Evaluation of Electrocardiographic Leads Using Conventional ST-segment Depression and ST-segment Depression/Heart Rate Hysteresis for Diagnosing of Coronary Artery Disease in Women Population: The Finnish Cardiovascular Study

ANONYMIZED

Abstract. Studies have shown that ST-segment depression/heart rate hysteresis improves the limited diagnosing accuracy of exercise electrocardiography in detection of coronary artery disease in women. To the best of our knowledge, the methods developed lack comprehensive comparison of a lead-by-lead basis and have been validated with limited number of female populations. The study aimed to evaluate the effect of the 12 electrocardiographic leads on the diagnostic performance of ST-segment depression/heart rate hysteresis and the traditional ST-segment depression at maximum exercise. This study analyzed 239 women participating in the Finnish Cardiovascular Study. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the overall diagnostic performance. The areas under the ROC curve for ST-segment depression/heart rate hysteresis in all leads were more than 80%, while leads V1 and aVL achieved the smallest area, 73% and 33% respectively. Almost all leads for the conventional ST-segment depression at peak achieved below 70% areas under the ROC curve. At 80% of specificity, the sensitivity values obtained for the variable ST-segment depression/heart rate hysteresis were promising in all leads except in leads V1 and aVL. This study suggests that except leads V1 and aVL, all leads can be applied when ST-segment depression/heart rate hysteresis is used for diagnosing of coronary artery disease in women. The diagnostic performance of conventional ST-segment depression at peak exercise was limited for diagnosing of coronary artery disease in women.

Keywords: electrocardiographic leads, coronary artery disease, ST/HR hysteresis, women.

1 Introduction

Previous studies revealed that conventional ST-segment depression at peak exercise showed limited diagnostic accuracy, about 70% at positive criterion of 0.1mV for detection of coronary artery disease (CAD) [1,2]. ST-segment depression/heart rate (ST/HR) hysteresis improves the identification of CAD when compared with other methods [1-7]. However, most of these studies mainly included men, and few studies that considered women made the analysis with limited number of female populations. Beside this, these studies missed to consider the effect of the 12 electrocardiographic (ECG) leads on the diagnostic performance of ST/HR hysteresis in women population.

This indicates that further studies should be conducted to validate the performance of ST/HR hysteresis in a larger women population in all ECG leads. The objective of this study was to evaluate ECG leads using ST-segment depression and ST/HR hysteresis for diagnosing of CAD in women population**.**

2 Materials and methods

2.1 Study cohort

A total of 239 women (mean age, 56.1 ± 14.0 years) who participated in the Finnish Cardiovascular Study data cohort (FINCAVAS) [8] was analyzed. The patients were divided into two groups; angiographically proven CAD (CAD) and low likelihood of CAD (LLC) based on angiography-proven results and clinical history, respectively. The CAD study category comprised 138 patients who had previously undergone angiography and had ≥ 50% luminal diameter narrowing in at least one major epicardial coronary artery. 101 female patients who did not use any cardiac medications, had low probability of CAD after the exercise test based on the opinion of a supervising physician and who did not report chest pain during the exercise test were included in the LLC group.

The exercise ECG stress tests were performed at Tampere University Hospital using a bicycle ergometer with electrical brakes, wherein the Mason–Likar modification of the standard 12-lead system was applied [9]. The entire exercise test covered the resting phase where in the patient was laid in the supine position for 10 min until the recovery phase, that was started immediately after the exercise phase and lasted at least 5 min after the exercise. The initial workload was 20-30 W and the load was increased stepwise by 10-20 W every minute.

Diagnostic ECG Variables: The variables used in this study were ST/HR hysteresis and ST-segment depression at peak exercise. All the 12 leads were involved and analyzed for the variables used for diagnosing of CAD in women population. ST/HR hysteresis and ST-segment depression at peak exercise were analyzed for each lead from the data recorded at 500 Hz with modified CASE/CardioSoft software (V.1.84; GE Healthcare, Freiburg, Germany).

ST/HR hysteresis: The novel diagnostic variable, S/HR hysteresis, associates the magnitude of conventional ST-segment depression and heart rate (HR). The variable utilizes both exercise and postexercise recovery phase of exercise ECG test to improve the performance of diagnosis CAD. Integration of the difference in ST-segment depression between the exercise and recovery phases over the HR from the three minutes HR of recovery to the maximum HR of the exercise test was the first step to calculate the variable ST/HR hysteresis. Then, the integral obtained from the first step was divided by the HR difference over the integration interval to normalize the ST/HR hysteresis with respect to the recovery HR decrement. The final output obtained was ST/HR hysteresis with dimension in millivolt (mV) [3].

ST-segment depression: The conventional ST-segment amplitudes were measured to the nearest 10 μV at a point 60 ms after the QRS offset (J-point) on a computerized exercise ECG system. This study used ST-segment depression values at peak exercise (STpeak). The recommended positive test criterion is ≥1.0 mm ST depression, i.e. ≤−0.1 mV ST-segment value.

Statistical analysis. Kolmogorov-Smirnov (K–S) test was applied to check normal distribution of the variables. Accordingly, non-normal distribution was observed between all variables except age ($p = 0.200$) in both CAD and LLC study group and HR max ($p = 0.200$) in LLC. Homogeneity of the variables was tested using non-parametric Levene's test. Age, body mass index (BMI), not active smoker, and Max workload are equal in both study group while the rest variables were significantly different. The mean values with standard deviations were calculated for continuous study variables. The Chi-square test was performed for the comparison of discrete variables of the exercise test and the analysis of significant differences between CAD and LLC groups in the clinical characteristics of the study data. Quantitative variables were examined using an independent sample *t*-test; if the distribution was not normal, the Mann–Whitney U test was used. To evaluate the diagnostic ability of the study variables, ST/HR hysteresis and the traditional ST-segment depression in the 12 ECG leads, the receiver operating characteristic (ROC) curves were used, and the values of the area under the curves were calculated. The sensitivity values at 80% specificity and the cut-off points that yield specificity of 80% in all leads for both variables were determined. All tests were considered significant at the level of $\alpha \leq 0.05$. Statistical analysis was performed using IBM SPSS Statistics (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp).

3. Results

3.1. Clinical characteristics of the study population

Table 1 presents the clinical characteristics and statistical comparisons between the CAD and LLC study groups. Age, BMI, maximum heart rate (HRmax), and maximum (max) workload are expressed as mean ± standard deviation, whereas other parameters are presented as percentages. The patients in the CAD category were older, more often on cardiac medication, had a history of acute myocardial infarction, had lower HR max, more often had diabetes than those in the LLC categories ($p < 0.001$). The LLC patients had lower BMI, did not use any cardiac medications, did not report chest pain during exercise, and Max workload was higher when compared with the CAD group ($p < 0.001$).

Table 1. Mean, standard deviation, percentages, and p-values of clinical characteristics of the study groups.

Characteristics	CAD (n=138)	LLC (n=101)	p-values
Age (years)	62.4 ± 9.9	46.7 ± 13.6	< 0.001
BMI (kg/m^2)	28.4 ± 5.1	25.8 ± 5.1	< 0.001
Not active smoker (%)	84.1	78.2	0.277
Diabetes, type 2 (%)	14.5	1.0	< 0.001
HR max (beats/min)	134.9 ± 28.7	168.2 ± 16.6	< 0.001
Max workload (watts)	84.6 ± 37.2	124.5 ± 41.2	< 0.001
History of MI (%)	13.8	0	0.001
Chest pain in ET (%)	15.9	0	< 0.001
ATR antagonists (%)	15.2	0	< 0.001
Diuretics (%)	29.7	0	< 0.001
ACE (%)	28.3	0	< 0.001
Ca channel blockers (%)	23.2	0	< 0.001
β-blockers (%)	84.8	0	0.001

CAD, coronary artery disease; LLC, low likelihood of CAD; n, number of patients; BMI, body mass index; MI, myocardial infarction; HR, heart rate; ACE, angiotensin-converting enzyme; ATR, angiotensin II receptor; ET, exercise test.

Electrocardiography variables. The areas under the ROC curves of the 12 ECG leads for the ST/HR hysteresis and for the conventional ST-segment depression are presented in Fig. 1 and Fig. 2, respectively. ST/HR hysteresis showed good diagnostic performance (ROC area ≥ 80%) in all leads, except in leads V1 and aVL. On the other hand, only lead I showed moderate performance (ROC area ≥ 70%) for the variable ST-segment depression at maximum exercise to diagnose CAD in women.

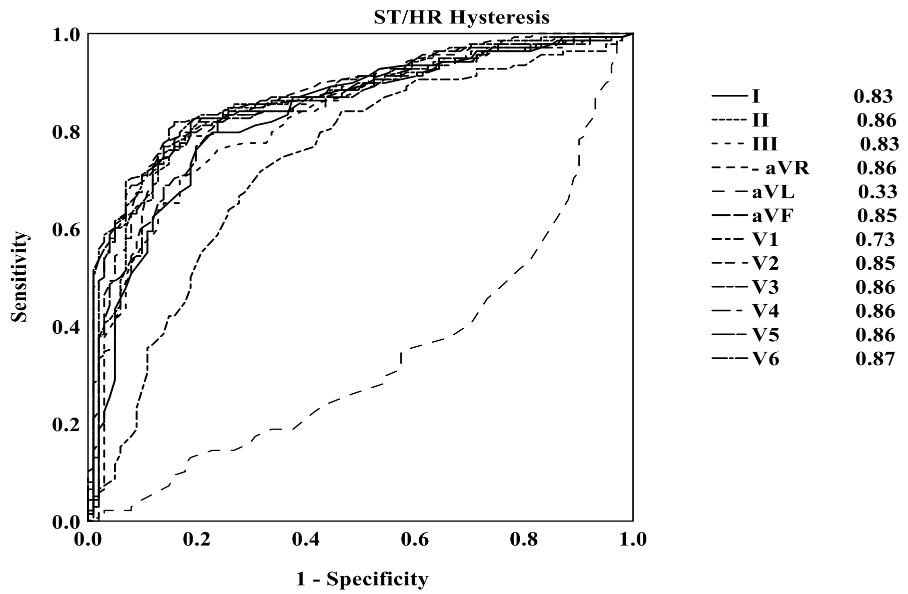

Fig. 1. The receiver operating characteristic (ROC) curves and areas under the curves for ST/HR hysteresis

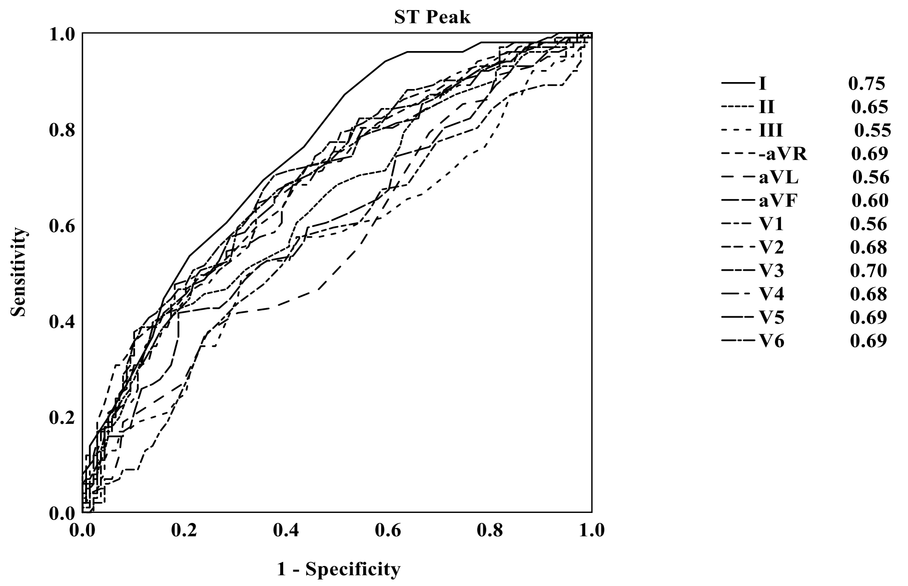

Fig. 2. The receiver operating characteristic (ROC) curves and areas under the curves for ST-segment depression at peak exercise.

Table 2 presents the sensitivity at 80% specificity and cut-off points that yield specificity of 80% of all leads for the ST/HR hysteresis and ST-segment depression at peak exercise. When sensitivity values of the variables at 80% specificity were compared for the ST/HR hysteresis, only leads V1 and aVL had remarkably lower sensitivity while all the rest leads had good sensitivity values between (71.7-82.6%). The sensitivity values obtained by the conventional ST-segment depression were below 50% for all leads, except for lead I, 53.5%.

Table 2. Sensitivity values at 80% specificity (%) and cut-off points at 80% of specificity of 12 electrocardiography leads for ST/HR hysteresis and ST-segment depression at peak exercise.

Leads	ST/HR Hysteresis		ST_{Peak}	
	Sensitivity at 80% specificity (%)	Cut-off points at 80% specificity (mV)	Sensitivity at 80% specificity (%)	Cut-off points at 80% specificity (mV)
I	76.1	0.00	53.5	-0.00
II	81.2	-0.02	43.5	-0.01
III	71.7	-0.02	24.8	0.01
-aVR	81.9	-0.01	48.5	0.01
aVL	13.8	0.02	27.0	0.03
aVF	76.8	-0.02	41.6	0.00
V1	55.1	-0.01	29.0	0.09
V2	79.0	-0.04	44.0	0.11
V3	80.4	-0.05	46.0	0.09
V4	79.7	-0.04	49.0	0.04
V5	82.6	-0.03	47.0	-0.01
V6	82.6	-0.02	45.0	-0.02

4. Discussion and conclusion

The results of this study indicate that ST/HR hysteresis shows improved diagnostic performance in diagnosing CAD in women when compared with ST-segment depression at peak exercise. The ROC analysis suggests that all the 12 ECG leads except, leads V1 and aVL have promising ability to discriminate CAD patients from patients with a low likelihood of CAD for ST/HR hysteresis. Only lead I shows moderate CAD identification capacity for ST-segment depression at peak exercise. Almost all ECG leads achieve higher sensitivity at 80% specificity for the study variable ST/HR hysteresis. These values were quite low in all leads for ST-segment depression at peak exercise. The results of this study showed that cut-off points that yield 80% of specificity were very similar (from 0.00 to -0.05 mV) for all ECG leads except for lead aVL (0.02) for ST/HR hysteresis. The cut-off points had larger variation in all ECG leads for the ST-segment depression at peak exercise. This implies that appropriate lead and lead-specific cut-off points should be considered when ST-segment depression at maximum exercise is used for detection of CAD.

Analyzing small sample data from single center is a limitation of the paper. In addition, this paper does not provide information on the sensitivity and specificity of the traditional ST-segment depression and ST/HR hysteresis when combined with other diagnostic methods, such as cardiac imaging.

In conclusion, the overall results of this study suggest that ST/HR hysteresis improves markedly the detection of CAD in the female population. The inappropriate overall diagnostic performance of the conventional ST-segment depression at the peak exercise was also observed.

Acknowledgments

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