Association of Coronary Artery Disease with Abnormal Exercise Electrocardiogram Testing in Hypertensive Patients

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ABSTRACT

Introduction: Coronary artery disease (CAD) is one of the most common causes of death worldwide. Twenty-five percent of people suffering the disease eventually die from sudden death or acute myocardial infarction. This study was established to determine the correlation between CAD and abnormal exercise electrocardiogram (ECG) testing, hypertension, and other associated risk factors. **Methods**: This cross-sectional study was performed on 384 hypertensive patients referred to Isfahan Shariati Hospital Exercise ECG Testing Center in 2011 and 2012. Patients who had irregularities in exercise ECG tests and also had a history of hypertension were selected. Patients with abnormal angiography findings were considered as patients with CAD. Sensitivity and false Positivity of exercise testing compared to angiography were calculated and the data were analyzed using SPSS software. **Results**: In this study of 384 hypertensive patients, angiography was suggestive of CAD in 310 patients. Among these patients who underwent exercise testing and angiography in order to diagnose ischemic heart disease or CAD, the most common risk factors were family history (56%), diabetes (54.2%), dyslipidemia (41.7%), smoking (40.9%), obesity (38.3%), alcohol (13%), addiction (13%), and anxiety (10.9%). The sensitivity and specificity of ECG exercise testing compared to angiography were calculated as 79% and 64%. **Conclusion**: According to the results obtained; a detailed history taking and assessing the known risks can assist clinicians to establish the most proper approach to CAD. Also depending on the assessed risk, patients with CAD can benefit from ECG exercise testing much more than strategies using cardiac computed tomography angiography primarily in order to minimize the costs and radiation exposure.

Keywords: Coronary Artery Disease, Electrocardiogram Exercise Test, Angiography

INTRODUCTION

Coronary artery disease (CAD) is one of the most common causes of death worldwide accounting for 40% of all the deaths occurring (1). Twenty-five percent of people with this disease die from sudden death or acute myocardial infarction (2). If mortality rates from CAD continue to rise, it is estimated that 23.4 million people would die from it in the year 2030 (3). The lasting, progressive, and disabling complications of the disease not only affect the patients but also is a huge burden on the whole community economically (4). Following symptoms such as weakness, shortness of breath, and chest pain are the more typical alarms for coronary artery disease and are seen mostly in men (5). Instead, women are more likely to be presented with non-typical symptoms. These symptoms include nausea, vomiting, abdominal pain, shortness of breath, back pain, and pain in the neck and jaw (6). Since it is not possible to make a definite diagnosis of the disease based on solely the clinical

presentations, determining the risk factors and estimating the chance of coronary artery disease in each individual, especially those with a positive family history, is the first step to discover future patients and prevent or at least delay the occurrence of cardiovascular complications (7). The most important risk factors known for CAD are age, smoking, hypertension, diabetes, dyslipidemia, and obesity (4, 8). With its variant demonstrations and high rates of mortality, further evaluation for proper diagnosis of CAD is a crucial but also a challenging matter. Further diagnostic evaluations are also depended on the assessment of these risk factors. For example, the proportion of abnormal exercise Electrocardiogram (ECG) testing among asymptomatic people is as low as 5 to 10 percent. So low-risk individuals are usually not recommended to be tested for exercise ECG since there is also a high probability of false positivity (9) On the other hand, exercise ECG testing is a non-invasive, inexpensive, and convenient method with fewer side effects than other

comparable invasive techniques (10). Therefore, if used at a proper time and be performed correctly, exercise ECG testing can be a great diagnostic factor in the evaluation of ischemic heart disease (11). Cardiac computed tomography angiography (CCTA) is also another non-invasive diagnostic test for CAD with more reliable findings because of its 97% of sensitivity, 90% of specificity, the positive predictive value of 93%, and the negative predictive value of 96% in the detection of CAD. But this method is costlier and the injection of contrast needed could result in some unwanted side effects (12, 13).

In order to determine the role of risk factors in CAD and more importantly to find out if exercise ECG testing can be a better diagnostic method for CAD in certain patients, this study was conducted to determine the correlation between coronary artery disease and abnormal exercise ECG testing in hypertensive patients. The results taken from this study can give us more information about CAD and may help in trying to prevent and reduce the costs of this devastating disease.

MATERIAL AND METHODS

This descriptive cross-sectional study was performed after being approved by the Research Committee of Islamic Azad University, Najafabad branch of Medical Sciences on all the 384 hypertensive patients referred to the Shariati Hospital Exercise ECG Testing Center in 2011 and 2012.

Inclusion criteria for this study was an abnormal exercise ECG test in patients with a prior history of hypertension. Taking into account the Helsinki statement, after the study goals were described for each patient and they were assured that their information would remain confidential, their informed written consent was obtained. 24 to 48 hours prior to the exercise ECG test, a series of drugs that could impair the test results such as Atenolol, Metoprolol, Propranolol, Nitrates, Diltiazem, and Verapamil was discontinued. The patients were fasting at least for 3 hours before the test, their chest hair was shaved and their skin got cleansed in order to prevent chest hair or greasiness of skin interfering in the results. After taking a full personal and familial medical history, individuals were placed on a treadmill with small electrocardiogram electrodes attached to their chest, abdomen, and arms. Then, patients were told to walk for 3 minutes on a treadmill while their cardiac electrical function and blood pressure were recorded simultaneously. The patients were demanded to walk faster as the test went on. Also, they were asked to inform the operator if they got bothered by any sort of pain especially in the chest any time during the exercise. After each session, their pulse rate was recorded and possible cardiac electrocardiogram changes were monitored. The test would be seized for the patients if they become severely tired or felt any sort of chest pain or if severe changes in the electrocardiogram were recorded. Eventually, the ECGs recorded from the patients were interpreted by a physician in detail and those who had a positive (abnormal) test and also had a history of hypertension were selected. Subsequent coronary angiography was the next diagnostic measurement in those patients who had electrocardiogram changes during exercise suggestive of coronary stenosis. Patients with impaired angiography were considered to have coronary artery disease. In order to calculate the false positivity and sensitivity of the exercise test, all the data were analyzed using SPSS software (IBM statistics for windows, version 22). Mean and standard deviation for quantitative variables and the absolute and relative ratio of qualitative variables were calculated. The Chi-square test was used for the statistical analysis of variables and the significance level was set at 0.05.

RESULTS

384 patients with hypertension who had a positive exercise ECG test for coronary artery disease were taken into the study. Then angiography was performed on each of those individuals. Angiography results suggesting CAD were seen in 310 of those patients.

The mean age of all the patients was 59.9 ± 7.94. The mean age of patients with abnormal angiography was 60 ± 7.83 and the mean age of patients who had normal angiography was 59.3 ± 8 years. No significant differences were observed between the ages of these study groups.

64.3% of all the participated patients were males and 35.7% of them were females. Of those who tested positive in angiography and therefore considered as coronary artery disease patients, 64.2% were males and 35.8% were females. Although in patients with normal angiography findings 64.9% of the patients were males. As a result, based on the Chi-square test, there was a significant difference in gender of the patients and the incidence of hypertension and coronary artery disease, which was higher in males than in females.

Among the hypertensive patients who underwent exercise ECG testing and angiography to diagnose coronary ischemia or coronary artery disease, the most frequent related risk factors

Table 1. Ratio of relative and absolute risk factors by sexuality in patients who went under exercise test.

Risk Factor	Men		Women	
	Yes	No	Yes	No
diabetic	38.1%(92)	61.9%(153)	83.2%(114)	16.8%(23)
fatness	37.7%(93)	63.3%(154)	39.4%(54)	60.6%(83)
dyslipidemia	42.1%(104)	57.9%(143)	40.9%(56)	59.1%(81)
Family history	45.3%(112)	54.7%(135)	75.2%(103)	24.8%(34)
Use alcohol	13.4%(33)	86.6%(214)	12.4%(17)	87.6%(120)
Use cigarette	56.7%(140)	43.3%(107)	12.4%(17)	87.6%(120)
addiction	13.4%(33)	86.6%(214)	12.4%(17)	87.6%(120)
anxiety	13.4%(33)	86.6%(214)	6.6%(9)	93.4%(128)

were family history, diabetes, obesity, dyslipidemia, smoking, stress, alcohol use, and addiction, respectively (Table 1 and 2).

To establish the efficacy and diagnostic value of the exercise ECG testing, considering the 384 patients who had abnormal results of exercise ECG testing and the 310 patients whose CAD was confirmed by angiography findings, the sensitivity and specificity of exercise testing compared to angiography were 79% and 64%.

DISCUSSION

This study aimed to evaluate the sensitivity and accuracy of diagnostic methods of exercise testing in comparison with an-

Table 2. Ratio of relative and absolute risk factors by sexuality in patients with abnormal findings in angiography.

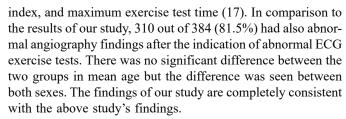|	Men		Women	
Risk Factor	Yes	No	Yes	No
diabetic	17.8%(44)	82.2%(203)	22.6%(31)	77.4%(106)
fatness	35.6%(88)	64.4%(159)	40.1%(55)	59.9%(82)
dyslipidemia	17.8%(44)	82.2%(203)	43.1%(59)	56.9%(78)
Family history	17.8%(44)	82.2%(203)	62%(85)	38%(52)
Use alcohol	6.1%(15)	93.9%(232)	8.8%(12)	92.2%(125)
Use cigarette	45.7%(113)	54.3%(134)	8.8%(12)	91.2%(125)
addiction	6.1%(15)	93.9%(232)	8.8%(12)	91.2%(125)
anxiety	17.8%(44)	82.2%(203)	8.8%(12)	91.2%(125)

giography among hypertensive patients suffering from CAD and also to evaluate the risk factors related to CAD. According to the findings, there was no statistical difference between the mean ages of our study groups. But there was a significant difference between the genders, in which CAD was more common in men. The most common risk factor in patients with CAD was a positive family or personal history of obesity and smoking.

In a study conducted by Nader Agha-Khani and colleagues in 2014, the results conducted on 500 patients showed a significant relationship between cardiovascular risk factors (including diabetes, hypertension, age, high fat, smoking, and family history of cardiovascular disease) and abnormal exercise ECG testing. But there was no relationship between sex and the CAD (14). These results are compatible with our findings gathered on risk factors except for the relationship between sex and CAD. We believe it is due to the fact that women refer to clinics with angina pectoris more often with less extensive CAD, and less severe ischemia than men (15).

Moreover, it was shown in our study that sensitivity and specificity of the diagnostic method of exercise test compared to angiography were 79% and 64%, respectively.

In other studies by using horizontal exercise ST-depression at least 0.1 mV or 1 mm at 60–80 ms after the J-point to indicate a positive test, the reported sensitivities and specificities for the detection of CAD range between 23–100% (mean 68%) and 17–100% (mean 77%), respectively. These statistics are in coherence with the study we conducted (16).

In Mohammad pour's study in 2011, the study was done on patients who were tested by exercise ECG test and coronary angiography. Of 125 patients with positive ECG results, 24 (19.2%) had normal coronary angiography and 101 (80.8%) had one to three veins with stenosis above 50%. Apart from variable ECG findings in exercise tests, the age and sex of the patients were also studied. The mean age of the subjects was not significantly different between the groups, but the ratio of normal patients to patients with coronary artery disease was different in both sexes. The most important exercise ECG test findings that had the greatest impact on patient classification for disease severity were ST-segment depression, ST/HR, HRr

index, and maximum exercise test time (17). In comparison to the results of our study, 310 out of 384 (81.5%) had also abnormal angiography findings after the indication of abnormal ECG exercise tests. There was no significant difference between the two groups in mean age but the difference was seen between both sexes. The findings of our study are completely consistent with the above study's findings.

In another study conducted by Barth S et al. between 2009 and 2014, in a total population of 1352 patients of the German Cardiac Computed Tomography Registry who had previously undergone stress tests, cardiac computed tomography angiography (CCTA) was carried out on the coronary arteries with suspected CAD. According to stress test results, there was no difference in the incidence of an obstructive CAD in patients with and without ischemia in the stress test. By combining our studies, we can conduct that exercise testing and angiography could play an important role in the diagnostics of CAD (18).

SG Kozlov et al. in a study including 390 patients aged 70 years old and more, with suspected stable ischemic heart disease, who underwent coronary artery angiography. Among 72 patients with atypical angina and non-angina pain who underwent exercise treadmill testing and had unequivocal results, 38 (53 %) had obstructive CAD. exercise treadmill testing for detection of obstructive CAD had a sensitivity of 79 %, a specificity of 82 % which is not far from the results we demonstrated in our study (19).

Adrián I Löffler and colleagues also performed a retrospective study on 412 patients who underwent exercise stress testing for the evaluation of chest pain and underwent diagnostic coronary angiography. They found that positive stress ECG test, abnormal stress imaging, left ventricular ejection fraction, and male gender were independent predictors of high-risk (more than 70% stenosis) CAD. The strongest predictor was positive stress ECG (20).

In a meta-analysis composed of 13 trials on 10,315 patients, compared with functional stress testing, CCTA was associated with a reduced incidence of myocardial infarction but an increased incidence of invasive coronary angiography, revascularization, CAD diagnoses, and prescriptions for statins and aspirin. Despite these differences, CCTA is not associated with a reduction in mortality or hospitalizations (21).

Also, in the article conducted by James K. Min and colleagues, it is concluded that Initial exercise testing followed by imaging wherein exercise testing was equivocal or unable to be performed appeared more cost-effective than any strategy employing initial testing by imaging. And, as the pre-test likelihood of CAD varies, different modalities have been improved to reduce costs and enhanced effectiveness (22).

By comparing the results of our study and the above studies we can conclude that provisional use of myocardial perfusion imaging in patients with low functional capacity or abnormal stress ECG can be much more beneficial to minimize cost and radiation exposure.

CONCLUSION

Based on the results of these studies, it can be concluded that other than a significant positive correlation between blood pressure and coronary artery stenosis; there is a statistically significant difference between the genders too. And the most

common risk factors in patients with CAD are a positive family history of diabetes, obesity, and smoking. As a result, obtaining a detailed history can be a good predictor for coronary artery disease as a first-step diagnostic method. The sensitivity and specificity of the diagnostic method of exercise test compared to angiography were 79% and 64%, respectively. Therefore, depending on the severity of the disease, diagnosis of coronary artery stenosis by using exercise ECG testing combined with taking the history of patients into consideration has a trustworthy sensitivity and diagnostic accuracy.

In order to reduce the costs burdening the whole society and also improve the effectiveness of the approach to patients with suspected CAD, we suggest that more extensive studies should be performed to compare the numbers of coronary stenosis diagnosed by angiography with those diagnosed by exercise testing and also more studies must be established in developing strategies to find the most reliable and cost-benefit diagnostic procedures for cardiovascular disease, especially coronary artery disease.

ETHICAL CONSIDERATION

This study was registered at Research Committee of Islamic Azad University, Najafabad branch of Medical Sciences, Isfahan, Iran. A written informed consent was taken from patients for participating in this study. All the personal information remained anonymous.

CONFLICT OF INTRESETS

There are no conflicts of interest in terms of the present manuscript.

REFRENCES

1. Babapour B, Khaledi A. Prevalence of Coronary Artery Disease among the Candidate Patients for Cardiac Valve's Surgery in Tehran - Imam Khomeini Hospital (1999-2003). Journal of Ardabil University of Medical Sciences. 2007;7(3):254-8.
2. Salarifar M, Kazemeini S.M, Haji Zeinali A.M. Prevalence of Coronary Artery Disease and related risk factors in first degree relatives of patients with premature CAD Tehran Heart Center. Tehran University Medical Journal. 2008;65(1):49-54.
3. Gaziano TA, Bitton A, Anand S, Abrahams-Gessel S, Murphy A. Growing epidemic of coronary heart disease in low-and middle-income countries. Current problems in cardiology. 2010;35(2):72-115.
4. Akbar-Zadeh F, Hejazi E, Kooshavar H, Pezeshkian M. Prevalence of cardiovascular diseases and cardiac risk factors in northwestern Tabriz. Med J Tabriz Univ Med Sci Health Serv. 2003;59(11).
5. DeVon HA, Zerwic JJ. Symptoms of acute coronary syndromes: are there gender differences? A review of the literature. Heart & Lung. 2002;31(4):235-45.
6. Milner KA, Funk M, Arnold A, Vaccarino V. Typical symptoms are predictive of acute coronary syndromes in women. American heart journal. 2002;143(2):283-8.
7. Fodor JG, Tzerovska R. Coronary heart disease: is gender important? Journal of Men's Health and Gender. 2004;1(1):32-7.
8. Chou R, Arora B, Dana T, Fu R, Walker M, Humphrey L. Screening asymptomatic adults with resting or exercise electrocardiography: a review of the evidence for the US Preventive Services Task Force. Annals of internal medicine. 2011;155(6):375-85.
9. Shahverdi E, Khani MA. Cardiology & Cardiovascular Medicine Journal. 2016.
10. Myers J, Arena R, Franklin B, Pina I, Kraus WE, McInnis K, et al. Recommendations for clinical exercise laboratories: a scientific statement from the American Heart Association. Circulation. 2009;119(24):3144-61.
11. Asadi H, Darvishi N. The study of results of exercise test in the age 40-60 suffering from atypical chest pain referring to Tohid Hospital in Sanandaj in second half of 1377. Scientific Journal of Kurdestan University of medical Sciences. 2000;14(4):37-3.
12. Tsarpalis K. Coronary Computed Tomographic Angiography and Potential for Overtreatment. JAMA Intern Med. 2018;178(3):435-6.
13. Taylor AJ, Cerqueira M, Hodgson JM, Mark D, Min J, O'Gara P, et al. ACCF/SCCT/ACR/AHA/ASE/ASNC/NASCI/SCAI/SCMR 2010 Appropriate Use Criteria for Cardiac Computed Tomography. A Report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, the Society of Cardiovascular Computed Tomography, the American College of Radiology, the American Heart Association, the American Society of Echocardiography, the American Society of Nuclear Cardiology, the North American Society for Cardiovascular Imaging, the Society for Cardiovascular Angiography and Interventions, and the Society for Cardiovascular Magnetic Resonance. Circulation. 2010;122(21):e525-55.
14. Aghakhani N, Sharif Nia H, Shamabadi G, TaGhipour B, Nikoonejad A. Survey of the relationship between cardiovascular risk factors and results of exercise test on patients referring to a hospital in Urmia in 2009. Community Health Journal. 2017;7(4):54-61.
15. Reynolds HR, Shaw LJ, Min JK, Spertus JA, Chaitman BR, Berman DS, et al. Association of Sex With Severity of Coronary Artery Disease, Ischemia, and Symptom Burden in Patients With Moderate or Severe Ischemia: Secondary Analysis of the ISCHEMIA Randomized Clinical Trial. JAMA Cardiol. 2020;5(7):773-86.
16. Montalescot G, Sechtem U, Achenbach S, Andreotti F, Arden C, Budaj A, et al. 2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology. Eur Heart J. 2013;34(38):2949-3003.
17. MOHAMMADPOUR TR, BABAEE G, MAHMOUDI M, Memariani A, MOHSENI A. Evaluation of exercise test variables in diagnosis and prediction of the severity of coronary artery disease by fuzzy discriminant analysis. 2002.
18. Barth S, Marwan M, Hausleiter J, Moshage W, Korosoglou G, Leber A, et al. Coronary computed tomography angiography (CCTA) in patients with suspected stable coronary artery disease (CAD): diagnostic impact and clinical consequences in the German Cardiac CT Registry depending on stress test results. Int J Cardiovasc Imaging. 2019;35(4):741-8.
19. Kozlov SG, Chernova OV, Shitov VN, Matveeva MA, Alekseeva IA, Saidova MA. [The Diagnostic Accuracy of Exercise Treadmill Testing and Stress Echocardiography for the Detection of Obstructive Coronary Artery Disease in Patients Aged ≥ 70 Years]. Kardiologiia. 2019;59(10):23-30.
20. Löffler AI, Perez MV, Nketiah EO, Bourque JM, Keeley EC. Usefulness of Achieving ≥10 METs With a Negative Stress Electrocardiogram to Screen for High-Risk Obstructive Coronary Artery Disease in Patients Referred for Coronary Angiography After Exercise Stress Testing. Am J Cardiol. 2018;121(3):289-93.
21. Foy AJ, Dhruva SS, Peterson B, Mandrola JM, Morgan DJ, Redberg RF. Coronary Computed Tomography Angiography vs Functional Stress Testing for Patients With Suspected Coronary Artery Disease: A Systematic Review and Meta-analysis. JAMA Intern Med. 2017;177(11):1623-31.
22. Min JK, Gilmore A, Jones EC, Berman DS, Stuijfzand WJ, Shaw LJ, et al. Cost-effectiveness of diagnostic evaluation strategies for individuals with stable chest pain syndrome and suspected coronary artery disease. Clin Imaging. 2017;43:97-105.