Original Article

Evaluation of the Diagnostic Value and Prognostic Role of Positive Exercise Stress Echocardiography in Coronary Artery Disease

Hamideh Khesali[1], MD; Niloufar Samiei[2], MD; Niloufar Akbari Parsa[3*], MD; Mahrokh Dalir[1]; Nasim Jafari[1]; Soheil Hassanipour[3], PhD

ABSTRACT

Background: Despite steps in lifestyle changes and preventive measures, the incidence of heart disease is still rising. Coronary artery disease (CAD) is the world's leading cause of death; thus, the early detection of this disease can significantly reduce its mortality rate. We evaluated the diagnostic value and prognostic role of positive exercise stress echocardiography in CAD.

Methods: The present retrospective study was performed on 350 patients with symptoms of IHD referred for exercise stress echocardiography between 2004 and 2017. The obtained data were analyzed using the SPSS software.

Results: Ischemic electrocardiographic (ECG) changes, the regional wall motion abnormality (RWMA) score index, the metabolic equivalent, and the peak left ventricular ejection fraction were associated with CAD (P=0.004, P=0.000, P=0.02, and P=0.000, respectively). The incidence of ventricular arrhythmias was associated with sudden cardiac death and myocardial infarction (P=0.00). Ischemic ECG changes were significantly associated with myocardial infarction and the need for percutaneous coronary interventions in the future (P=0.04 and P=0.03). The relationship between left ventricular dilation and sudden cardiac death was significant (P=0.01), and RWMAs were significantly associated with myocardial infarction (P=0.03). However, dyspnea and chest pain had no association with cardiac events.

Conclusions: Positive exercise stress echocardiography was associated with sudden cardiac death, myocardial infarction, and the need for future coronary revascularization, and its diagnostic and predictive role was observed in ischemic heart disease and predicting future cardiac events. ***(Iranian Heart Journal 2023; 24(2): 69-76)***

KEYWORDS: Ischemic heart disease, Prognostic value, Exercise stress echocardiography

[1] Echocardiography Research Center, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, IR Iran.
[2] Heart Valve Disease Research Center, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, IR Iran.
[3] Cardiovascular Diseases Research Center, Department of Cardiology, Heshmat Hospital, School of Medicine, Guilan University of Medical Sciences, Rasht, IR Iran.

***Corresponding Author:** Niloufar Akbari Parsa, MD; Cardiovascular Diseases Research Center, Department of Cardiology, Heshmat Hospital, School of Medicine, Guilan University of Medical Sciences, Rasht, IR Iran.
Email: dr.niloufar.parsa@gmail.com **Tel:** +989113359748

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Ischemic heart disease (IHD) is the leading cause of death the world over. During the last decades, heart attack prevention strategies have been on the agenda of major health organizations. [1,2] Methods of predicting myocardial infarction (MI) can be effective in identifying individuals at high risk. [3]
One of the routine methods of diagnosing patients with coronary artery disease (CAD) and predicting major adverse cardiovascular events is the stress echocardiography test, a valuable tool in assessing regional wall motion abnormalities (RWMAs) in patients with suspected CAD. This method is a combination of 2D echocardiography and physical or medical stress, during which myocardial ischemia is diagnosed with the aid of stress induction and the examination of the signs and symptoms of damaged tissue at a specific myocardial wall or segment. [4,5]
Myocardial ischemia results in a cascade of events in which different biochemical and clinical markers appear hierarchically in a specific time sequence. [6] Flow heterogeneity is the first indicator of ischemia, followed by metabolic changes, changes in the mechanical function of the affected area due to the lack of oxygen, and in the next stage, echocardiographic changes and the occurrence of pain. A decreased coronary flow reserve is the common pathophysiological mechanism of ischemia. [6, 7]
Today, the diagnostic value and predictive role of stress echocardiography in ischemic and non-ischemic diseases have been considered, [8] and the full medical treatment and close follow-up of patients with positive stress echocardiography are deemed significant issues in preventing adverse outcomes. [8, 9]
The evaluation of various factors, including symptoms (eg, dyspnea and chest pain), functional class, ischemic electrocardiographic (ECG) changes during exercise, RWMAs, left ventricular (LV) dilation, the severity of ischemic mitral regurgitation, increased LV filling pressure, elevated pulmonary arterial pressure (PAP), and ventricular arrhythmias can be effective in diagnosing the severity of IHD and predicting the risk of future cardiac events. [10, 11]
Objectives: The present study aimed to evaluate the diagnostic value and predictive role of positive exercise stress echocardiography in IHD.

METHODS

Study Design
The current retrospective study was performed on all patients who underwent exercise stress echocardiography between November 2004 and August 2017. Patients with positive test results who underwent coronary angiography in our center were included in the study.

Participants
The inclusion criteria consisted of a positive test result, age between 18 and 70 years, undergoing coronary angiography, and the provision of consent to participate in the study. The exclusion criteria were non-response to telephone calls and noncardiac death during the follow-up.

Variables
After the research plan was approved by the institutional ethics committee, all patients who underwent stress echocardiography with exercise (the treadmill) for the diagnosis of IHD in the defined period and had positive results were included in the study. Information such as demographic characteristics, risk factors, previous noninvasive test results, stress echocardiography findings, and coronary angiography findings was entered into a questionnaire, and the study population was followed up by phone calls to record cardiovascular events and mortality.
Then, the data were analyzed to determine the role of this diagnostic modality in the study of IHD.

Statistical Analysis

Quantitative data were expressed as the mean ± the standard deviation, and qualitative data were expressed as frequencies and frequency percentages. The data were entered into the SPSS software, version 25, and frequencies were calculated using descriptive statistical tests.

Ethical Considerations

The proposal was approved by the institutional ethics committee (code: IR.RHC.REC.1400.063). The patients' information was coded and registered anonymously. Consent was obtained from the study participants by contacting them to access the information recorded in their files. The researcher did not have the right to access or contact the participants before obtaining their consent. The confidentiality of patient information was considered.

RESULTS

Participants

The mean age of the study population, composed of 350 patients, was 59.8 years. The demographic findings of the studied patients are presented in Table 1.

Table 1: Demographic characteristics

Parameter	Mean± SD (N=350)
Age, y	59.82 ± 11.42
Body mass index, kg/m^2	27.93 ± 4.75
Body surface area, m^2	1.81 ± 0.20
Systolic blood pressure, mm Hg	134.84 ± 18.82
Diastolic blood pressure, mm Hg	81.05 ± 12.19
HEART RATE	74.06 ± 13.19
LEFT VENTRICULAR EJECTION FRACTION	50.22 ± 7.81

Descriptive Data

Descriptive and clinical characteristics can be seen in Table 2. The findings demonstrated that 55% of the studied patients were male, and 45% were female. In addition, 41% of the study population had diabetes, 60% had high blood pressure, 49% had hyperlipidemia, and 35% had a family history of IHD.

Chief Results

The evaluation of the relationships between the variables studied in exercise stress echocardiography and coronary angiography is presented in Table 3. The results showed that among the studied variables, ischemic ECG changes were associated with coronary angiography results (P<0.05). No significant relationships were observed between angiography results and dyspnea, chest pain, and LV dilation (P>0.05).

The results also demonstrated that the mean metabolic equivalent, ST-segment deviation (mm), the LV ejection fraction at the peak of stress, the peak LV filling pressure, the RWMA score index, and the peak systolic PAP had significant relationships with angiography results (P<0.05) (Table 3).

The evaluation of the relationships between the variables studied in echocardiography and cardiac events associated with IHD is demonstrated in Table 4. The incidence of dyspnea and chest pain during stress echocardiography was not associated with the occurrence of heart events during the follow-up (P>0.05). However, the incidence of ventricular arrhythmias was associated with sudden cardiac death and MI during the follow-up (P=0.00). The amount of ischemic ECG change at the peak of stress was significantly associated with MI and the need for future percutaneous coronary interventions (P=0.04 and P=0.03).

The study of the relationship between LV dilation and the incidence of cardiac events during the follow-up showed that among cardiac events, this variable was significantly associated with sudden cardiac death (P=0.01). The RWMA score index, the peak LV ejection fraction, the peak LV filling pressure, and the peak systolic PAP were significantly associated with sudden cardiac death and MI during the follow-up (P<0.05). The findings are presented in Table 4.

The areas under the receiver operating characteristic (ROC) curve and 95% confidence intervals for the RWMA score index, the peak heart rate, the peak systolic blood pressure, the peak diastolic blood pressure, the percentage of maximal heart rate, and clinical outcomes in our patients with IHD can be seen in Table 5.

Table 2: Descriptive and clinical characteristics of the studied patients

Characteristic	Parameter	Frequency	%
Sex	male	192	54.9
	female	157	44.9
DM	no	206	58.9
	yes	144	41.1
HTN	no	140	40.0
	yes	210	60.0
HLP	no	176	50.3
	yes	174	49.7
MI history	no	340	97.1
	yes	10	2.9
POSITIVE FH	no	228	65.1
	yes	122	34.9
PCI HISTORY	no	298	85.1
	yes	52	14.9
CABG HISTORY	no	333	95.1
	yes	17	4.9
SMOKING	no	258	73.7
	yes	92	26.3

DM, Diabetes mellitus; HTN, Hypertension; HLP, Hyperlipidemia; MI, Myocardial infarction; FH, Family history; PCI, Percutaneous coronary intervention; CABG, Coronary artery bypass grafting

Table 3: Evaluation of the relationships between stress echocardiography and angiography

Characteristic	CAG	Normal	Minimal CAD	Slow Flow	Mild CAD	SVD	2VD	3VD	Total	*P* value
Percentage(%)										
Stage	1.0	66.7	0.0	0.0	0.0	33.3	0.0	0.0	100.0	0.14
	2.0	28.0	0.0	4.0	12.0	16.0	8.0	32.0	100.0	
	3.0	18.6	11.4	7.1	4.3	15.7	24.3	18.6	100.0	
	4.0	9.1	13.6	0.0	13.6	18.2	31.8	13.6	100.0	
	5.0	25.0	0.0	0.0	0.0	75.0	0.0	0.0	100.0	
Chest pain	no	22.2	4.8	5.6	11.1	17.5	20.6	18.3	100.0	0.61
	yes	17.0	6.8	5.7	6.8	19.3	17.0	27.3	100.0	
Dyspnea	no	20.8	5.8	4.6	10.4	19.7	20.2	18.5	100.0	0.15
	yes	17.1	4.9	9.8	4.9	12.2	14.6	36.6	100.0	
ECG change	no	26.5	7.1	9.2	11.2	17.3	17.3	11.2	100.0	0.004
	yes	14.7	4.3	2.6	7.8	19.0	20.7	31.0	100.0	
Arrhythmia	no	23.1	3.8	4.5	9.6	21.8	20.5	16.7	100.0	0.004
	yes	12.1	10.3	8.6	8.6	8.6	15.5	36.2	100.0	
LV dilation	no	19.9	6.1	6.1	10.2	18.4	19.9	19.4	100.0	0.06
	yes	22.2	0.0	0.0	0.0	16.7	11.1	50.0	100.0	
Mean										
METS		8.96	10.47	7.95	9.06	9.75	9.06	7.57	8.95	0.02
ECG mm		0.53	0.66	0.41	0.55	0.84	1.07	1.44	0.89	0.000

Peak LVEF		58.37	55.83	45.8	55.750	50.12	50.00	46.38	51.54	0.000
Peak filling		8.62	9.41	9.50	8.77	9.89	10.96	12.72	10.31	0.000
RWMASI		1.24	1.28	1.52	1.38	1.42	1.54	1.69	1.46	0.000
Peak sPAP		38.14	44.25	37.50	37.85	38.38	40.85	41.85	39.79	0.04

CAG, Coronary angiography; CAD, Coronary artery disease; SVD, Single-vessel disease; 2VD, Two-vessel disease; 3VD, Three-vessel disease; ECG, Electrocardiogram; LV, Left ventricle; METs, Metabolic equivalent; LVEF, Left ventricular ejection fraction; RWMASi, Regional wall motion abnormality score index; sPAP, Systolic pulmonary artery pressure

Table 4: Evaluation of the relationships between the variables examined in positive echocardiography and cardiac events

Characteristic		Sudden Cardiac Death		*P* value	MI		*P* value	PCI		*P* value	CABG		*P* value
	Parameter	no	yes		no	yes		no	yes		no	yes	
Percentage (%)													
Chest pain	no	87.8	12.2	0.47	87.2	12.8	0.57	86.5	13.5	0.30	94.2	5.8	0.19
	yes	84.7	15.3		90.8	9.2		90.8	9.2		92.9	7.1	
Dyspnea	no	86.8	13.2	0.85	85.8	14.2	0.70	87.7	12.3	0.65	92.9	7.1	0.25
	yes	85.7	14.3		88.1	11.9		90.5	9.5		97.6	2.4	
ECG change	no	86	14.0	0.78	90.7	9.3	0.03	92.2	7.8	0.04	93.8	6.2	0.94
	yes	87.2	12.8		81.6	18.4		84.0	16.0		93.6	6.4	
Arrhythmia	no	92.7	7.3	0.00	91.6	8.4	0.00	88.2	11.8	0.99	94.9	5.1	0.21
	yes	72.4	27.6		73.7	26.3		88.2	11.8		90.8	9.2	
LV dilation	no	88.1	11.9	0.01	87.3	12.7	0.07	88.1	11.9	0.92	94.5	5.5	0.06
	yes	66.7	33.3		72.2	27.8		88.9	11.1		83.3	16.7	
RWMA	no	85.7	14.3	0.36	91.7	8.3	0.03	85.2	14.8	0.81	89.2	10.8	0.47
	yes	82.0	18.0		86.0	14.0		88.2	11.8		83.2	16.8	
Mean													
METS		9.12	7.00	0.01	9.05	8.20	0.26	9.08	8.10	0.23	8.99	8.52	.642
ECG mm		0.79	0.85	0.92	0.74	1.17	0.016	0.76	1.06	0.07	.80	0.75	0.86
Peak LVEF		52.84	40.88	0.000	52.46	43.57	0.007	51.51	49.16	0.28	51.36	49.37	0.51
Peak filling		9.96	13.912	0.000	10.01	13.54	0.007	10.41	11.10	0.10	10.42	11.50	0.10
RWMASI		1.37	1.94	0.000	1.39	1.81	0.000	1.44	1.51	0.16	1.43	1.82	0.10
Peak sPAP		39.39	46.47	0.000	39.13	47.85	0.000	40.09	42.16	0.86	40.20	42.37	0.001

MI, Myocardial infarction; PCI, Percutaneous coronary intervention; CABG, Coronary artery bypass graft; ECG, Electrocardiogram; LV, Left ventricle; RWMA, Regional wall motion abnormality; METs, Metabolic equivalent; LVEF, Left ventricular ejection fraction; RWMASI, Regional wall motion abnormality score index; sPAP, Systolic pulmonary artery pressure

Table 5: Areas under the ROC curve and 95% confidence intervals for RWMASI, Peak HR, Peak SBP, Peak DBP, Percentage of maximal HR, and clinical outcomes in patients with ischemic heart disease

	ROC and 95% CI		
Variable	Death	MI	PCI
RWMASI	0.796 (CI: 0.628-0.965) *P*= 0.010	0.729 (CI: 0.377-1.000) *P*= 0.179	0.706 (CI: 0.388-1.000) *P*= 0.256
Peak HR	0.616 (CI: 0.376-0.856) *P*= 0.309	0.682 (CI: 0.434-0.931) *P*= 0.285	0.794 (CI: 0.621-0.966) *P*= 0.106
Peak SBP	0.526 (CI: 0.262-0.789) *P*= 0.823	0.653 (CI: 0.321-0.985) *P*= 0.258	0.492 (CI: 0.257-0.727) *P*= 0.965
Peak DBP	0.534 (CI:0.251-0.816) *P*= 0.770	0.671 (CI: 0.230-1.000) *P*= 0.317	0.571 (CI: 0.308-0.835) *P*= 0.694
Percentage of maximal HR	0.595 (CI: 0354-0.837) *P*= 0.405	0.698 (CI: 0.433-0.963) *P*= 0246	0.825 (CI: 0.665-0.986) *P*= 0.074

ROC, Receiver operating characteristic; CI, Confidence interval; RWMASI, Regional wall motion abnormality score index; HR, Heart rate; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; CABG, Coronary artery bypass grafting; MI, Myocardial infarction; PCI, Percutaneous coronary intervention

DISCUSSION

CAD is the cause of more than half of all deaths from cardiovascular diseases and is the major fatal disease in the world. [1,2] Indubitably, the early detection and treatment of this disease can prevent future major adverse cardiovascular events.

The present study was performed to evaluate the diagnostic value and predictive role of positive exercise stress echocardiography in IHD. Our findings demonstrated that exercise stress echocardiography was a tool capable of diagnosing CAD. Ortega et al [11] in 2017 examined the long-term predictive value of echocardiography and showed that this method had a good ability to diagnose acute coronary syndromes. Their results also showed that the positive findings of echocardiography and atrial fibrillation were significantly related to each other. Another similar study reported that the normal findings of stress echocardiography were associated with an appropriate prognosis in patients and could effectively classify patients into ischemic and nonischemic groups in terms of risk. It was also observed that the number of ischemic segments was a significant predictor of cardiac complications. [12]

We found that the incidence of ventricular arrhythmias was associated with sudden cardiac death and MI. The amount of ST-segment deviation (mm) at the peak of stress was significantly associated with MI and the need for future coronary revascularization. In addition, at the peak of stress, LV dilation was significantly associated with sudden cardiac death. These findings indicated the usefulness of exercise echocardiography in identifying and predicting the risk of major adverse cardiovascular events.

Ludka et al [13] in a study on patients with congestive heart failure showed that stress echocardiography was highly useful for identifying the risk and prognosis of the disease and that the classification of patients based on prognosis could be helpful in reducing the complications of the disease. Another observational study in Italy on 8050 patients reported that those with positive stress echocardiography were at higher risk of cardiac events and mortality than those with negative tests. [14]

In exercise stress echocardiography, the assessment of RWMAs is mainly considered by the cardiologist. [15] In the present study, the RWMA score index was associated with MI during the follow-up. Additionally, the peak LVEF, the peak LV filling pressure, and the peak systolic PAP were associated with sudden cardiac death and MI. In a similar prospective study, Innocenti et al [16] concluded that stress echocardiography had a favorable prognostic value in patients with chest pain referred to the emergency department. Their assessments during the follow-up showed that a high RWMA score index during activity was associated with a poor prognosis and the risk of cardiovascular events. Another study reported RWMAs as an efficient predictor in the diagnosis and identification of cardiac events. [17-19]

In another study, Marques et al [20] reported the sensitivity and specificity of stress echocardiography in predicting cardiac events at about 73% and 90%, respectively. Considering various fundamental studies and the results of the present study, stress echocardiography is a method capable of diagnosing and evaluating the prognosis of IHD.

In general, the present research showed that exercise stress echocardiography could play an effective role in diagnosing CAD and predicting future cardiovascular events.

Limitations

One of the limitations of the present study is the incompleteness of patient information, especially regarding patients undergoing parts of the diagnostic tests in other centers or patients studied a long time ago with outdated contact information. One of the strengths of this retrospective study is the 13-year follow-up of the studied patients and the reasonable sample size.

CONCLUSIONS

According to the findings of the present study, it appears that positive exercise stress echocardiography is significantly effective in diagnosing CAD and predicting sudden cardiac death, MI, and the need for coronary revascularization in the future. In addition, ischemic ECG changes, the RWMA score index, LV dilation at the peak of stress, and the incidence of ventricular arrhythmias were associated with cardiovascular events during the follow-up. Therefore, the evaluation of influential variables during stress echocardiography in patients can provide valuable prognostic information regarding myocardial ischemia. It is recommended that further studies be performed in several medical centers.

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Conflict of Interest

The authors do not have any conflicts of interest.

Disclosures

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