Right-sided Chest Leads in Exercise Testing for Detection of Coronary Restenosis

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ABSTRACT

Background: The incorporation of right-sided chest leads (V_3R through V_5R) into standard exercise testing has been reported to improve its diagnostic utility.

Hypothesis: The purpose of this study was to evaluate any improvement in the ability of exercise testing in detecting restenosis, using additional V_3R through V_5R leads, in asymptomatic patients undergoing percutaneous coronary intervention (PCI) in the right coronary artery (RCA) or/and left circumflex (LCX).

Methods: We studied 172 consecutive patients (54 ± 7 years old, 106 males) undergoing PCI in RCA or/and LCX. A treadmill test had been performed before PCI. Six months later, all patients underwent a second treadmill test and arteriography in order to detect silent ischemia due to restenosis. Recordings during exercise were obtained with the standard 12-leads plus V_3R through V_5R .

Results: Out of 172 patients, 106 had stenosis in RCA, 35 in LCX, and 31 in both vessels while 6 months later, restenosis was detected in 8 (for RCA), 3 (for LCX), and 3 (for both vessels) patients respectively. Sensitivity, specificity, positive prognostic value, negative prognostic value, and accuracy of exercise testing performed post PCI were ameliorated using V_3R through V_5R (79% vs 57%, 97% vs 80%, 69% vs 21%, 98% vs 95%, and 95% vs 78% respectively, $P < .05$ for all except negative prognostic value). Maximal exercise-induced ST-segment deviation (in mm) was not changed post PCI in 12 leads (1.4 ± 0.2 vs 1.5 ± 0.2 , $P = \text{NS}$) while it was decreased in V_3R through V_5R (0.2 ± 0.2 vs 1.2 ± 0.3 , $P < .01$).

Conclusions: The addition of V_3R through V_5R improves the diagnostic ability of standard exercise testing in detecting silent ischemia due to restenosis in patients undergoing PCI in RCA or/and LCX.

Introduction

Percutaneous coronary intervention (PCI) using implantable stents has become a well-established technique for myocardial revascularization of patients with coronary artery disease (CAD). However, in-stent restenosis does occur within 6 months of stenting (in 20%–30% of cases with bare metal stents and in <10% of cases with drug-eluting stents).¹ Angiographically apparent restenosis does not always lead to recurrent angina. A significant proportion of patients with restenosis are asymptomatic.^{2–4} A major clinical problem is the strategy for follow-up evaluation and noninvasive detection of restenosis among asymptomatic patients since silent ischemia has been reported as a predictor of mortality and cardiac events in patients with CAD.^{5–8}

Exercise electrocardiography post PCI is commonly used to stratify risk and to aid in the assessment of restenosis, and it appears to be well tolerated.^{9–10} However, it is an insensitive predictor of restenosis with sensitivities ranging from 33% to 58%, significantly less than those from single-photon emission computed tomography (SPECT).¹¹

Besides, exercise testing is poor at reflecting disease in the circumflex territory.

The number and type of leads used in exercise ECG vary widely. Preliminary results from 2 studies suggest that incorporation of ST-segment deviation in right chest leads may improve sensitivity of the exercise testing (with no apparent decrease in specificity) mainly because of increased sensitivity in the detection of significant stenosis of the right coronary artery (RCA) and left circumflex coronary artery (LCX).^{12,13}

The purpose of this study was to evaluate any possible improvement in the diagnostic ability of exercise testing in detecting silent restenosis, using additional right-sided chest leads, in patients undergoing PCI in RCA or/and LCX.

Methods

Patients

From 2004 to 2007, 358 consecutive patients underwent PCI in our laboratory; 186 (52%) underwent PCI in RCA or/and LCX and 172 (92%) agreed to participate in our

study and did not have any exclusion criterion. A maximal treadmill exercise testing had been performed before PCI. Six months after the successful PCI, all patients, although asymptomatic, underwent (as a routine) a second treadmill test and a second coronary arteriography in order to detect possible silent ischemia due to restenosis. All patients were treated with drugs indicated for coronary heart disease: antiplatelet agents (aspirin or clopidogrel or both), angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB), β -blocker, calcium-blocker, and/or statin.

Excluded from the study were patients with left or right bundle branch block, left or right ventricular hypertrophy, ventricular preexcitation, a history of myocardial infarction, valvular or congenital heart disease, those who had undergone aortocoronary bypass surgery or previous coronary angioplasty, and those who were receiving digitalis. β -Blockers, dihydropyridines, and nitrates were discontinued for at least 5 half-lives before the exercise test.

The study was approved by our hospital's ethics committee and written informed consent for participation in the study was obtained from all patients. Investigations were in accordance with the Declaration of Helsinki.

Treadmill Exercise Testing

All patients performed a maximal exercise testing on a GE Marquette 15-Lead ECG Analysis/GE Case T-2000 Series Treadmill System (GE Medical Systems, Milwaukee, WI), according to the multistage Bruce protocol. Each patient had an ECG recorded with the standard 12 chest leads and 3 additional right-sided chest leads (V_3R , V_4R , and V_5R). The positions of standard and right-sided chest leads were as previously described.¹⁴

Exercise was terminated whenever a patient had severe angina, physical exhaustion, dyspnea, or severe arrhythmias. In the absence of symptoms, the test was terminated at the occurrence of ≥ 2 mm ST-segment depression or ≥ 1 mm ST-segment elevation, an exaggerated blood pressure response ($\geq 250/115$ mm Hg), or a decrease in systolic blood pressure ≥ 20 mm Hg.¹⁵

The interpretation of exercise testing included appearance of symptoms, exercise capability, hemodynamic response, and ECG response.

The diagnosis of coronary artery disease or/and restenosis was based on the standard ST-segment deviation criteria (≥ 1 mm of additional horizontal or downsloping depression measured at 60 ms after the J-point or ≥ 1.5 mm of additional upsloping depression measured at 80 ms after the J-point or ≥ 1 mm of elevation measured at the J-point).¹⁵ Concerning the V_3R through V_5R leads, ST-segment deviation ≥ 1 mm was considered a positive result. Furthermore the exercise testing was considered positive when typical pain was reproduced, if systolic blood

pressure dropped at least 20 mm Hg, or if severe ventricular arrhythmia developed.

Measurements on the electrocardiograms were made by 2 of the investigators (using a magnifying lens) who were unaware of the results of angiography. The respective intraobserver and interobserver variabilities were 0.07 ± 0.05 and 0.08 ± 0.04 mm (correlation coefficients, 0.98 and 0.99) for ST-segment deviation. Disagreements between observers were resolved by a third interpreter.

Coronary Arteriography and Percutaneous Coronary Intervention

All patients underwent left ventriculography in the 30-degree right anterior oblique projection, at 40 frames/second. All patients underwent selective coronary arteriography, using the percutaneous (Judkins) technique. The left coronary artery was visualized in the 60-degree left anterior oblique, in the 30-degree right anterior oblique, and in the left lateral position, with a 30-degree cranial angulation. The RCA was visualized in the 60-degree left anterior oblique and the 30-degree right anterior oblique position. Significant coronary stenosis was considered in the presence of $>70\%$ diameter narrowing in the lumen of the RCA and the LCX. The interpretation was performed by 2 investigators who were unaware of exercise testing results.

A bare metal stent (BMS) was implanted during PCI in the culprit lesions in 81 (47%) patients while a drug-eluting stent (DES) was implanted in 91 (53%) patients.

Statistical Analysis

Continuous variables are reported as mean $\pm$ SD and categorical variables as observed number (percentage). A student *t* test was used to compare differences between subgroups for continuous variables once normality was demonstrated (Shapiro-Wilks test); otherwise, a nonparametric test (Wilcoxon test) was used. Differences between categorical variables were analyzed with χ^2 test (with the use of Yates correction) or Fisher exact *t* test. All tests were 2-sided. Differences were considered as statistically significant for $P < 0.05$. Data analysis was performed with SPSS 15.0 statistical software (2006 SPSS Inc., Chicago, IL, Version 12.0).

Results

Patient's baseline characteristics are demonstrated in Table 1. Most of the patients were males, smokers with dyslipidemia. One-vessel disease was found in 141 patients (82%) while 31 patients (18%) suffered from 2-vessel disease.

Exercise parameters of the study population are presented in Table 2. Six months after a successful PCI most exercise parameters were ameliorated: exercise duration, maximum heart rate, time to ST-segment depression of 1 mm, maximum ST-segment depression in right chest leads, incidence of anginal discomfort.

Table 1. Baseline Characteristics of the Studied Patients

Patients (n = 172)	
Age, years	54 ± 7
Gender (M/F)	106 (62)/66 (38)
Smokers	131 (76)
Hypertension	29 (17)
Diabetes mellitus	23 (13)
Dyslipidemia	108 (63)
1-vessel disease (RCA or LCX)	141 (82)
RCA	106 (62)
LCX	35 (20)
2-vessel disease (RCA and LCX)	31 (18)
Abbreviations: LCX = left circumflex coronary artery; RCA = right coronary artery.	
Age is reported as mean ± standard deviation when all other variables are reported as an observed number (percentage).	

From 172 patients undergoing PCI, 106 (62%) had significant stenosis in RCA, 35 (20%) in LCX, and 31 (18%) in both RCA and LCX. Six months after a successful PCI, restenosis was detected with arteriography in 14 patients: 8 (57%) in RCA, 3 (21%) in LCX, and 3 (21%) in both RCA and LCX.

Exercise testing (ET) results for the 172 patients are presented in Table 3. Based on these results, sensitivity (Se), specificity (Sp), positive prognostic value (Ppv), negative prognostic value (Npv), and diagnostic accuracy (Ac) were calculated for the standard 12-leads ET and the right-sided chest leads (V₃R through V₅R) ET before and post PCI (Figure). They were all ameliorated using V₃R through V₅R leads.

Discussion

The results of this study indicate that the standard 12-leads ET is a rather insensitive diagnostic tool for the detection of coronary artery disease, especially regarding RCA or/and LCX or/and coronary restenosis after a successful PCI regarding RCA or/and LCX with a sensitivity of 53% and 57% respectively. These percentages are in agreement with those previously reported¹⁵ and significantly less than those from other noninvasive techniques like SPECT (87%¹⁶ and 87%¹¹ respectively) or stress echocardiography (86%¹⁷ and 63%¹¹ respectively).

The addition of V₃R through V₅R leads in the standard 12-leads (according to our results) makes ET much more sensitive in detecting coronary artery disease and restenosis (especially in RCA or/and LCX). It also improves specificity, prognostic value, and accuracy of the exercise treadmill test

Table 2. Exercise Parameters of the Studied Patients.

Parameters	Before PCI	Post PCI	P Value
Exercise duration (sec)	385 ± 12	481 ± 18	.03
Maximal heart rate (beats/min)	152 ± 7	176 ± 8	.02
Maximal systolic blood pressure (mm Hg)	172 ± 11	181 ± 10	NS
Time to ST-segment depression of 1 mm (sec)	228 ± 15	298 ± 12	.03
Maximal ST-segment depression (mm):			
Inferior leads (II, III, aVF)	1.7 ± 0.2	1.5 ± 0.3	NS
Lateral leads (I, aVL, V ₄ through V ₆)	1.4 ± 0.3	1.3 ± 0.2	NS
Right-sided chest leads:			
V ₃ R	1.2 ± 0.3	0.2 ± 0.2	<.01
V ₄ R	1.1 ± 0.3	0.3 ± 0.1	<.01
V ₅ R	1.3 ± 0.4	0.1 ± 0.1	<.001
Patients with exercise-induced angina [n/total n (%)]	81/172 (47)	10/172 (6)	<.01
Abbreviations: NS = not significant; PCI = percutaneous coronary intervention.			
Angina is reported as observed number (percentage) when all other variables are reported as mean ± standard deviation.			

in detecting restenosis 6 months after a successful PCI in RCA or/and LCX.

Therefore, a positive 15-leads (standard 12-leads and V₃R through V₅R) ET makes restenosis quite possible while a negative exercise response practically excludes severe restenosis in RCA or/and LCX when performed 6 months post PCI.

The value of 12-leads ET at late (6 months) follow-up of patients treated with PCI is scarce. The results of our study (Se, Sp, Ppv, Npv, and Ac up to 57%, 80%, 21%, 95%, and 78% respectively for the standard 12-leads ET in detecting asymptomatic coronary restenosis 6 months after PCI) are similar to those from other studies evaluating noninvasive techniques in detecting restenosis^{15–17}.

A meta-analysis from Garzon et al¹¹ reported that the Se, Sp, and Ac of 12-leads exercise electrocardiography for the detection of restenosis after PCI was 46%, 77%, and 62% respectively. The use of nuclear imaging increases Se up to 87% and Sp up to 78%. Echocardiographic stress imaging also increases Se up to 63% and Sp up to 87%.

A review study from Dori et al¹⁸ reported that Se, Sp, Ppv, Npv, and Ac of 12-leads exercise stress testing were 54%, 70%, 64%, 61%, and 62% respectively; of myocardial perfusion imaging were 83%, 79%, 80%, 85%, and 82%

Table 3. Positive Exercise Testing in the Studied Patients

		Standard 12-leads ET	Right-sided Chest Leads (V ₃ R through V ₅ R) ET
Before PCI	1-vessel disease (n = 141)	67/141 (48%)	122/141 (87%)
	RCA (n = 106)	51/106 (48%)	93/106 (88%)
	LCX (n = 35)	16/35 (46%)	29/35 (83%)
	2-vessel disease (n = 31)	25/31 (81%)	28/31 (90%)
	Any vessel disease (n = 172)	92/172 (53%)	150/172 (87%)
Post PCI	1-vessel disease (n = 11)	7/11 (64%)	9/11 (82%)
	RCA (n = 8)	5/8 (63%)	7/8 (88%)
	LCX (n = 3)	2/3 (67%)	2/3 (67%)
	2-vessel disease (n = 3)	1/3 (33%)	2/3 (67%)
	Any vessel disease (n = 14)	8/14 (57%)	11/14 (79%)
	No restenosis (n = 158)	31/158 (20%)	5/158 (3%)

Abbreviations: 1-vessel disease = RCA or LCX; 2-vessel disease = RCA and LCX, Any vessel disease = RCA or/and LCX; ET = exercise testing; LCX = left circumflex coronary artery; RCA = right coronary artery.

Figure 1. Diagnostic ability of exercise testing (ET) in detecting restenosis 6 months post PCI.

respectively; and of stress echocardiography were 82%, 86%, 88%, 79%, and 84% respectively, when performed to detect restenosis in patients after successful percutaneous transluminal coronary angioplasty.

In recent studies, Isaaz et al¹⁹ evaluated stress SPECT imaging performed routinely at 6 months in asymptomatic patients for predicting angiographic restenosis after successful direct percutaneous intervention for acute ST-elevation myocardial infarction and reported Se, Sp, Ppv, Npv, and Ac up to 73%, 62%, 29%, 92%, and 64% respectively while Chalela et al²⁰ evaluated exercise stress testing before

and after successful multivessel percutaneous transluminal coronary angioplasty and found Se, Sp, and Ac up to 61%, 63%, and 62% respectively.

No previous data are available concerning the ability of a 15-lead (standard 12-leads and 3 right-sided chest leads) ET to detect coronary restenosis. According to our results, incorporation of right-sided chest leads improved the reliability of the technique (Se, Sp, Ppv, Npv, and Ac up to 79%, 97%, 69%, 98%, and 95% respectively) in levels similar or even better to them from SPECT and stress echocardiography.^{10,11,18,19}

The improvement in the ability of exercise testing in detecting coronary artery disease and restenosis in RCA and LCX with the use of right-sided chest leads seems reasonable since V₃R through V₅R leads (which are located symmetrically to V₃R through V₅R in the right hemithorax) "view" the inferolateral surface of the heart which is dominantly supplied from RCA and LCX.

The use of V₄R, as an additional lead in the exercise test, was initially reported to improve detection of RCA stenosis.^{21,22} ST-segment alterations in certain combinations of precordial leads (V₁ and V₂) and right-sided chest leads (V₃R and V₄R) are suggested to be indicative of the culprit vessel in patients with myocardial infarction during the dobutamine stress test.²³ Furthermore, we previously demonstrated that additional right-sided chest leads contributed to 1-vessel disease detection in 14% of patients with left anterior descending coronary artery stenosis, in 64% of patients with RCA stenosis, and in 41% of patients with LCX stenosis.¹²

Conclusions

The 15-leads exercise testing has proven to be a useful diagnostic tool for restenosis in RCA or/and LCX after a successful PCI. With such high specificity and negative prognostic value, it seems to be a perfect test for excluding restenosis. Its reliability is similar to that of other noninvasive methods like SPECT and stress echocardiography. Since this technique is widely available, low in cost, and highly accurate we should consider it as a diagnostic tool of choice for coronary restenosis.

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