# Comparing the Efficacy of Electrocardiographic Leads in Recovery Phase in Detecting Coronary Artery Disease in Women

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## Abstract

*Different methods have been suggested to improve the limited diagnosing accuracy of exercise electrocardiography in detection of coronary artery disease (CAD) in women. To the best of our knowledge, the methods developed lack comprehensive comparison of a lead-by-lead basis. This study aimed to compare the diagnostic performance of ST segment depression and T wave alternans (TWA) at peak, 1 and 3 min of the recovery phase in leads I, aVL, V1 and V5. The study included 245 women participating in the Finnish Cardiovascular Study. Receiver operating characteristic curve (ROC) curve analysis was performed to evaluate the overall diagnostic performance. The areas under the ROC curve for ST segment depression at peak, 1 and 3 min of the recovery phase in leads I and $V_5$ were more than 80%, while leads $V_1$ and aVL achieved the smallest area. For TWA, the largest areas were obtained at 3 min of the recovery phase. At 80% of specificity, different cut-points were achieved for ST segment depression but the same cut-points for TWA at 1 and 3 min of the recovery phase. This study suggests that the limited diagnostic accuracy of ST segment depression to detect CAD can be improved by determining the appropriate lead and lead specific cut-point selection. TWA rather depends on determining the best time point of recovery phase for diagnosis of CAD in women.*

## 1. Introduction

Previous studies revealed that when using the traditional ST segment depression method used to diagnose CAD, different cut-points should be applied for the different leads [1 - 3]. Besides this, studies [3 - 5] introduced the inclusion of the recovery phase in the analysis to increase the diagnostic capacity of the exercise test. However, these studies mainly included men, and women were under-represented. This indicates that further studies should be conducted to investigate appropriate cut points for specific leads to increase the performance of conventional ST segment depression.

The objective of this study was to compare the diagnostic performances of electrocardiographic leads I, aVL, V1 and V5, and the effect of lead selection on the analyses of ST segment depression and TWA in the discrimination of patients with angiographically proven CAD and patients with a low likelihood of CAD.

## 2. Materials and methods

### 2.1. Study cohort

The Finnish Cardiovascular Study data cohort (FINCAVAS) [6] was analyzed in this study. A total of 245 women (mean age, 56.1 ± 14.0 years) participated in the study. 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. The CAD study category comprised 138 female patients who had previously undergone angiography and had ≥ 50% luminal diameter narrowing in at least one major epicardial coronary artery. The criterion of a time difference between the exercise ECG and angiography was less than 180 days. 107 women were included in LLC study category. 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 this study category.

The exercise ECG stress tests were performed at Tampere University Hospital (TAUH) using a bicycle ergometer with electrical brakes, wherein the Mason–Likar modification of the standard 12-lead system was applied [7]. 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 20-30W and the load was increased stepwise by 10-20W every minute. The amplitudes of ST segment depression and TWA were determined using Cardiac Assessment System for Exercise Testing (CASE) (GE Healthcare) of the recovery phase in leads I, aVL, V1 and V5.

## 2.2. Statistical analysis

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 samples Student's t-test. To evaluate the diagnostic ability of the study variables, ST segment depression and TWA at peak, 1 and 3 min of recovery 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 cut off values that yield specificity of 80% of leads I, aVL, V1 and V5 for the ST segment depression and TWA at peak, 1 and 3 min of the recovery phase 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 26.0. Armonk, NY: IBM Corp).

Table1. Mean, standard deviation, percentages, and p values of clinical characteristics of the study groups. The p values compare the CAD and LLC groups.

| Characteristics | CAD (n=138) | LLC (n=107) | *P* value |
|---|---|---|---|
| Age (years) | 62.8 ± 9.9 | 46.9 ± 13.5 | < 0.001 |
| BMI (kg/m$^2$) | 28.3 ± 5.0 | 25.8 ± 5.1 | < 0.001 |
| Not active smoker (%) | 84.5 | 78.8 | 0.252 |
| Diabetes, type 2 (%) | 15.1 | 1.0 | < 0.001 |
| HR max (beats/min) | 134.9 ± 29.5 | 167.6± 16.9 | < 0.001 |
| Max workload (watts) | 84.5 ± 38.4 | 123.6 ± 40.9 | < 0.001 |
| History of MI (%) | 14.6 | 0 | 0.001 |
| Chest pain in ET (%) | 16.2 | 0 | < 0.001 |
| ATR antagonists (%) | 14.8 | 0 | < 0.001 |
| Diuretics (%) | 29.6 | 0 | < 0.001 |
| ACE %) | 28.2 | 0 | < 0.001 |
| β-blockers (%) | 85.2 | 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.

# 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, body mass index (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 ($p < 0.001$).

## 3.2. Electrocardiography Variables

The area under the ROC curves of leads V5, I, V 1, and aVL for the ST segment depression and TWA at peak, 1 and 3 min of the recovery phase are presented in Fig. 1. For ST segment depression, leads V5 and I showed good diagnostic performance while leads V1 and aVL showed limited performance to detect CAD in the female population. On the other hand, regarding TWA, leads V1 and aVL showed good performance at 1 and 3 min of the recovery phase.

Table 2 presents areas under ROC curves, the sensitivity at 80% specificity and cut off values that yield specificity of 80% of leads V5, I, V1 and aVL for the ST segment depression and TWA at peak, 1 and 3 min of the recovery phase. When sensitivity values of the variables at 80% specificity were compared (Table 2), lead I had quite good sensitivity of 70%, 73% and 76% at peak, 1 and 3 min, respectively of the recovery phase for ST segment depression. The corresponding values for lead V5 were 66%, 63% and 63%. Leads V1 and aVL had remarkably lower sensitivity at a level of 20–40%. Promising sensitivity values were obtained at 80% specificity for the variable TWA at 3 min of the recovery phase for each selected lead, V5 (75%), I (70%), V1 (71%) and aVL (77%). At 1 min of the recovery phase for TWA, sensitivity values at 80 % specificity were 62%, 64%, 65% and 62% for leads V5, I, V1 and aVL respectively, whereas the corresponding sensitivity values at peak of the recovery phase for the selected leads were below 50%.

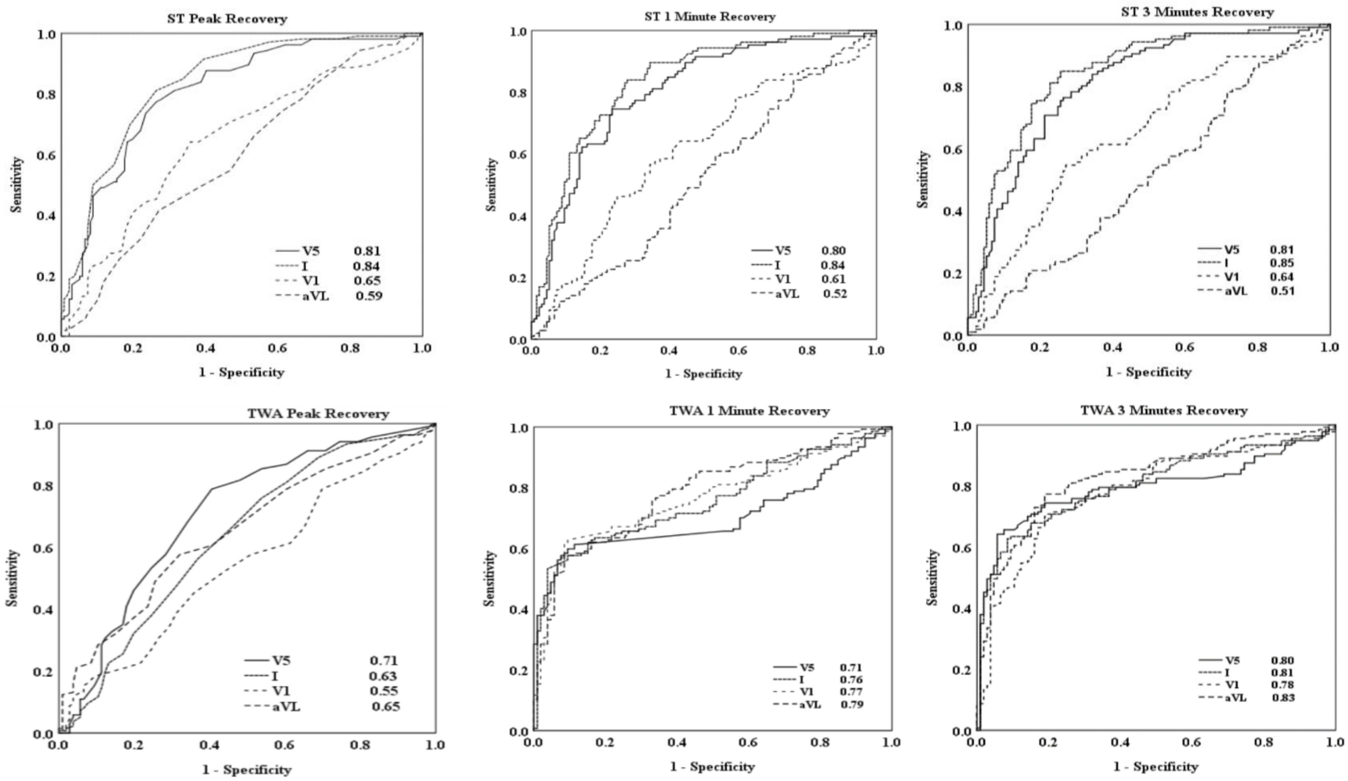


Figure 1. The receiver operating characteristic (ROC) curves and areas under the curves for ST segment depression at peak, 1 and 3 min of the recovery phase, respectively (row 1), and for TWA at peak, 1and 3 min of the recovery phase, respectively (row 2) in leads V5, I, V1 and aVL.

Table 2. The areas under receiver operating characteristics (ROC) curves, sensitivity values at 80% specificity (%) and cut-off points at 80% of specificity of leads V5, I, V1 and aVL for ST segment depression and TWA at peak, 1 and 3 min of the recovery phase.

| | ST peak rec | ST 1 rec | ST 3 rec | TWA peak rec | TWA 1 rec | TWA 3 rec |
|---|---|---|---|---|---|---|
| **Lead V5** ROC area | 0.81 | 0.80 | 0.81 | 0.71 | 0.71 | 0.80 |
| Sensitivity at 80% specificity | 66 | 63 | 63 | 46 | 62 | 75 |
| Cut-off points at 80% specificity (mV) | 0.05 | 0.02 | 0.03 | 0.01 | 0.00 | 0.00 |
| **Lead I** ROC area | 0.84 | 0.84 | 0.85 | 0.63 | 0.76 | 0.81 |
| Sensitivity at 80% specificity | 70 | 73 | 76 | 32 | 64 | 70 |
| Cut-off points at 80% specificity (mV) | 0.02 | 0.00 | 0.00 | 0.01 | 0.00 | 0.00 |
| **Lead V1** ROC area | 0.65 | 0.61 | 0.64 | 0.55 | 0.77 | 0.78 |
| Sensitivity at 80% specificity | 41 | 34 | 37 | 23 | 65 | 71 |
| Cut-off points at 80% specificity (mV) | 0.12 | 0.10 | 0.10 | 0.02 | 0.00 | 0.00 |
| **Lead aVL** ROC area | 0.59 | 0.52 | 0.51 | 0.35 | 0.79 | 0.83 |
| Sensitivity at 80% specificity | 32 | 21 | 21 | 37 | 62 | 77 |
| Cut-off points at 80% specificity (mV) | 0.04 | 0.02 | 0.02 | 0.01 | 0.00 | 0.00 |

STpeakrec = ST-segment value at peak recovery; ST1rec = ST-segment value at one minute recovery; ST3rec = ST-segment value at 3 min recovery; TWApeakrec = TWA value at peak recovery; TWA1rec = TWA value at one minute recovery; TWA3rec = TWA value at 3 min recovery.

## 4. Discussion and conclusion

The results of this study indicate that the performance of ST segment depression in diagnosing CAD in women depends both on the lead selection and on the definition of cut-off values for the selected leads of the recovery phase. These results are in line with results from the previous studies [1,2,8]. On the other hand, TWA seems to be relatively insensitive with respect to lead selection and the lead-specific cut-off points for CAD diagnosis in women. Beside this, the results obtained from this study reveal that leads V1 and aVL that show limited performance to detect CAD for ST segment depression significantly increase the diagnostic performance of exercise electrocardiography in the detection of CAD in women at 1 and 3 min of the recovery phase regarding TWA.

Referring to the ROC curves for the ST-segment depression at peak, 1 and 3 min of the recovery phase (Fig. 1), chest lead V5 and limb lead I showed the highest diagnostic performance for CAD detection in women. However, this study found different cut-points that yield 80 % of specificity for leads V5 and I at peak, 1 min and 3 min of the recovery phase. The results imply that lead-specific analysis should be considered. The areas under the ROC curves (Fig. 1 and Table 2) for the leads V1 and aVL were very small. This study suggests the exclusion of these leads when the traditional ST segment depression was applied to diagnose CAD in women, which was also supported by previous studies [9,10].

The areas under the ROC curves for TWA indicate that lead and cut-point specific analysis is not as sensitive as the ST segment depression. Areas under the ROC curves for all selected leads are quite similar at 1and 3 min of the recovery phase for the TWA method. From this point of view, the most important results were that the chest lead V1 and limb lead aVL, which had limited performance of CAD detection for ST segment depression, showed very good capacity of CAD detection in this female population at 1 min and even more promising results at 3 min of the recovery phase. The cutoff-values that yield 80% of specificity were the same (0.00) at 1 and 3 min of the recovery phase for all selected leads for the TWA method.

Considering only leads V5, I, V1and aVL in the analysis was one of the limitations of this study. Since the analysis is only at the recovery phase, the study did not consider the TWA value at heart rate < 125 beats per minute should be taken for the analysis.

In conclusion, the results of this study suggest that appropriate lead and lead-specific cut-off points should be considered whenever conventional ST segment analysis is used for detection of CAD in the recovery phase. However, when we apply TWA for CAD detection in women, more attention should be given not to the lead and lead specific cut-off points selection but rather what time point of recovery phase should be used for diagnosis.

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