ORIGINAL ARTICLE

Predictive Value of Exercise Stress Test–Induced ST–Segment Changes in Leads V₁ and aVR in Determining Angiographic Coronary Involvement

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Background: The significance of electrocardiographic changes during exercise tolerance testing for distinguishing occluded artery is not well known. We tried to determine the role of ST elevation in leads aVR and V₁ during exercise in detecting stenosis of left main coronary artery and proximal left anterior descending artery.

Methods: ST segment changes during exercise in 230 patients, who underwent diagnostic angiography, were documented. The association of ST elevation in lead aVR, V₁, leads aVR + V₁, and STE in leads aVR + V₁ with ST depression in other leads with pattern of coronary stenosis were investigated.

Results: Left main and proximal left anterior artery stenosis were more common in patients with ST elevation in lead aVR ($P < 0.001$ for both). Similar association was found in the presence of ST elevation in lead V₁. The presence of ST elevation ≥ 1 mm in lead aVR had a sensitivity of 100% and 94.3% for detecting left main and left anterior descending artery stenosis, respectively. The specificity was 33.5% and 26.6%, respectively. ST elevation in leads aVR + V₁ had a sensitivity of 74.4% and 65.9% and a specificity of 68.5% and 64.4% for detecting left main and left anterior descending arteries stenosis, respectively.

Conclusion: ST elevation in lead aVR is highly sensitive for left main and proximal left anterior descending artery lesions. Using ST elevation in lead V₁ in addition to lead aVR as a positive finding increases the specificity with a further decrease in sensitivity.

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exercise test; electrocardiography; coronary artery disease; coronary angiography

INTRODUCTION

Electrocardiographic (ECG) findings during exercise tolerance testing (ETT) provide important information for better management of patients with suspected coronary artery disease (CAD).¹ Although ST segment is frequently evaluated to identify exercise-induced changes,^{1,2} ST segment depression (STD) that is the most common positive finding in ETT does not reveal information about the site of occlusion in coronary arteries.¹ On the other hand, knowing the location of coronary stenosis may influence the therapeutic approach

and estimate the prognosis of the patients.³ Although different criteria on resting ECG have been established for predicting the site of occlusion during acute coronary syndrome,^{4,5} the value of ECG findings during ETT in patients with suspected CAD is not well studied in this regard.

Acute obstruction of left main coronary artery (LMCA) or proximal left anterior descending (LAD) leads to ST segment elevation (STE) in lead aVR.^{6,7} Recently, STE in lead aVR, which is not routinely considered in practice, is suggested as a sign of LMCA or ostial LAD during ETT as well.^{8–12} Moreover, STE in lead V₁ may also provide

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valuable information for detecting the location of stenosis during ETT.^{8–10,13} However, the diagnostic value of these findings is not consistent in different studies.^{10–12,14} Since acute obstruction of LMCA is associated with severe hemodynamic changes and a high mortality rate, timely diagnosis and early proper interventions are of great importance.^{15,16}

Regarding these facts, we sought to investigate the role of exercise-induced ST segment elevation in leads aVR and V₁ alone and in combination, in determining the significant stenosis of LMCA and LAD artery. We also studied the association of these electrocardiographic findings during ETT with resting left ventricular ejection fraction (LVEF) measured by echocardiography.

METHOD AND MATERIALS

In this cohort study, from March 2013 through December 2014, 230 consecutive patients who were candidates for diagnostic coronary angiography and had undergone exercise tolerance testing according to Bruce standard protocol were included. Patients who had electrocardiographic evidence of bundle branch blocks, ventricular hypertrophy, ventricular arrhythmias, or preexcitation syndrome, history of myocardial infarction, coronary artery bypass grafting, or percutaneous coronary intervention were excluded from the study.

Comprehensive demographic data and coronary risk factors as well as the results of two-dimensional echocardiography were recorded for each patient. Based on angiographic data, the involvement of coronary arteries and severity of stenosis were documented in each patient. A cardiologist manually determined the presence and magnitude of electrocardiographic changes in all leads during exercise tolerance testing.

In four separate analysis, patients were grouped based on the magnitude of ST elevation in lead aVR, based on the magnitude of ST elevation in lead V₁, the presence or absence of ST elevation in leads aVR + V₁, and presence or absence of ST elevation in leads aVR + V₁ with concomitant ST depression in other leads. They were compared regarding demographic, echocardiographic, electrocardiographic, and angiographic findings in different settings.

Significant ST depression was considered as horizontal or down-sloping ST depression ≥ 1 mm at 60–80 ms after the J-point. Significant ST elevation (STE) was defined as the development of

J-point elevation ≥ 1 mm at 60 ms after the J-point.¹ In lead aVR, only horizontal or up-sloping STE was considered significant.

A reduction of at least 50 percent of the luminal diameter of coronary artery was considered as significant stenosis. Lesions of LAD artery were allocated into two groups. The lesions from the origin of LAD to the first septal or diagonal branch were defined as proximal and the lesions distal to the first septal or diagonal branch were defined as nonproximal including both middle and distal lesions.

Institutional Review Board Committee at Tabriz University of Medical sciences reviewed and approved the design of the study. The study was exempted from informed consent due to its descriptive design. However, complete patient privacy was maintained during whole study.

Statistical Analysis

Data were analyzed with statistical software SPSS (SPSS Inc. Released 2009. PASW Statistics for Windows, Version 18.0. Chicago, IL, USA). Continuous variables were stated as the mean $\pm$ standard deviation and categorical variables were presented as frequencies and percentages. Chi-square analysis test was used to compare the frequencies of categorical variables. Independent *t*-test was conducted to compare continuous variables among study groups. Sensitivity and specificity analysis were performed using common statistical methods. A P value of <0.05 was considered statistically significant.

RESULTS

Baseline Characteristics

The mean age of 230 studied patients was 55.96 ± 8.91 years. Out of 230 patients, 159 (69.1%) were male and 71 (30.9%) were female. Family history of cardiovascular diseases was present in 29 patients (12.6%) and 64 patients (27.8%) were active smokers. History of hyperlipidemia, history of diabetes mellitus, and history of hypertension were present in 75 patients (32.6%), 44 patients (19.1%), and 119 patients (51.7%), respectively. Body mass index of 30 kg/m^2 or more was present in 17 patients (7.4%). Mean left ventricular ejection fraction in total population was $53.09\% \pm 6.68\%$.

ST elevation ≥ 1 mm in lead V_1 was present in 105 patients (45.7%). The remaining 125 patients (54.3%) did not have significant STE in lead V_1 . ST elevation ≥ 1 mm in lead aVR was present in 166 patients (72.2%). The remaining 64 patients (27.8%) did not have significant STE in lead aVR. Significant STE in both lead aVR and V_1 was present in 89 patients (38.7%). Significant STE in lead aVR and V_1 with concomitant ST depression in other leads was present in 72 patients (31.3%).

Comparison of Patients with and Those without ST Segment Elevation in Lead V_1

The patients were allocated into three groups based on the magnitude of ST segment elevation in lead V_1 . There were no significant differences among three groups, regarding mean age, sex, and prevalence of coronary risk factors. Prevalence of reduced LVEF was not different in patients of three groups (Table 1). Treadmill score ≤ -11 was significantly more common in patients with STE in lead V_1 (78.8% in group with STE ≥ 2 mm, 55.6% in group with $1 \text{ mm} \leq \text{STE} < 2$ mm and 19.2% in group with STE < 1 mm, $P < 0.001$). Mitral regurgitation $> 2+$ was significantly more common in patients with STE in lead V_1 (36.4% in group with STE ≥ 2 mm, 13.9% in group with $1 \text{ mm} \leq \text{STE} < 2$ mm, and 8.8% in group with STE < 1 mm, $P < 0.001$). STD ≥ 1 mm in leads V_4 – V_6 was significantly more prevalent in patients with STE in lead V_1 (84.8% in group with STE ≥ 2 mm, 76.3% in group with $1 \text{ mm} \leq \text{STE} < 2$ mm, and 51.2% in group with STE < 1 mm, $P < 0.001$). STD in inferior leads was also more common in patients with STE in lead V_1 (72.7% in group with STE ≥ 2 mm, 63.8% in group with $1 \text{ mm} \leq \text{STE} < 2$ mm, and 51.2% in group with STE < 1 mm, $P < 0.04$).

Left main coronary artery stenosis was significantly more prevalent in the group with STE in lead V_1 (48.5% in group with STE ≥ 2 mm, 18.1% in group with $1 \text{ mm} \leq \text{STE} < 2$ mm and 8% in group with STE < 1 mm, $P < 0.001$). Significant LAD stenosis and significant left circumflex (LCX) stenosis were also more common in the group with STE in lead V_1 . However, prevalence of significant right coronary artery stenosis was not different.

Considering the lesions of LAD artery, proximal LAD stenosis was significantly more common in patients with STE in lead V_1 (84.8% in group with STE ≥ 2 mm, 62% in group with

$1 \text{ mm} \leq \text{STE} < 2$ mm, and 58% in group with STE < 1 mm, $P < 0.02$) (Table 1).

Comparison of Patients with and Those without ST Segment Elevation in Lead aVR

The patients were allocated into three groups based on the magnitude of ST segment elevation in lead aVR. There were no significant differences among three groups, regarding mean age, sex, and prevalence of coronary risk factors except for prevalence of smoking (43.3% in group with STE ≥ 2 mm, 21.7% in group with $1 \text{ mm} \leq \text{STE} < 2$ mm, 23.4% in group with STE < 1 mm, $P = 0.01$) (Table 2). Prevalence of reduced LVEF was significantly higher in patients with STE in lead aVR (53.3% in group with STE ≥ 2 mm, 37.7% in group with $1 \text{ mm} \leq \text{STE} < 2$ mm, and 26.6% in group with STE < 1 mm, $P < 0.001$). Treadmill score ≤ -11 was significantly more common in patients with STE in lead aVR (73.3% in group with STE ≥ 2 mm, 31.1% in group with $1 \text{ mm} \leq \text{STE} < 2$ mm and 20.3% in group with STE < 1 mm, $P < 0.001$). Mitral regurgitation $> 2+$ was significantly more common in patients with STE in lead aVR (23.3% in group with STE ≥ 2 mm, 13.2% in group with $1 \text{ mm} \leq \text{STE} < 2$ mm, and 7.8% in group with STE < 1 mm, $P = 0.04$). STD ≥ 1 mm in leads V_4 – V_6 was significantly more prevalent in patients with STE in lead aVR (81.6% in group with STE ≥ 2 mm, 65% in group with $1 \text{ mm} \leq \text{STE} < 2$ mm, and 59.3% in group with STE < 1 mm, $P < 0.02$). STD in inferior leads was significantly different in patients of three groups with highest percent in the group with STE ≥ 2 mm (73.3% in group with STE ≥ 2 mm, 51.8% in group with $1 \text{ mm} \leq \text{STE} < 2$ mm, and 54.6% in group with STE < 1 mm, $P = 0.02$).

Left main coronary artery stenosis was significantly more common in the group with STE in lead aVR (41.7% in group with STE ≥ 2 mm, 13.8% in group with $1 \text{ mm} \leq \text{STE} < 2$ mm, and no case in group with STE < 1 mm, $P < 0.001$). Significant LAD stenosis, significant LCX stenosis, and significant right coronary artery (RCA) stenosis were more prevalent in the group with STE in lead aVR (Table 2).

Regarding the site of occlusion in LAD artery, proximal LAD stenosis was significantly more common in patients with STE in lead aVR (90.2% in group with STE ≥ 2 mm, 56.9% in group with

Table 1. Comparison of Patients with Regard to ST Segment Elevation in Lead V₁

	STE <1 mm N = 125 N (%)	1 ≤ STE <2 mm N = 72 N (%)	STE ≥2 mm N = 33 N (%)	P Value
Gender (male)	85 (68)	50 (69.4)	24 (72.7)	0.87
Age (years)	55.82 ± 8.96	55.24 ± 8.30	57.97 ± 9.90	0.34
Smoking	29 (23.2)	23 (31.9)	12 (36.4)	0.21
Family history	14 (11.2)	10 (13.9)	5 (15.2)	0.77
Hyperlipidemia	43 (34.4)	22 (30.6)	10 (30.3)	0.82
Diabetes	20 (16)	13 (18.1)	11 (33.3)	0.08
Hypertension	68 (54.4)	34 (47.2)	17 (51.5)	0.62
Peripheral artery disease	3 (2.4)	0 (0)	3 (9.1)	0.03
Body mass index (≥30)	117 (93.6)	66 (91.7)	30 (90.9)	0.81
Reduced left ventricular ejection fraction (%)	81 (64.8)	44 (61.1)	16 (48.5)	0.23
ST depression ≥1 mm (V ₄ -V ₆ leads)	73 (58.4)	55 (76)	28 (84.8)	<0.001
ST depression ≥1 mm (inferior leads)	64 (51.2)	46 (63.8)	24 (72.7)	0.04
Treadmill Score (≥ -11)	24 (19.2)	40 (55.6)	26 (78.8)	<0.001
Mitral regurgitation >2+	11 (8.8)	10 (13.9)	12 (36.4)	<0.001
Angiographic findings				
1VD	38 (30.4)	21 (29.2)	10 (30.3)	
2VD	21 (16.8)	17 (23.6)	5 (15.2)	
3VD	11 (8.8)	13 (18.1)	2 (6.1)	
Isolated LM	1 (0.8)	0 (0)	0 (0)	
LM + 1VD	3 (2.4)	6 (8.3)	3 (9.1)	
LM + 2VD	5 (4)	3 (4.2)	7 (21.2)	
LM + 3VD	1 (0.8)	4 (5.6)	6 (18.2)	
Minimal	7 (5.6)	1 (1.4)	0 (0)	
Normal	38 (30.4)	7 (9.7)	0 (0)	
LMCA stenosis	10 (8)	13 (18.1)	16 (48.5)	<0.001
LAD stenosis	50 (40)	50 (69.4)	33 (100)	<0.001
RCA stenosis	45 (36)	33 (48.6)	14 (42.4)	0.38
LCX stenosis	36 (28.8)	36 (50)	14 (42.4)	0.01
Site of LAD lesion				
Proximal	29 (58)	31 (62)	28 (84.8)	
Middle/distal	21 (42)	19 (38)	5 (15.1)	0.02
Proximal LAD stenosis >90%	9 (31)	18 (58.1)	19 (70.4)	0.01
RCA chronic total obstruction	8 (6.4)	10 (13.9)	5 (15.2)	0.14
LCX chronic total obstruction	3 (2.4)	4 (5.6)	3 (9.1)	0.20
LAD chronic total obstruction	4 (3.2)	8 (11.1)	9 (27.3)	<0.001
Dominance				
Left	6 (4.8)	4 (5.6)	2 (6.1)	
Codominance	5 (4)	10 (13.9)	6 (18.2)	
Right	114 (91.2)	58 (80.6)	25 (75.8)	0.06
Collateral				
RCA	7 (46.7)	10 (50)	11 (73.3)	
LCX	0 (0)	1 (5)	0 (0)	
LAD	8 (53.3)	9 (45)	4 (26.7)	0.41

1/2/3 VD = 1/2/3 vessel disease; LAD = left anterior descending; LCX = left circumflex artery; LMCA = left main coronary artery; RCA = right coronary artery; STE = ST elevation.

Table 2. Comparison of Patients with Regard to ST Segment Elevation in Lead aVR

	STE <1 mm N = 64 N (%)	1 ≤ STE <2 mm N = 106 N (%)	STE ≥2 mm N = 60 N (%)	P Value
Gender (male)	42 (65.6)	75 (70.8)	42 (70)	0.77
Age (years)	19/9 ± 84/55	14/9 ± 23/56	30/8 ± 60/55	0.9
Smoking	15 (23.4)	23 (21.7)	26 (43.3)	0.01
Family history	7 (10.9)	12 (11.3)	10 (16.7)	0.54
Hyperlipidemia	20 (31.3)	34 (32.1)	21 (35)	0.89
Diabetes	10 (15.6)	19 (17.9)	15 (25)	0.40
Hypertension	34 (53.1)	57 (53.8)	28 (46.7)	0.66
Peripheral artery disease	1 (1.6)	3 (2.8)	2 (3.3)	0.81
Body Mass Index (≥30)	4 (6.3)	7 (6.6)	6 (10)	0.67
Reduced left ventricular ejection fraction	17 (26.6)	40 (37.7)	32 (53.3)	0.01
ST depression ≥1 mm (V ₄ -V ₆ leads)	38 (59.3)	69 (65)	49 (81.6)	0.02
ST depression ≥1 mm (inferior leads)	35 (54.6)	55 (51.8)	44 (73.3)	0.02
Treadmill score (≥ -11)	13 (20.3)	33 (31.1)	44 (73.3)	<0.001
Mitral regurgitation >2+	5 (7.8)	14 (13.2)	14 (23.2)	0.04
Angiography				
1VD	20 (31.3)	38 (35.8)	11 (18.3)	
2VD	8 (12.5)	23 (21.7)	12 (20)	
3VD	2 (3.1)	13 (12.3)	11 (18.3)	
Isolated LM	0 (0)	0 (0)	1 (1.7)	
LM + 1VD	0 (0)	4 (3.8)	8 (13.3)	
LM + 2VD	0 (0)	6 (5.7)	9 (15)	
LM + 3VD	0 (0)	4 (3.8)	7 (11.7)	
Minimal	5 (7.8)	3 (2.8)	(0)0	
Normal	29 (45.3)	15 (14.2)	1 (1.7)	
LMCA stenosis	0 (0)	14 (13.8)	25 (41.7)	<0.001
LAD stenosis	17 (26.6)	65 (61.3)	51 (85)	<0.001
RCA stenosis	14 (21.9)	45 (42.5)	33 (55)	0.001
LCX stenosis	11 (17.2)	43 (40.6)	32 (53.3)	<0.001
Site of LAD lesion				
Proximal	5 (29.4)	37 (56.9)	46 (90.2)	
Middle/distal	12 (66.6)	28 (43.1)	5 (9.8)	<0.001
Proximal LAD stenosis >90%	1 (20)	16 (43.2)	29 (64.4)	0.05
RCA chronic total obstruction	3 (4.7)	9 (8.5)	11 (18.3)	0.03
LCX chronic total obstruction	1 (1.6)	2 (1.9)	7 (11.7)	0.01
LAD chronic total obstruction	4 (6.3)	7 (6.6)	10 (16.7)	0.06
Dominance				
Left	2 (3.1)	6 (5.7)	4 (6.7)	0.34
Codominance	7 (10.9)	8 (7.5)	6 (10)	
Right	55 (85.9)	92 (68.8)	50 (83.3)	

(continued)

Table 2. *Continued*

	STE <1 mm N = 64 N (%)	1 ≤ STE <2 mm N = 106 N (%)	STE ≥2 mm N = 60 N (%)	P Value
Collateral				
RCA	5 (62.5)	7 (43.8)	16 (61.5)	0.12
LCX	1 (12.5)	0 (0)	0 (0)	
LAD	2 (25)	9 (56.3)	10 (38.5)	

1/2/3 VD = 1/2/3 vessel disease; LAD = left anterior descending; LCX = left circumflex artery; LMCA = left main coronary artery; RCA = right coronary artery; STE = ST elevation.

1 mm ≤ STE <2 mm, and 29.4% in group with STE <1 mm, $P < 0.001$).

Comparison of Patients with and Those without ST Segment Elevation in Leads aVR + V₁

The patients were allocated into two groups based on the presence and absence of ST segment elevation in both aVR and V₁ leads. There were no significant differences between two groups, regarding mean age, sex, and prevalence of coronary risk factors (Table 3). Prevalence of reduced LVEF was not significantly different between two groups. Treadmill score ≤−11 was significantly more common in patients with STE in leads aVR + V₁ (65.2% vs 22.7%, $P < 0.001$). Mitral regurgitation >2+ was significantly more common in patients with STE in leads aVR + V₁ (24.7% vs 7.8%, $P = 0.001$). STD ≥1 mm in leads V₄–V₆ was significantly more prevalent in patients with STE in leads aVR + V₁ (80.8% vs 59.5%, $P < 0.001$). STD ≥1 mm in inferior leads was significantly more prevalent in patients with STE in leads aVR + V₁ (66.2% vs 53.1%, $P = 0.04$). LMCA stenosis was present in 32.6% of patients with STE in lead aVR + V₁ and in 7.1% of patients without this finding ($P < 0.001$). LAD stenosis and LCX stenosis were also significantly more prevalent in patients with STE in lead aVR + V₁. LAD stenosis was present in 83.1% of patients with STE in leads aVR + V₁ and it was present in 41.8% of patients without this finding. The prevalence of LCX stenosis was 50.6% in patients with STE in leads aVR + V₁ and it was 29.1% in patients without this finding. Considering the site of stenosis in LAD artery, proximal LAD stenosis was significantly more common in patients with STE in leads aVR + V₁ (78.4% vs 50.8%, $P = 0.003$).

Comparison of Patients with and Those without ST Segment Elevation in Leads aVR + V₁ and Concomitant ST Depression in Other Leads

The patients were allocated into two groups based on the presence and absence of ST segment elevation in aVR + V₁ leads and concomitant ST depression in other leads. There were no significant differences between two groups, regarding mean age, sex, and prevalence of coronary risk factors except for smoking which was more prevalent in patients with STE in leads aVR + V₁ and STD in other leads (Table 4). Prevalence of reduced LVEF was not significantly different between two groups. Treadmill score ≤−11 was significantly more common in patients with STE in leads aVR + V₁ and STD in other leads (75% vs 22.8%, $P < 0.001$). Mitral regurgitation >2+ was significantly more common in patients with STE in leads aVR + V₁ and STD in other leads (22.2% vs 10.8%, $P = 0.02$). STD ≥1 mm in leads V₄–V₆ was significantly more prevalent in patients with STE in leads aVR + V₁ and STD in other leads (100% vs 53.1%, $P < 0.001$). STD ≥1 mm in inferior leads was not significantly different in two groups (65.3% vs 55.1%, $P = 0.14$).

Left main coronary artery stenosis was present in 31.9% of patients with STE in leads aVR + V₁ and STD in other leads and in 10.1% of patients without this finding ($P < 0.001$). LAD stenosis and LCX stenosis were also significantly more prevalent in patients with STE in leads aVR + V₁ and STD in other leads. LAD stenosis was present in 68.1% of patients with STE in leads aVR + V₁ and STD in other leads and it was present in 44.9% of patients without this finding. The prevalence of LCX stenosis was 52.8% in patients with STE in leads aVR + V₁ and STD in other leads and 30.4% in patients without this finding. Proximal LAD culprit lesion was

Table 3. Comparison of Patients with Regard to ST Segment Elevation in Leads aVR + V₁

	ST Elevation in Leads aVR + V ₁		P Value
	No N = 141 N (%)	Yes N = 89 N (%)	
Gender (male)	96 (68.1)	63 (70.8)	0.67
Age (years)	56.38 ± 9.04	55.70 ± 8.85	0.57
Smoking	34 (24.1)	30 (33.7)	0.11
Family history	16 (11.3)	13 (14.6)	0.50
Hyperlipidemia	49 (34.9)	26 (29.2)	0.38
Diabetes	22 (15.6)	22 (24.7)	0.09
Hypertension	76 (53.9)	43 (48.3)	0.41
Peripheral artery disease	3 (2.1)	3 (3.4)	0.70
Body mass index (≥30)	9 (6.4)	8 (9)	0.46
Reduced left ventricular ejection fraction	48 (34)	41 (46.1)	0.07
ST depression ≥1 mm (V ₄ –V ₆ leads)	84 (59.5)	72 (80.8)	<0.001
ST depression ≥1 mm (inferior leads)	75 (53.1)	59 (66.2)	0.04
Treadmill score (≥ –11)	32 (22.7)	58 (65.2)	<0.001
Mitral regurgitation >2+	11 (7.8)	22 (24.7)	<0.001
Angiographic findings			
1VD	44 (31.2)	25 (28.1)	
2VD	25 (17.7)	18 (20.2)	
3VD	13 (9.2)	13 (14.6)	
Isolated LMCA	1 (0.7)	0 (0)	
LMCA + 1VD	3 (2.1)	9 (10.1)	
LMCA + 2VD	5 (3.5)	10 (11.2)	
LMCA + 3VD	1 (0.7)	10 (11.2)	
Minimal	7 (5)	1 (1.1)	
Normal coronary	42 (29.8)	3 (3.4)	
LMCA stenosis	10 (7.1)	29 (32.6)	<0.001
LAD stenosis	59 (41.8)	74 (83.1)	<0.001
RCA stenosis	51 (63.2)	41 (46.1)	0.14
LCX stenosis	41 (29.1)	45 (50.6)	0.001
Site of LAD lesion			
Proximal	30 (50.8)	58 (78.4)	
Middle/distal	29 (49.2)	16 (21.6)	0.003
Proximal LAD stenosis ≥90%	9 (30)	37 (64.9)	0.002
RCA chronic total obstruction	10 (7.1)	13 (14.6)	0.06
LCX chronic total obstruction	4 (2.8)	6 (6.7)	0.19
LAD chronic total obstruction	6 (4.3)	15 (16.9)	0.001
Dominance			
Left	7 (5)	5 (5.6)	
Codominance	8 (5.7)	13 (14.6)	
Right	126 (89.4)	71 (79.8)	0.07

(continued)

Table 3. *Continued*

	ST Elevation in Leads aVR + V ₁		P Value
	No N = 141 N (%)	Yes N = 89 N (%)	
Collateral			
RCA	10 (50)	18 (60)	
LCX	1 (5)	0 (0)	
LAD	9 (45)	12 (40)	0.41

1/2/3 VD = 1/2/3 vessel disease; LAD = left anterior descending; LCX = left circumflex artery; LMCA = left main coronary artery; RCA = right coronary artery.

significantly more common in patients with STE in leads aVR + V₁ and concomitant STD in other leads. (79% vs 54.9%, $P = 0.003$).

Sensitivity, Specificity, Positive Predictive Value (PPV), and Negative Predictive Value (NPP) of Electrocardiographic Findings for Detecting LMCA Stenosis and LAD Stenosis

The presence of STE ≥ 1 mm in lead aVR had sensitivity of 100% and specificity of 33.5% for detecting LMCA stenosis. The presence of STE ≥ 1 mm in lead V₁ had sensitivity of 74.6% and specificity of 60.2% for detecting LMCA stenosis. When considering STE in both leads aVR and V₁ as the positive ECG finding, sensitivity and specificity for detecting LMCA stenosis were 74.4% and 68.5%, respectively. The presence of STE in leads aVR + V₁ with STD in other leads had a sensitivity of 59% and specificity of 74.4% for detecting LMCA lesions (Table 5).

The presence of STE ≥ 1 mm in lead aVR had sensitivity of 94.3% and specificity of 26.6% for detecting proximal LAD stenosis. The presence of STE ≥ 1 mm in lead V₁ had sensitivity of 67% and specificity of 46.6% for detecting proximal LAD stenosis. By considering STE in both leads aVR and V₁ as the positive ECG finding, sensitivity and specificity for detecting proximal LAD stenosis were 65.9% and 64.4%, respectively. The presence of STE in lead aVR + V₁ with STD in other leads had a sensitivity of 55.6% and specificity of 71.1% for detecting proximal LAD lesions (Table 5).

DISCUSSION

According to the results of this study, exercise-induced ST segment elevation in lead aVR as well

as in lead V₁ is useful for identifying significant LMCA and proximal LAD stenosis. Although diagnostic angiography is the definite test to determine the site of occlusion in patients with CAD,¹⁷ as shown in this study, ECG changes during ETT may also be helpful for distinguishing the occluded artery at an earlier time. For this reason, the significance of ST segment elevation during ETT in lead aVR or V₁ for differentiating proximal LAD or LMCA stenosis is emphasized recently.^{9–14,18,19}

Lead aVR is assumed as an intracavitary lead, which looks toward the atria from the apex and can be derived from leads I and II. In fact, counterclockwise progression from lead II to lead I constitutes the perspective that inverted aVR represents. Although lead aVR is a calculated lead, the contained information improves clinical recognition of ECG patterns.²⁰ STE in lead aVR may result from proximal LAD occlusion due to transmural ischemia in the basal portion of the interventricular septum. LMCA stenosis or multi-vessel disease may also cause STE in lead aVR by global subendomyocardial ischemia during acute coronary syndrome.²¹

The results of this study imply that in patients with suspected CAD, stenosis of LMCA and LAD artery is associated with ST segment elevation in lead aVR and V₁ during ETT. The presence of STE in lead aVR is highly sensitive for LMCA lesions and in the absence of STE in lead aVR stenosis of LMCA is unlikely. However, considering a specificity of 33.5%, the presence of STE in lead aVR cannot reliably confirm the LMCA stenosis. Even in the presence of STE ≥ 2 mm in lead aVR, only 41.7% of the patients had significant stenosis in LMCA. Nevertheless, the presence of STE in both leads (aVR + V₁) increases the specificity for LMCA stenosis to 68.5%.

Table 4. Comparison of Patients with Regard to ST Segment Elevation in Leads aVR + V₁ with Concomitant ST Depression in Other Leads

	ST Elevation in Leads aVR + V ₁ and ST Depression in Other Leads		P Value
	No N = 158 N (%)	Yes N = 72 N (%)	
Gender (male)	105 (66.5)	54 (75)	0.19
Age (years)	45/9 ± 84/56	66/8 ± 56/55	0.32
Smoking	37 (23.4)	27 (37.5)	0.03
Family history	18 (11.4)	11 (15.3)	0.41
Hyperlipidemia	55 (34.8)	20 (27.8)	0.29
Diabetes	25 (15.8)	19 (26.4)	0.06
Hypertension	84 (53.2)	35 (48.6)	0.52
Peripheral artery disease	3 (1.9)	3 (4.2)	0.38
Body mass index (≥30)	10 (6.3)	7 (9.7)	0.36
Reduced left ventricular ejection fraction	57 (36.1)	32 (44.4)	0.23
ST depression ≥1 mm (V ₄ -V ₆)	84 (53.1)	72 (100)	<0.001
ST depression ≥1 mm (inferior leads)	87 (55.1)	47 (65.2)	0.14
Treadmill score (≥ -11)	36 (22.8)	54 (75)	<0.001
Mitral regurgitation >2+	17 (10.8)	16 (22.2)	0.02
Angiographic findings			
1VD	49 (31)	20 (27.8)	
2VD	27 (17.1)	16 (22.2)	
3VD	15 (9.5)	11 (15.3)	
Isolated LMCA	1 (0.6)	0 (0)	
LMCA + 1VD	6 (3.8)	6 (8.3)	
LMCA + 2VD	7 (4.4)	8 (11.1)	
LMCA + 3VD	2 (1.3)	9 (12.5)	
Minimal	7 (4.4)	1 (1.4)	
Normal	44 (27.8)	1 (1.4)	
LMCA stenosis	16 (10.1)	23 (31.9)	<0.001
LAD stenosis	71 (44.9)	62 (68.1)	<0.001
RCA stenosis	57 (36.1)	35 (48.6)	0.07
LCX stenosis	48 (30.4)	38 (52.8)	0.001
Site of LAD lesion			
Proximal	39 (54.9)	49 (79)	
Middle/distal	32 (45.1)	13 (21)	0.003
Proximal LAD stenosis >90%	16 (41)	30 (62.5)	0.05
RCA chronic total obstruction	12 (7.6)	11 (15.3)	0.07
LCX chronic total obstruction	5 (3.2)	5 (6.9)	0.29
LAD chronic total obstruction	10 (6.9)	11 (15.3)	0.03
Dominance			
Left	7 (4.4)	5 (6.9)	
Codominance	10 (6.3)	11 (15.3)	
Right	141 (89.2)	56 (77.8)	0.06

(continued)

Table 4. *Continued*

	ST Elevation in Leads aVR + V ₁ and ST Depression in Other Leads		P Value
	No N = 158 N (%)	Yes N = 72 N (%)	
Collateral			
RCA	14 (56)	14 (56)	
LCX	1 (4)	0 (0)	
LAD	10 (40)	11 (44)	0.59

1/2/3 VD = 1/2/3 vessel disease; LAD = left anterior descending; LCX = left circumflex artery; LMCA = left main coronary artery; RCA = right coronary artery.

Regarding the diagnostic value of ETT for detecting proximal LAD stenosis, STE in lead aVR has a high sensitivity of 94.3% but a low specificity of 26.6%. However, the presence of STE in lead V₁ in addition to STE in lead aVR increases the specificity of the finding for confirming the proximal LAD stenosis. Furthermore, a positive ETT result with concomitant STE in leads aVR + V₁ increases the specificity and decreases the sensitivity for detecting proximal LAD or LMCA stenosis.

The findings of various studies regarding the association of STE in lead aVR and V₁ during

ETT with LMCA or LAD stenosis are consistent with our results.^{9–14,18,19} Michaelides et al. have investigated the significance of ST deviation in lead V₁ in ETT for localizing the site of stenosis in 198 patients with single-vessel disease. Their study revealed the association of STE in lead V₁ with LAD occlusion.¹³ In another study by Michaelides et al. STE in lead aVR with concomitant STD in lead V₅ during ETT was indicative of LAD occlusion in patients with single-vessel disease.¹⁹ In an article published by Neill et al.,¹⁸ STE in lead aVR during ETT in patients with chest pain, was related to the ischemia of anterior

Table 5. Sensitivity, Specificity, Positive Predictive Value, and Negative Predictive Values for Detecting Stenosis of Left Main Coronary Artery, Left Anterior Descending Artery, and Its Proximal Lesions

	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
For left main coronary artery				
STE (V ₁)	74.6	60.2	27.6	92
STE (aVR)	100	33.5	23.5	100
STE (V ₁ + aVR)	74.4	68.5	32.6	92.9
STE (V ₁ + aVR) + STD (others)	59	74.4	31.9	90
For left anterior descending				
STE (V ₁)	62.4	77.3	79.1	60
STE (aVR)	87.2	48.5	70	73.4
STE (V ₁ + aVR)	55.6	85.4	83.2	58.2
STE (V ₁ + aVR) + STD (others)	46.6	89.7	86.1	55.1
For proximal left anterior descending ^a				
STE (V ₁)	67	46.6	71	42
STE (aVR)	94.3	26.6	71.5	70.5
STE (V ₁ + aVR)	65.9	64.4	78.3	49.1
STE (V ₁ + aVR) + STD (others)	55.6	71.1	79	45

STD = ST depression; STE = ST elevation. ^aThe values are calculated for distinguishing proximal versus nonproximal lesions in patients with left anterior descending artery stenosis.

ventricular wall detected by (99 m) Tc-sestamibi scanning, and also LAD lesions. Rostoff et al. published an article in which exercise induced STE in lead aVR and V₁ in patients with chronic stable angina, and strongly positive exercise test results was assessed. In their study, isolated STE in lead aVR had a sensitivity of 85% and specificity of 50% for detecting LMCA lesions. In patients with LMCA lesions, unlike significant STE in lead aVR during exercise testing, ST segment changes in lead V₁ were not significant.⁹ Another study by Katircibas et al. demonstrated that in patients with treadmill score ≤ -11 , STE in lead aVR during ETT had a sensitivity of 92.9% and specificity of 48.6% for detecting LMCA stenosis. Combining STE in lead aVR and STE in lead V₁ increased the specificity of the finding to 81.6% with a decrease in sensitivity to 85.7%.¹⁰ Although they included only patients with treadmill score ≤ -11 , the effect of combining two criteria on sensitivity and specificity is consistent with our results. Information presented by Ozmen et al. showed that for detecting LMCA stenosis, STE in lead aVR during ETT had a sensitivity and specificity of 84% and 88%, respectively. However, in their study only patients with a positive ETT were included.¹⁴ Uthamalingam et al.¹¹ have shown that exercise-induced ST elevation in lead aVR is the strongest predictor for LMCA or ostial LAD stenosis with a sensitivity of 75% and specificity of 81%. In another study, Maganis et al. investigated the association of different exercise-induced ECG changes with the presence of myocardial ischemia, detected by myocardial perfusion imaging scintigrams during maximum exercise stress phase. According to their results, in patients with suspected CAD referred to exercise testing, STE in lead aVR had a sensitivity and specificity of 53.1% and 78.3%, for detecting the presence of ischemic myocardium.¹² Despite notable differences in diagnostic ability of STE in lead aVR or lead V₁ in various studies, this may be explained by inclusion of different patient population in these studies with varying risk of CAD.

As shown in our study, STE in lead aVR and STE in lead V₁ during ETT are both associated with a more severe disease presented by a higher number of patients with treadmill score ≤ -11 . In addition, reduced left ventricular ejection fraction was more common in patients with STE in lead aVR, but not in patients with STE in lead V₁.

Although not studied in the present report, these findings highlight the possible prognostic value of ST segment changes in these leads during ETT, a matter that needs further investigations. Nevertheless, STE in lead aVR is described as a predictor of worse clinical complications and higher mortality in patients with non-ST segment myocardial infarction.²² Furthermore, in a big study investigating the prognostic value of ST segment changes in lead aVR in ST elevation myocardial infarction, patients with STE in lead aVR had a higher mortality rate in both inferior wall and anterior wall infarction.²³ However, in another report, STE in lead aVR was associated with a poor prognosis in inferior wall, but not in anterior wall myocardial infarction.²⁴

Limitations

This study included patients of real-life setting. This means that patients with positive ETT findings were more likely to undergo cardiac catheterization and consequently be included in the study. Furthermore, due to a low number of patients with isolated LMCA stenosis, we could not separately explore this subgroup of patients.

CONCLUSIONS

Exercise-induced ST elevation in lead aVR is highly sensitive for LMCA lesions. The presence of LMCA stenosis is unlikely in the absence of STE in lead aVR during ETT. The presence of STE in lead V₁ in addition to STE in lead aVR increases specificity for LMCA stenosis. STE in lead aVR is also highly sensitive for proximal LAD stenosis. The presence of STE in lead V₁ in addition to STE in lead aVR increases the specificity for confirming the diagnosis.

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