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Original Article

Accuracy of exercise tolerance test in the diagnosis of coronary artery disease in patients with left dominant coronary circulation

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ABSTRACT

Background: Exercise is a physiologic stress that helps the physicians to clarify the presence or absence of cardiovascular disease which may be obscure at rest. Although it is sensitive, its specificity is affected by several parameters, such as some metabolic conditions, some structural heart diseases, and some baseline electrocardiogram abnormalities. Currently, the relationship between coronary dominance and accuracy of EET is not examined. Therefore, this study was conducted to determine the potential impact of coronary dominance on the accuracy of EET.

Methods: In this retrospective study, data were gathered from 720 patients from four medical centers. The pattern of dominancy was determined, and the coronary dominance pattern of the patients who had normal angiograms despite abnormal EETs was compared to that from all the patients.

Results: Among the patients who had a normal angiogram despite an abnormal EET, 27% were left dominant while the frequency of left dominancy in the whole population of the study was only 10.9% ($P = 0.013$). There were no significant differences in baseline characteristics, such as age and sex, between the two studied groups.

Conclusion: The results indicated that the presence of left dominance in patients who had normal angiograms despite an abnormal EET was significantly higher than general population. Therefore, left dominance may be considered a confounding factor for EET, producing false positive results.

1. Introduction

Exercise is a physiologic stress that helps one to clarify the presence or absence of cardiovascular disease which may be obscure at rest. Electrocardiographic exercise test (EET, also known as exercise tolerance test [ETT]), is one of the most frequent non-invasive clinical modalities used for this purpose. This inexpensive test is mainly used to elicit the likelihood and extent of myocardial ischemia indirectly.[1,2] Although it is sensitive and helpful in detecting coronary artery disease (CAD), its specificity is affected by several parameters which can lead to false positive results.[2] EET is less specific in patients with some metabolic conditions (anemia, glucose load, hyperventilation, and hypokalemia), some structural heart diseases (severe aortic stenosis, mitral valve prolapsed, severe aortic or mitral regurgitation, cardiomyopathies, and left ventricular hypertrophy), marked resting ST segment depression, intraventricular conduction disturbances, pre-excitation syndromes, severe hypertension, severe hypoxia, sudden excessive exercise, supra-ventricular arrhythmias or digitalis therapy.[3] Furthermore, currently EET plays a gate keeper role for angiography and only patients with a positive test result are referred for further studies. This leads to a decrease in the rate of true-negative test results, which eventually increases the sensitivity and decreases the specificity (post-referral bias).[3]

In addition, the pattern of coronary artery disease would also affect the specificity and sensitivity of the test. In patients who underwent coronary angiography, EET sensitivity is approximately 68% and specificity is 77%. The sensitivity for those with single vessel disease varies from 25% to 71% with the involved vessel, being most sensitive to lesion in the left anterior descending coronary artery, followed by abnormalities in the right coronary artery and the least sensitivity is noticed in patients suffering from isolated lesions of left circumflex coronary artery. These figures for

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Table 1
Comparison of coronary dominance, age and sex between the patients with normal angiogram despite an abnormal exercise tolerance test and all of the patients.

	Patients with normal angiogram despite an abnormal EET[a] ($n=39$)	All of the patients excluding false positives ($n=681$)	P value
Right dominant (%)	67.6	83.3	0.013
Left dominant (%)	27	10.9	
Codominant (%)	5.4	5.9	
Age (mean years ± SD)	53.09 ± 9.56	56.1 ± 10.93	0.45
Male (%)	53.1	42.3	0.25
Female (%)	46.9	57.7	
Family history of premature coronary disease (%)	17.94	20.12	0.09
Urban residence (%)	26.7	22.1	0.12
Rural residence (%)	74.3	77.9	

[a] EET = exercise tolerance test.

patients with multivessel CAD are 81% sensitivity and 66% specificity. This may rise to 86% and 53%, respectively for the patients with left main or three-vessel coronary artery disease.[4] Finally, according to Bayes' theorem, the specificity and sensitivity of the test is affected by the baseline frequency of the disease in the studied population (pretest probability).[3]

Currently, to the best of our knowledge, nothing is known about the relationship between coronary dominance and accuracy of EET. Therefore, we conducted this study to determine the potential impact of coronary dominance on the accuracy of EET.

2. Methods

In this retrospective study, data were gathered from 720 patients from four medical centers who had undergone angiography during the year 2013. Information regarding age, sex, coronary dominance, the presence of coronary artery disease or microvascular dysfunction (also known as cardiac syndrome X), the reason for performing angiography, lab data, medications, and echocardiographic findings including valvular heart disease, left ventricular hypertrophy, etc. were collected. Among those who were referred for coronary angiography due to abnormal EETs, those who had mentioned confounding factors were excluded. All the patients' angiographies and EETs were reviewed by our research team to exclude potential misinterpretations and biases. Coronary angiogram was considered as the gold standard of the study, and the coronary dominance pattern of the patients who had normal angiograms despite abnormal EETs was compared to all of the patients.

3. Statistical analysis

All statistical analyses were performed using the statistical Package for Social Sciences version 17.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were described as mean ± SD and we analyzed them with t-test and Mann–Whitney U test when appropriate. Fisher's exact test was used for analysis of categorical variables. Several statistical diagnostic measures of electrocardiographic exercise testing including sensitivity, specificity, positive predictive value, negative predictive value, likelihood ratio, and accuracy of EET were calculated for all patients and those with right and left dominant coronary circulation.

4. Results

In this study, angiographic data were gathered from four medical centers from two cities of Iran, Shiraz and Rasht. A total of 720 profiles were included in the study. Among those who were referred for coronary angiography, 102 were referred due to an abnormal EET. Among them, 39 had a normal angiogram despite having an abnormal EET. From these 39 patients, none had baseline ECG abnormalities including pre-excitation, LVH, resting ST segment depression and intraventricular conduction defects. The only baseline abnormality was presence of the left anterior fascicular blocks with left axis deviation in three patients. Baseline echocardiogram among these patients revealed normal systolic function among all and there were no other significant structural abnormalities including severe valvular heart diseases. Baseline laboratory data were within the normal range regarding kidney function and electrolyte abnormality although four patients suffered from a controlled diabetes type II. The presence of left dominance in patients who had normal angiograms despite an abnormal EET was significantly higher than all of the patients ($P=0.013$) (Table 1). No significant difference in age and sex was observed between these groups ($P=0.45$ and $P=0.25$, respectively).

Among all the studied subjects, a total of 248 patients had no significant obstructive coronary lesions. Excluding those with false positive ETT, the pattern of dominance among these patients was 82.6% right dominant, 12.3% left dominant, and 5.1% co-dominant. When considering this population as the control group, performing the previous analysis was again significant ($P=0.019$). The specificity of EET was 11.9% for all patients. This parameter was 13.8% in the right dominant coronary circulation and 9% in those with left dominancy. The full data for statistical diagnostic measures of electrocardiographic exercise testing is provided in Table 2.

5. Discussion

These results confirm that the presence of left dominance in patients who have normal angiograms despite an abnormal EET is significantly higher than general population. Therefore, left dominance may be considered a confounding factor for EET, producing false positive results. In other words, the specificity of EET in diagnosis of patients with CAD is lower in patients with left dominance.

To the best of our knowledge, it is for the first time that the impact of left dominance on EET results is investigated. The accuracy of EET in diagnosis of CAD is dependent on the age, gender, clinical features of the patient and the prevalence of CAD;

Table 2
Statistical diagnostic measures of electrocardiographic exercise testing among the patients with right and left dominant coronary circulation.

	Sensitivity	Specificity	+LR	−LR	PPV	NPV	Accuracy
Total	98.3%	11.9%	1.11	0.14	61.4%	83.3%	62.7%
Right dominant	100%	13.8%	1.16	0.00	67.1%	100%	69%
Left dominant	80%	9%	0.8	2.2	28.5%	50%	31%

Abbreviations: +LR = positive likelihood ratio, −LR = negative likelihood ratio, PPV = positive predictive value, NPV = negative predictive value.

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