Significance of Exercise-Induced ST Changes in Leads aVR, V₅, and V₁. Discrimination of Patients with Single- or Multivessel Coronary Artery Disease

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Summary

Background: It is known that exercise-induced ST-segment elevation in lead V₁ (V₁-E) detects left anterior descending (LAD) stenosis. It was also postulated that ST elevation in aVR and simultaneous ST depression in V₅ (aVR-E + V₅-D) is a marker of ischemia due to significant stenosis of the LAD in patients with single-vessel disease.

Hypothesis: This study was undertaken to investigate the significance of the concomitant appearance of both electrocardiographic (ECG) ischemic markers, and of each of them alone during exercise, to detect either LAD stenosis as single-vessel coronary artery disease (CAD), or multivessel CAD involving LAD stenosis.

Methods: A total of 196 consecutive patients (152 men and 44 women, mean age 54 ± 7 years) with at least one of these ECG markers, who underwent treadmill exercise testing with the Bruce protocol and coronary arteriography, were studied.

Results: Patients were divided into three groups. In Group A (83 patients with V₁-E + aVR-E & V₅-D), 93% of patients with single-vessel disease had significant LAD stenosis ($p < 0.001$), whereas 75% of patients with double-vessel disease had significant stenoses of the LAD and the left circumflex (LCx) coronary arteries ($p < 0.01$). In Group B (97 patients with aVR-E & V₅-D but without V₁-E), 43% of patients with single-vessel disease had significant LAD stenosis ($p < 0.08$),

whereas 85% of patients with double-vessel disease had significant stenoses of the LAD and the right coronary artery (RCA) ($p < 0.01$). In Group C (16 patients with only V₁-E), 60% of patients with single-vessel disease had significant LAD stenosis ($p < 0.05$), whereas 75% of patients with double-vessel disease had significant LAD and LCx stenoses ($p < 0.05$).

Conclusions: The concomitant appearance of exercise-induced ST elevation in lead V₁, ST elevation in lead aVR, and ST depression in lead V₅, as well as the isolated appearance of ST elevation in lead V₁ detect significant LAD stenosis as single-vessel disease, or significant stenoses of LAD and LCx arteries in patients with double-vessel disease, whereas the appearance of ST elevation in aVR & ST depression in V₅ but without ST elevation in V₁ correlates strongly with significant LAD and RCA stenoses and usually indicates double-vessel disease.

Key words: exercise testing, ST-segment deviation, lead V₁, lead aVR, coronary artery disease, left anterior descending artery stenosis

Introduction

During the last decades, exercise testing has been used as a valuable, noninvasive, widely available, cost-effective, and low-risk tool for the assessment of patients with known or suspected coronary artery disease (CAD). However, traditional evaluation of ST-segment depression has not been useful for localizing the ischemic myocardial area supplied by the significantly narrowed coronary vessel.¹ On the other hand, the appearance of exercise-induced ST-segment elevation, although significantly less frequent than ST depression, seems to indicate a particular myocardial region, with ischemia either by coronary spasm or by severe narrowing of the coronary vessels in patients without prior myocardial infarction.^{2–7} Consequently, the estimation of ST elevation in particular leads might be useful for identifying ischemic my-

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Received: October 10, 2001

Accepted with revision: April 25, 2002

ocardial regions during exercise testing. Progress in this field appears to be promising, as reported recently by two studies, in which the value of ST elevation in the “pseudo-intracavitary” lead aVR and in lead V₁ was appreciated. It was postulated⁸ that ST-segment changes in lead V₁ discriminate the diseased coronary vessel. The appearance of ST elevation or ST depression in lead V₁ was strongly related to left anterior descending (LAD) disease or right coronary artery (RCA) disease, respectively. Likewise, another study⁹ showed that concomitant exercise-induced ST elevation in lead aVR and ST depression in lead V₅ correlated with LAD disease. Thallium-201 scintigraphy data confirmed the existence of reversible perfusion defect(s) in the myocardial area(s) supplied by the respective coronary artery(ies).

Consequently, it was speculated that the simultaneous appearance of (1) ST-segment elevation in lead V₁ (V₁-E) and (2) concomitant ST-segment elevation in lead aVR and ST-segment depression in lead V₅ (aVR-E & V₅-D) might be a stronger exercise-induced electrocardiographic (ECG) combined marker indicating ischemia in the myocardial region supplied by a significantly narrowed LAD. This study was undertaken to test this hypothesis by comparing the simultaneous appearance of both markers with each of them alone, as well as the possible significance of each marker for identifying patients with single- or multivessel CAD in relation to the location of the narrowed vessel(s).

Materials and Methods

Study Population

Of a total of 880 individuals with known or suspected coronary artery disease, who underwent treadmill exercise testing in our laboratory with the Bruce protocol between 1999 and 2000, 196 patients (152 men and 44 women, mean age 54 ± 7 years, range 39–68 years), who developed significant exercise-induced ST-segment deviation in lead V₁ and/or in leads aVR and V₅, were included in the study. In addition to exercise testing, all patients underwent coronary arteriography within 2 months of exercise testing. Patients with left or right bundle-branch block, left or right ventricular hypertrophy, ventricular preexcitation, prior myocardial infarction, sole ST-segment elevation in lead aVR or sole ST-segment depression in lead V₅, a history of coronary angioplasty or aorto-coronary bypass surgery, valvular heart disease, as well as patients receiving digitalis were excluded from the study. Patient characteristics are presented in Table I. The study was approved by our hospital's Ethical Committee, and written informed consent was obtained from all participants.

Patients were divided into three groups. Group A consisted of 83 patients with exercise-induced ST elevation in lead V₁ as well as concomitant ST elevation in lead aVR and ST depression in lead V₅ (V₁-E and aVR-E & V₅-D). Group B consisted of 97 patients with concomitant ST elevation in lead aVR and ST depression in lead V₅ (aVR-E & V₅-D) but without ST elevation in lead V₁ (V₁-E). Group C consisted of 16 patients

TABLE I Patient characteristics

	Group A (n = 83)	Group B (n = 97)	Group C (n = 16)	p Value
Males/females	66/17	74/23	12/4	NS
Age (years)	52 ± 8	55 ± 7	53 ± 7	NS
Arterial hypertension (%)	7 (8)	9 (9)	2 (12.5)	NS
Hypercholesterolemia (%)	28 (34)	32 (33)	6 (37.5)	NS
Smokers (%)	39 (47)	48 (50)	7 (44)	NS

Abbreviation: NS = not significant.

with isolated ST elevation in lead V₁ (V₁-E), without ST deviation in leads V₅ and aVR.

Exercise Testing

Exercise testing was carried out on a Quinton 5000 treadmill system (Quinton Instruments Co. Seattle, Wash., USA) according to the multistage Bruce protocol. During the procedure, leads V₁, aVF, and V₅ were continuously monitored. A 12-lead ECG tracing was recorded every min. Cuff blood pressure was measured every min and before every stage change. Exercise endpoints included achieving target heart rate, development of maximal ST-segment depression of ≥ 3 mm, excessive blood pressure (BP) increase (systolic BP ≥ 230 mmHg and diastolic BP ≥ 130 mmHg), development of severe angina, incapacitating fatigue, dyspnea, and severe ventricular arrhythmias. An exercise test result was considered positive if there was (1) a horizontal or downsloping ST-segment depression of at least 1 mm, 60 ms after the J point, or (2) an upsloping ST-segment depression of ≥ 1.5 mm, 80 ms after the J point, or (3) an ST-segment elevation of at least 1 mm.¹⁰ All medications were discontinued for at least five half-lives before exercise testing performance. The interpretation was carried out by two independent investigators. Intra- and inter-observer variability for ST-segment changes were 0.08 ± 0.06 and 0.09 ± 0.05 mm, respectively.

Coronary Arteriography and Left Ventriculography

All patients underwent left ventriculography in the 30° right anterior oblique projection at 40 frames/s. The area-length method¹¹ was used for calculation of left ventricular ejection fraction. All patients underwent selective coronary arteriography using the percutaneous (Judkins) technique. The left coronary artery was visualized in the 60° left anterior oblique, in the 30° right anterior oblique, and in the left lateral with 30° cranial angulation positions. The RCA was visualized in the 60° left anterior oblique and the 30° right anterior oblique positions. Significant CAD was diagnosed when there was a diameter narrowing of $\geq 70\%$ in the lumen of the LAD, the left circumflex (LCx), and the RCA, or a diameter narrowing $\geq 50\%$ of left main coronary artery. The interpretation was performed by two investigators who were blinded to exercise testing results. Coronary arteriography findings are shown in Table II.

TABLE II Coronary arteriography results

Coronary artery disease	Number of patients (%)
Normal arteries	5/196 (2.5)
Single-vessel disease	71/196 (36)
LAD	59/71 (83)
RCA	4/71 (6)
LCx	8/71 (11)
Double-vessel disease	78/196 (40)
LAD and RCA	52/78 (66.5)
LAD and LCx	21/78 (27)
RCA and LCx	5/78 (6.5)
Triple-vessel disease	42/196 (21.5)

Abbreviations: LAD = left anterior descending coronary artery, RCA = right coronary artery, LCx = left circumflex coronary artery.

Statistical Analysis

Values are expressed as mean $\pm$ standard deviation (SD). Comparisons among groups were performed with chi-square analysis and two-way analysis of variance with multiple comparisons, as appropriate. Statistical significance was assumed for $p < 0.05$.

Results

In Group A (83 patients with V_1 -E and aVR-E & V_5 -D), 52 (93%) of the 56 (68%) patients with single-vessel disease had significant LAD stenosis, 1 (2%) had significant RCA stenosis, and 3 (5%) had significant LCx stenosis ($p < 0.001$). In the same group, 12 (75%) of 16 (19%) patients with double-vessel disease had significant LAD and LCx stenoses, 2 (12.5%) had significant LAD and RCA stenoses, and 2 (12.5%) had significant RCA and LCx stenoses ($p < 0.01$). Furthermore, nine (11%) patients had triple-vessel disease while two (2%) had normal coronary arteries.

In Group B (97 patients with aVR-E & V_5 -D but without V_1 -E), of seven (7%) patients with single-vessel disease, three (43%) had significant LAD stenosis, two (28.5%) had significant RCA stenosis, and two (28.5%) had significant LCx stenosis ($p < 0.08$). In the same group, 49 (84.5%) of 58 (60%) patients with double-vessel disease had significant LAD and RCA stenoses, 6 (10.5%) had significant LAD and LCx stenoses, and 3 (5%) had significant RCA and LCx stenoses ($p < 0.01$). Thirty-one (32%) patients had triple-vessel disease while 1 (1%) had normal coronary arteries.

In Group C (16 patients with isolated V_1 -E), five (60%) of eight (50%) patients with single-vessel disease had significant LAD stenosis, one (12%) patient had significant RCA stenosis, and two (28%) had significant LCx stenosis ($p < 0.05$). In the same group, three (75%) of four (25%) patients with double-vessel disease had significant LAD and LCx stenoses, one patient (25%) had significant LAD and RCA stenoses, whereas no patient had significant RCA and LCx stenoses ($p < 0.05$). Moreover, two (12.5%) patients had triple-vessel disease and

FIG. 1 Results in Group A (83 patients with V_1 -E and aVR-E & V_5 -D). Overall coronary arteriography findings and significant stenoses in patients with single- and double-vessel disease. LAD = left anterior descending coronary artery, LCx = left circumflex coronary artery, RCA = right coronary artery, VD = vessel disease, V_1 -E = elevation in lead V_1 , aVR-E & V_5 -D = ST elevation in lead aVR with simultaneous depression in lead V_5 .

FIG. 2 Results in Group B (97 patients with aVR-E & V_5 -D but without V_1 -E). Overall coronary arteriography findings and significant stenoses in patients with single- and double-vessel disease. Abbreviations as in Figure 1.

FIG. 3 Results in Group C (16 patients with isolated V₁-E). Overall coronary arteriography findings and significant stenoses in patients with single- and double-vessel disease. Abbreviations as in Figure 1.

two (12.5%) had normal coronary arteries. As shown from these results, exercise-induced concomitant ST changes in leads V₁, aVR, and V₅ mostly detect single-vessel disease, especially LAD disease, while the appearance of ST changes in leads aVR and V₅, but without ST elevation in V₁, mostly detects double-vessel disease with the contribution of LAD and RCA arteries, and furthermore multivessel disease.

Results are shown in Figures 1–3. Table III shows the ST-segment changes in all leads during exercise of the studied population, while Table IV shows the sensitivity, the specificity, and the positive and negative predictive values of the three ECG ischemic markers regarding the different types of coronary artery stenoses.

Discussion

Up to the present, leads aVR and V₁ have been underestimated during the evaluation of exercise testing electrocardiography. Lead V₁ is defined as an anteroseptal lead; however, lead V₁ also tends to be oriented toward the cavity of the heart. It is known that ST-segment elevation in a precordial lead could deflect not only the subepicardial ischemia of a proximal myocardial segment, but also the subendocardial ischemia in a distal myocardial area. Exercise-induced ST-segment elevation has been attributed to ventricular wall motion abnormalities,^{4, 12} ventricular aneurysms,^{5, 12} and ischemia due to either coronary vasospasm² or severe proximal coronary stenosis,^{3–6} whereas exercise-induced ST-segment depression in lead V₁ has been attributed to significant RCA stenosis.¹³

In previous studies it has been postulated that transmural anterior wall ischemia during maximal exercise testing may

TABLE III Exercise-induced ST-segment changes in all leads

	Group A (n = 83)	Group B (n = 97)	Group C (n = 16)
I and/or II and/or III	10	12	4
AVR	83	97	—
I and/or aVL	5	7	3
V ₁	83	—	16
V ₂ and/or V ₃	2	7	1
V ₄ and/or V ₆	12	11	2
V ₅	83	97	—

TABLE IV Sensitivity, specificity, and positive and negative predictive values of the three electrocardiographic ischemic markers regarding the different types of coronary artery stenoses

	Sensitivity	Specificity	Positive predictive value	Negative predictive value
A = V ₁ -E + aVR-E + V ₅ -D				
Single-VD (%)	79	78.5	67.5	87
Double-VD (%)	20.5	43	19	45
Triple-VD (%)	21.5	52	11	71
LAD (%)	86.6	63.6	92.8	46.6
RCA (%)	25	18	2	80
LCx (%)	43	17	5	73
LAD + RCA (%)	4	46	12.5	19
LAD + LCx (%)	70.5	93	75	85.5
RCA + LCx (%)	40	81	12.5	95
B = aVR-E + V ₅ -D				
Single-VD (%)	10	28	7	37
Double-VD (%)	74.5	67	60	80
Triple-VD (%)	74	57	32	89
LAD (%)	5	63.5	43	11
RCA (%)	50	92.5	28.5	97
LCx (%)	28.5	92	28.5	92
LAD + RCA (%)	94	65	84.5	85
LAD + LCx (%)	29.5	9	10	25
RCA + LCx (%)	60	25	5	90
C = V ₁ -E				
Single-VD (%)	11	93	50	65
Double-VD (%)	5	90	25	59
Triple-VD (%)	5	91	12.5	78
LAD (%)	8	73	62.5	13
RCA (%)	25	89.5	14	9.5
LCx (%)	28.5	90.5	25	92
LAD + RCA (%)	2	88.5	25	31
LAD + LCx (%)	14	98	75	76
RCA + LCx (%)	0	94.5	0	93

Abbreviations: LAD = left anterior descending coronary artery, RCA = right coronary artery, LCx = left circumflex coronary artery, VD = vessel-disease, V₁-E = elevation in lead V₁, aVR-E = elevation in lead aVR, V₅-D = depression in lead V₅.

result in ST-segment elevation in lead V₁, whereas transmural ischemia of the posterior wall may lead to ST-segment depression in lead V₁.⁸

Lead aVR is orientated toward the cavity, behaving as a "pseudo-intracavitary" lead and consequently detects intraventricular amplitudes of the left ventricle. On the other hand, lead V₅ detects extraventricular amplitudes of the same myocardial areas.¹⁴

Recently it was shown that ST-segment elevation in lead V₁,⁸ as well as simultaneous ST-segment elevation in lead aVR and ST-segment depression in lead V₅⁹ indicate ischemia in myocardial areas supplied by the significantly narrowed LAD coronary artery in patients with single-vessel disease. It seemed logical to assume that the combination of these two ECG findings would be more sensitive in identifying the significant stenosis of the LAD coronary artery, which produces exercise-induced ischemia in these patients.

Indeed, the main finding of this study is that the combination of (1) exercise-induced ST-segment elevation in lead V₁ and (2) the concomitant ST-segment elevation in lead aVR and ST-segment depression in lead V₅, is useful as a stronger marker of ischemia in the myocardial area supplied by a significantly narrowed LAD coronary artery in comparison with each ischemic marker independently.

Furthermore, the importance of this finding was investigated in patients with double-vessel disease. This inquiry revealed that patients with double-vessel disease and exercise-induced ST-segment elevation in leads V₁ and aVR, as well as ST-segment depression in lead V₅, are more likely to suffer from significant stenoses of the LAD and the LCx coronary arteries.

The exclusive appearance of exercise-induced ST-segment elevation in lead V₁ in patients with double-vessel disease seems to be also a useful ischemic marker that correlates with LAD and LCx stenoses, although no definite conclusions can be drawn from this study because of the small patients sample of this particular group. It is interesting that patients with double-vessel disease and exercise-induced concomitant ST-segment elevation in lead aVR and ST-segment depression in lead V₅ without ST-segment elevation in lead V₁ exhibited mostly significant LAD and RCA stenoses. This could be explained by exercise-induced ST-depression in lead V₁ in patients with RCA stenosis, which might compensate the tendency for the ST segment to elevate because of the LAD stenosis. Furthermore, the ECG finding B (aVR-E + V₅-D) seems to be a better predictor of double- and triple-vessel disease (60 vs. 19%, $p < 0.001$, and 32 vs. 11%, $p = 0.001$, respectively) than ECG finding A (V₁-E + aVR-E + V₅-D), which could be explained by the same compensative mechanism (Table V).

Conclusion

It was concluded that (1) the concomitant appearance of exercise-induced ST-segment elevation in lead V₁ and in lead aVR with simultaneous ST-segment depression in lead V₅, or the isolated appearance of ST-segment elevation in lead V₁ mostly detects single-vessel disease and correlates strongly

TABLE V Associations between the number of diseased coronary arteries and the presence of different combinations of ST-segment alterations

ST alterations	Single-vessel disease	Double-vessel disease	Triple-vessel disease
Group A (%)	67.5	19	11
Group B (%)	7	60	32
Group C (%)	50	25	12.5

P values

Single-vessel disease: A vs. B: $p < 0.001$, A vs. C: $p = 0.098$, B vs. C: $p < 0.001$

Double-vessel disease: A vs. B: $p < 0.001$, A vs. C: $p = 0.366$, B vs. C: $p < 0.001$

Triple-vessel disease: A vs. B: $p = 0.001$, A vs. C: $p = 0.835$, B vs. C: $p = 0.003$

with significant narrowing of the LAD coronary artery as single-vessel disease, or with significant stenoses of the LAD and LCx coronary arteries as double-vessel disease, whereas (2) the appearance of ST-segment elevation in lead aVR and ST-segment depression in lead V₅ at the same time but without ST-segment elevation in lead V₁ usually indicates double-vessel disease (LAD and RCA) and mostly detects multivessel disease.

References

- Ellestad MH: Predictive implications. In *Stress Testing. Principles and Practice*, 4th ed., p.330–333. Philadelphia: F. A. Davis, 1996
- Specchia G, de Servi S, Falcone C, Angoli L, Mussini A, Bramucci E, Marioni GP, Ardissino D, Salerno J, Bobba P: Significance of exercise-induced ST-segment elevation in patients without myocardial infarction. *Circulation* 1981;63:46–53
- de Servi S, Falcone C, Gavazzi A, Mussini A, Bramucci E, Curti MT, Vecchio C, Specchia G, Bobba P: The exercise test in variant angina: Results in 114 patients. *Circulation* 1981;64:684–688
- Nosrati FJ, Froelicher VF: ST elevation during exercise testing. *Am J Cardiol* 1989;63:986–988
- Chahine RA, Lowery MH, Bauerlein EJ: Interpretation of the exercise-induced ST-segment elevation. *Am J Cardiol* 1993;72:100–102
- Gallik DM, Mahmarian JJ, Verani MS: Therapeutic significance of exercise-induced ST-segment elevation in patients without previous myocardial infarction. *Am J Cardiol* 1993;72:1–7
- Longhurst JC, Kraus WL: Exercise-induced ST elevation in patients without myocardial infarction. *Circulation* 1979;60:616–629
- Michaelides AP, Psomadaki ZD, Richter DJ, Dilaveris PE, Andrikopoulos GK, Kakaidis S, Stefanadis C, Gialafos JE, Toutouzas PK: Exercise-induced ST-segment changes in lead V₁ identify the significantly narrowed coronary artery in patients with single-vessel disease. *J Electrocardiol* 1999;32:7–13
- Michaelides AP, Psomadaki MD, Richter DJ, Dilaveris PE, Andrikopoulos GK, Stefanadis C, Gialafos JE, Toutouzas PK: Significance of exercise-induced simultaneous ST-segment changes in leads aVR and V₅. *Int J Cardiol* 1999;71:49–56
- Colby J, Hakki AH, Iskandrian AS, Mattleman S: Hemodynamic, angiographic, and scintigraphic correlates of positive exercise electrocardiograms: Emphasis on strongly positive exercise electrocardiograms. *J Am Coll Cardiol* 1983;2:21–29
- Grossman W: *Cardiac Catheterization and Angiography*, 3rd ed., p. 200–212, 294–298. Philadelphia: Lea & Febiger, 1986
- Chahine RA, Raizner AE, Ishimori T: The clinical significance of exercise-induced ST-segment elevation. *Circulation* 1976;54:209–213
- Waters DD, Chaitman BR, Bourassa MG, Tubau JF: Clinical and angiographic correlates of exercise-induced ST-segment elevation. Increased detection with multiple ECG leads. *Circulation* 1980;61:286–296
- Schamroth L: The genesis of the normal and abnormal electrocardiogram. In *The 12-Lead Electrocardiogram*, p. 5–14. Oxford: Blackwell Scientific Publications, 1989