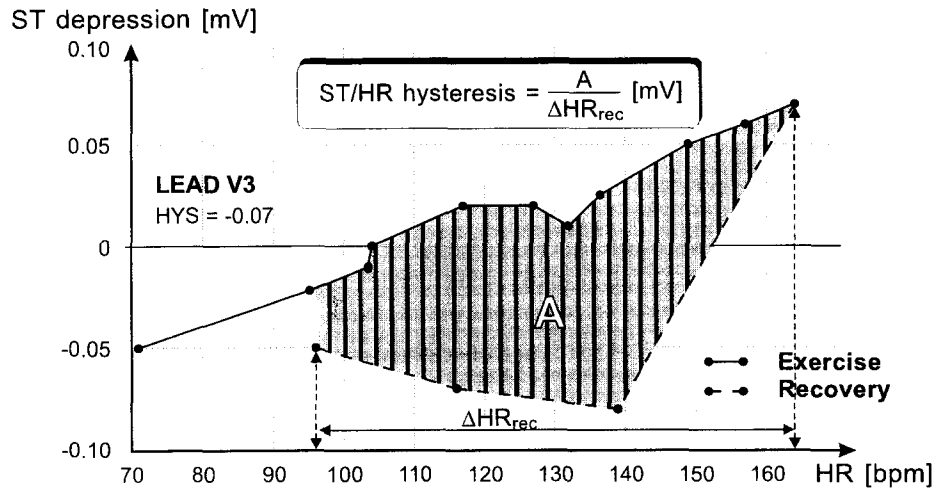

Fig. 1. ST/HR hysteresis method. ST segment depression and heart rate values during exercise and recovery phases. See text for more detailed description of the ST/HR hysteresis. A, area between the exercise and recovery phases up to 3 min of recovery; ΔHR_{rec}, maximum heart rate − minimum heart rate during 3 min of recovery.

Formation of the Lead Sets

The importance of the number of leads in the lead set was studied with lead sets having at first 2 leads (denoted by A_2), then 3 leads (A_3), and so on, up to all 12 leads (A_{12}). The maximum ST/HR hysteresis value, determined from each lead set (maximum search procedure), was used as the diagnostic classifier. The criterion for the inclusion of the next lead in the new lead set (from A_2 to A_{12}) was that the area under the receiver operating characteristic (ROC) curve of the new lead set should be as large as possible.

Data Analysis and Statistical Methods

The overall diagnostic performance of the individual leads and different lead sets was compared using ROC analysis. Taking into account the clinical utilization of the ST/HR hysteresis, the specificity and the sensitivity were defined using a fixed 0.01-mV partition value, which yielded the same specificity as the 0.1-mV criterion for the ST segment depression in our previous study (7). Furthermore, due to the quite bipartite nature of the study population, the sensitivity values at the fixed 80% specificity were also determined for each lead set.

Results

Individual Leads

The ROC areas for each individual lead using the ST/HR hysteresis are presented in Fig. 2. The high-

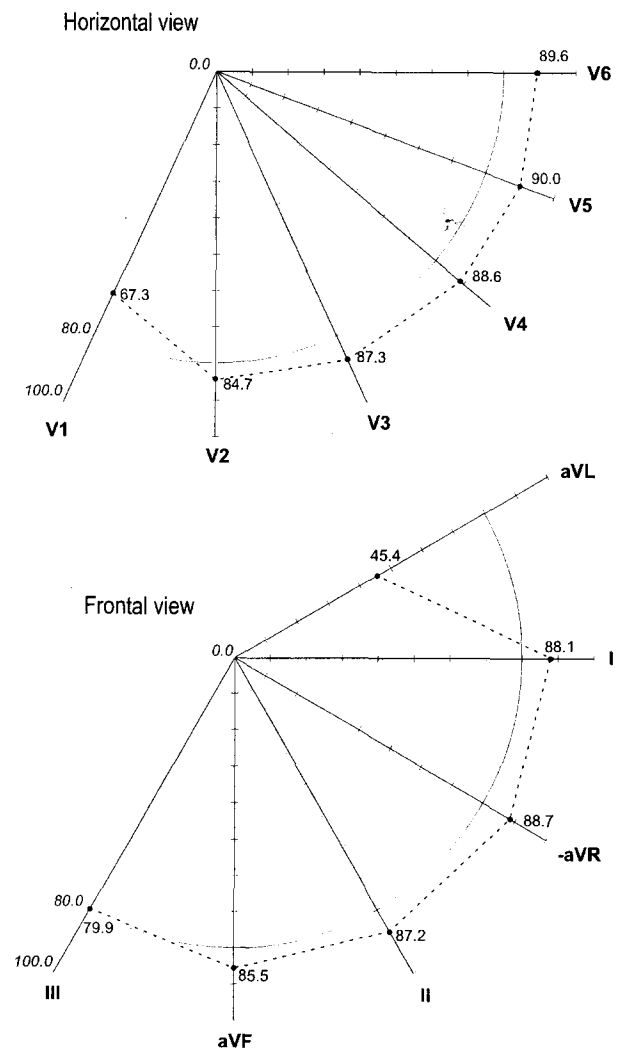

Fig. 2. The areas under the receiver operating characteristic (ROC) curve for each individual lead of the 12-lead system using ST/HR hysteresis.

est ROC area was in lead V_5 (90.0%) and the lowest was in lead aVL (45.6%). The value of less than 50% in lead aVL indicated that aVL should be used in inverted form in this study population (the ROC area for −aVL would be 54.6%). Noteworthy was that the ROC areas were very uniform, having more than 80% in each lead, except the leads aVL, V_1, and III.

Lead Sets

Figure 3 presents ROC areas for lead sets having 1 to 12 leads (the highest ROC area in lead sets A_1 to A_{12}). When more leads were included in the maximum search procedure, the ROC area started to increase. However, after 4 leads, no increase was achieved and after 8 leads the ROC area started to decrease. The deterioration of the ROC area was noticeable after 10 leads. The largest ROC area (90.7%) was in lead sets A_4, A_5, and A_6, and the smallest ROC-area was in A_{12} (79.8%, significantly smaller than in other lead sets).

In addition to ROC areas, the order of the inclusion of the leads is indicated in Fig. 3. Using the maximum value determined from lead V_5 and one other lead, the highest improvement in the ROC area was achieved using lead V_3. Further improvement was obtained by including leads V_6 and aVF in the lead set. A marked deterioration of the ROC area followed from the inclusion of leads V_1 and aVL in the maximum search procedure.

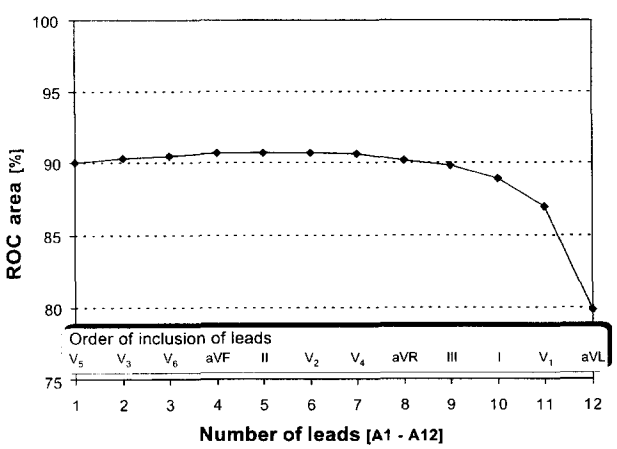

Fig. 3. The areas under receiver operating characteristic (ROC) curves for lead sets having 1 to 12 leads and the order of inclusion of leads in the corresponding lead sets. The diagnostic classifier was the maximum value of ST/HR hysteresis determined from the leads of each lead set.

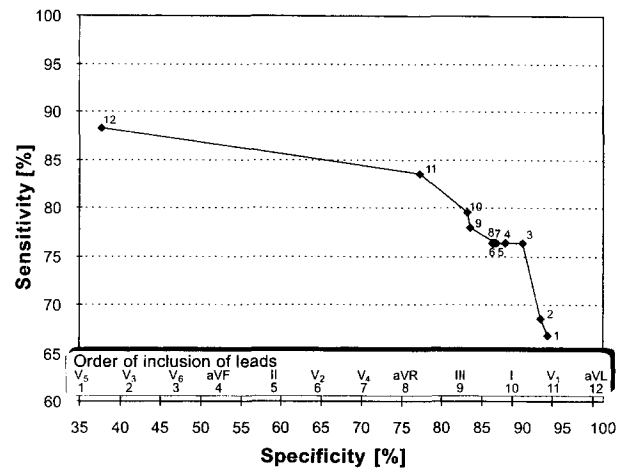

Fig. 4. The sensitivity and specificity values using the fixed 0.01-mV partition criterion for the maximum values of the ST/HR hysteresis defined from each lead sets. The number near to diamonds indicates the number of leads.

Figure 4 presents the sensitivity and specificity values obtained using the fixed 0.01 mV partition criterion for the maximum values of ST/HR hysteresis defined from each established lead set. The figure illustrates the concrete effect arising from the inclusion of the leads in the maximum search procedure from the viewpoint of clinical utilization: Including the leads in the analysis increases the sensitivity, but simultaneously the specificity of the ST/HR hysteresis decreases. Up to 3 leads, the increase rate in sensitivity was much higher than the decrease rate in specificity. After the inclusion of the fourth lead, the decrease in specificity was dominant. A decrease in specificity was noticeable in the case of lead sets A_{11} and A_{12} when the leads V_1 and aVL were included.

Figure 5 presents the sensitivity values at the fixed 80% specificity and the corresponding partition criteria for each lead set. The increase in sensitivity was very small, and the changes in sensitivity were insignificant up to 8 leads. After the inclusion of the ninth lead, the sensitivity started to diminish rapidly. However, the partition criterion at 80% specificity started to decrease already after the inclusion of the third lead. For lead set A_{11}, the partition criterion at 80% specificity was zero, and in lead set A_{12}, it was −0.01mV, indicating that the ST segment depression values on average were smaller during the recovery phase than in the exercise phase.

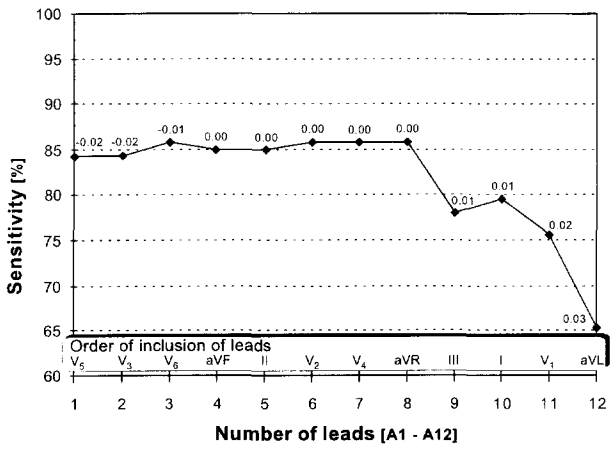

Fig. 5. The sensitivity values at the fixed 80% specificity and the corresponding partition criteria for each lead set.

Discussion

Individual Leads

According to this study, lead V_5 gave the most powerful overall diagnostic performance when using the ST/HR hysteresis in discrimination of patients with and without CAD. This is in accordance with many other studies (13–16), which have shown lead V_5 capable of detecting the majority of ischemic responses when a traditional criterion of 0.10-mV ST-segment depression is used. However, the ROC areas in all leads were very uniform, except in leads aVL and V_1 (the ROC areas were less than 70%). This result supports incontestably the previous finding (8,17) that leads aVL and V_1 are unreliable in the overall discrimination of patients with and without CAD. The obvious reason is that leads aVL and V_1 are quite susceptible to the rotation of the heart. Thus, these leads observe many ischemic responses as an ST segment elevation. Even more crucial is that the ST segment elevations are observed as ST segment depression among patients without CAD (decreasing the specificity).

Lead Sets and the Maximum Value

Several studies have demonstrated an improvement in the detection of CAD using multiple leads during the exercise test (18–21). It is obvious that increasing of the number of leads increases the sensitivity, but often a problem arises due to a decrease in specificity, and the diagnostic accuracy of the lead set does not necessary increase. In this study we noted that using the maximum value of the ST/HR hysteresis determined from the lead sets with different numbers of leads, the diagnostic capacities increased when more leads were included. However, this improvement reached the optimum with 3 to 5 leads, and after 8 leads the diagnostic capacities started to decrease considerably.

In this kind of population, the specificity of the test should be kept at a high level to avoid unnecessary further examinations. When observing the sensitivity values at the fixed 80% specificity in different lead sets, it was noted that the sensitivity remained equal up to 8 leads (Fig. 5), but at the same time the partition criterion decreased by 50%. The first impression might be that the maximum search procedure is not practical, and using the ST/HR hysteresis a single lead would be sufficient for the detection of CAD. However, this study also indicated that when the number of leads in the maximum search procedure is increased and the fixed partition criterion is used, the sensitivity of the ST/HR hysteresis was able to improve significantly without any marked decrease in specificity (Fig. 4). Of course, it must be kept in mind that the improvement in diagnostic accuracy depends greatly on the population with which we are working (ie, on the prevalence of CAD). It seems that for screening the use of several leads with the maximum search procedure is problematic, but for clinical utilization with patients who have been referred for exercise testing, the diagnostic accuracy of the ST/HR hysteresis can be improved significantly with the maximum search procedure. The optimum solution would be to specify the individual partition criteria for the different leads, but this requires a very large and carefully examined study population. However, particular attention should be paid to the selection of the leads if the maximum value of the ST/HR hysteresis is used over the different leads.

Conclusion

This study indicates that the selection of leads has a major importance when using the maximum value of the ST/HR hysteresis over the leads in the detection of CAD. It was possible to increase the diagnostic capacity of ST/HR hysteresis by anything from 4 up to a maximum of 8 leads. After that it started to decrease rapidly. Lead V_5 had the most powerful diagnostic capacity, whereas leads aVL and V_1 were very deficient and they should be

excluded when using the maximum value over the lead set.

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