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ORIGINAL ARTICLE

Diagnostic Accuracy of Combined Dobutamine Echocardiography and Electrocardiography in Patients with Suspected Chronic Coronary Syndrome

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ABSTRACT

Background: Diagnosis of chronic coronary syndrome is challenging. The role of exercise electrocardiography (ECG) decreased because of many artifacts and low diagnostic accuracy. Therefore, non-invasive stress imaging is the current approved recommendation for diagnosis of chronic coronary syndrome in patients with clinical pre-test probability of more than 15% or 5-15% with high clinical likelihood. Dobutamine echocardiography (Echo) is widely available but with limitations. Therefore, combined dobutamine Echo and ECG could improve the diagnostic accuracy. **Methods:** We performed a cross-sectional study in Zagazig university hospitals in the period between April 2023 and October 2023. We included all patients with suspected chronic coronary syndrome with clinical pre-test probability more than 5%. All patients underwent combined dobutamine Echo and ECG and invasive coronary angiography. Diagnostic accuracy of combined dobutamine Echo and ECG was compared with dobutamine Echo.**Results:** Among 50 patients with suspected chronic coronary syndrome, we found 37 patients had significant coronary artery disease (CAD) utilizing invasive coronary angiography compared with dobutamine Echo, combined Echo and ECG had more favorable sensitivity (97.1% vs 93.5%) and specificity (75% vs 57.9%) for prediction of significant CAD. **Conclusions:** With better diagnostic accuracy, combined dobutamine Echo and ECG is simple, cheap, and available non-invasive test for diagnosis of chronic coronary syndrome.

Keywords: dobutamine stress echocardiography, exercise ECG, myocardial ischemia.

INTRODUCTION

Coronary artery disease (CAD) is the most common cause of cardiovascular death worldwide. Many modalities are available for its diagnosis but with variable diagnostic accuracies and variable cost [1]. Individuals who are suspected of having CAD are categorized into low, intermediate, and high probabilities of CAD based on clinical pre-test probability, which takes into account factors such as age, gender, and chest pain criteria. For patients with a pretest probability of CAD equal to or more than 15% or 5-15% but with high clinical likelihood, the current guidelines recommend non-invasive stress test [2]. Among non-invasive stress tests, exercise electrocardiography (ECG) and

dobutamine echocardiography (Echo) are widely available and cheap options for diagnosis of stress induced CAD [3].

On one hand, exercise ECG has many limitations as artifacts, low sensitivity (68%), and low specificity (77%). Moreover, exercise ECG is useless in patients with movement limitations, left bundle branch block, atrial fibrillation, or left ventricular hypertrophy and resting ST-T waves changes [4]. On the other hand, dobutamine echo has better sensitivity (80%) and specificity (84%) for diagnosis of CAD. However, there are many limitations as poor Echo window, being subjective with interobserver variability, and respiratory motion artifacts [3].

We hypothesize that adding ECG monitoring to dobutamine Echo could improve the diagnostic accuracy and add an objective tool for better diagnosis of stress induced CAD.

METHODS

We performed a cross-sectional study in Zagazig university hospitals in the period between April 2023 and October 2023.

Inclusion criteria: All patients with suspected CAD who underwent both dobutamine Echo and invasive coronary angiography in Zagazig University Hospitals. The clinical pre-test probability of the study population was either more than 15% or between 5% and 15% but with high clinical likelihood of CAD. We evaluated the clinical pretest probability by considering age, gender, and characteristics of chest pain (all patients with suspected CAD who underwent both dobutamine Echo and invasive coronary angiography in Zagazig University Hospitals. The clinical pre-test probability of the study population was either more than 15% or between 5% and 15% but with high clinical likelihood of CAD. We evaluated the clinical pretest probability by considering age, gender, and characteristics of chest pain (Figure 1) [5]. The criteria of high likelihood of CAD involved the presence of risk factors as diabetes mellitus (DM), hypertension, dyslipidemia, smoking, positive family history of CAD, resting ECG changes, and coronary calcium by computed tomography (CT) [5].

Exclusion criteria: Patients with non-ischemic structural heart diseases as valvular heart disease and non-ischemic cardiomyopathies, patients with any form of arrhythmias, patients with pre-test probability of less than 5%, patients with very poor echo window, patients with serum creatinine of more than 2 mg/dl, patients with resting ischemic ECG changes and patients with resting wall motion abnormality in echocardiography.

Sample size: The study included a total of 50 participants.

Data Collection and Procedures:

We collected basic characteristics and risk factors for all patients including age, gender, body built, history of hypertension, diabetes mellitus, dyslipidemia, smoking, chronic kidney disease (CKD), peripheral vascular disease, and stroke. Furthermore, we checked for family history of premature cardiovascular disease defined as cardiovascular disease before 45 years old in males and 55 years old in females.

On the day of performing non-invasive test, we checked for pulse rate, blood pressure, and complete general and local examination to rule out structural heart disease. Resting ECG was performed using Sonoscope ECG device at voltage of 10 mm/mV and at speed of 25 mm/sec. Furthermore, we performed echocardiography examination using Siemens ACUSON X300 ultrasound machine with P4-2 1.8 MHZ transducer with tissue doppler imaging capability. We checked for LV end diastolic diameter (LVEDD), LV end systolic diameter (LVESD), LV ejection fraction (LV EF), E/é ratio, LA volume index (LAVI) and pulmonary artery systolic pressure (PASP).

All patients underwent dobutamine stress echocardiography (DSE) according to the standard protocol of diagnosis of stress induced wall motion abnormality. Dobutamine intravenous infusion was started at rate of 5 mcg/kg followed by 10, 20, … up to 40 mcg/kg. During each stage, we checked for any evidence of regional wall motion abnormality, increase in LV diastolic

diameter, increase in LV out flow tract gradient, and valve regurgitation [6].

The test was considered complete if the study showed new regional wall motion abnormality, the patient developed chest pain, dyspnea, ventricular arrythmia, the patient reached 85% of age predicted maximal heart rate without symptoms or regional wall motion abnormalities [6].

At the end of the test and before stopping dobutamine infusion another 12 lead ECG was performed. The interpretation of ECG was performed by a separate physician. Results of post-dobutamine ECG were kept secured till after performing coronary angiography.

All patients underwent coronary angiography using Philips (Germany), via either trans femoral or trans radial approach according to the operator choice. Coronary angiography was checked for presence of more than 50% stenosis in one or more of the epicardial coronary vessels [5].

Considering coronary angiography as the gold standard test for detection of significant coronary stenosis, the sensitivity and specificity were calculated for both dobutamine ECHO and combined dobutamine ECHO & ECG.

Ethical and administrative considerations: Institutional research board (IRB) committee of faculty of medicine, Zagazig university, Egypt has reviewed and accepted the study protocol with reference number (ZU.IRB #10484/8-3-2023). We obtained informed consent from all participants. The study was carried out according to the Ethical code of the World Medical Association (Declaration of Helsinki) for Studies including humans.

STATISTICAL ANALYSIS

SPSS v26 (IBM Inc., Armonk, NY, USA) was used for statistical analysis. The normality of the data distribution was assessed using the Shapiro-Wilks test and histograms. The Mann Whitney, chi-square, Fisher's exact, and unpaired student t-tests were employed. A statistically significant two-tailed P value was defined as < 0.05.

RESULTS

The study included a total of 50 participants with more than 5% pretest probability of ischemic heart disease, with a mean age of 42.3 ± 10.7 years. The gender distribution showed that 52% of the participants were male, while 48% were female. The average weight was 74.38 ± 11.52 kg, with a height of 1.71 ± 0.1 m, resulting in a mean body mass index (BMI) of 25.61 ± 4.8 kg/m^2.

Several cardiovascular risk factors were assessed in the study population. A significant proportion of participants had diabetes mellitus (42%), hypertension (42%), obesity 20%, and a history of smoking (36%). Hyperlipidemia was prevalent in 78% of the participants, indicating a high prevalence of lipid abnormalities. Additionally, 44% of participants reported a family history of coronary CAD. Details of the basic characteristics of the studied patients were presented in (Table 1).

Being the gold standard CA showed that 37 patients had more than 50% CA stenosis in one or more of the epicardial coronary arteries. Dobutamine ECHO alone showed sensitivity of 78.4% and specificity of 84.6% for detection of obstructive CAD. (Table 2). Adding ECG to dobutamine ECHO improved sensitivity to 89.2% and specificity to 92.3% (Table 3).

Table (1): Baseline characteristics of the study group.

Variables	The study population n=50	
Age (years)	42.3 ± 10.7	
Sex	Male	26 (52%)
	Female	24 (48%)
Weight (kg)	74.38 ± 11.52	
Height (m)	1.71 ± 0.1	
BMI (kg/m^2)	25.61 ± 4.8	
DM	21 (42%)	
HTN	21 (42%)	
Obesity	10 (20%)	
Smoking	18 (36%)	
Hyperlipidemia	39 (78%)	
Family history of CAD	22 (44%)	
Temperature (°C)	36.96 ± 0.35	
HR (beats/min)	67.82 ± 10.66	
SBP (mmHg)	131.84 ± 18.86	
DBP (mmHg)	82.5 ± 19.6	
RR (breaths/min)	14.04 ± 1.41	
Hb (g/dl)	13.21 ± 2.13	
TLC (*10^9/L)	7.75 ± 2	
Platelets (*10^9/L)	283.56 ± 87.67	
BUN (mg/dl)	15.62 ± 5.58	
Creatinine (mg/dl)	0.86 ± 0.17	
Cholesterol (mg/dl)	253.04 ± 55.13	
TG (mg/dl)	223.46 ± 87.43	
LDL (mg/dl)	158.32 ± 57.18	
HDL (mg/dl)	44.66 ± 7.37	
LVEDD	50 ± 3	
LVESD	30 ± 2	
EF	60 ± 3	
E/é	4 ± 1	
PASP	20 ± 5	

BMI: body mass index, DM: diabetes mellitus, HTN: hypertension, CAD: coronary artery disease, HR: heart rate, SBP: systolic blood pressure, DBP: diastolic blood pressure, RR: respiratory rate, Hb: hemoglobin, TLC: total leucocyte count, BUN: blood urea nitrogen, TG: triglycerides, LDL: low-density lipoprotein, HDL: high-density lipoprotein, LVEDD: left ventricular end diastolic diameter, LVESD: left ventricular end systolic diameter, EF: ejection fraction, PASP: pulmonary artery systolic pressure.

Table (2): Diagnostic value of dobutamine stress echocardiography in diagnosis of stress induced myocardial ischemia.

		Coronary angiography		P value
		Positive (n=37)	Negative (n=13)	
Dobutamine stress echocardiography	Positive	29 (78.4%)	2 (15.4%)	<0.001*
	Negative	8 (21.6%)	11 (84.6%)	
Sensitivity		93.55%		
Specificity		57.89%		
PPV		78.38%		
NPV		84.62%		
Accuracy		80%		

PPV: positive predictive value, NPV: negative predictive value, *: significant as P value ≤ 0.05.

Table (3): Diagnostic value of combination of exercise ECG and dobutamine stress echocardiography in diagnosis of stress induced myocardial ischemia.

		Coronary angiography		P value
		Positive (n=37)	Negative (n=13)	
Exercise ECG and dobutamine stress echocardiography	Positive	33 (89.2%)	1 (7.7%)	<0.001*
	Negative	4 (10.8%)	12 (92.3%)	
Sensitivity		97.06%		
Specificity		75%		
PPV		89.19%		
NPV		92.31%		
Accuracy		90%		

ECG: electrocardiogram, PPV: positive predictive value, NPV: negative predictive value, *: significant as P value ≤ 0.05.

	Typical		Atypical		Non-anginal		Dyspnoea[a]	
Age	M	W	M	W	M	W	M	W
30–39	3%	5%	4%	3%	1%	1%	0%	3%
40–49	22%	10%	10%	6%	3%	2%	12%	3%
50–59	32%	13%	17%	6%	11%	3%	20%	9%
60–69	44%	16%	26%	11%	22%	6%	27%	14%
70+	52%	27%	34%	19%	24%	10%	32%	12%

Figure 1: Pre-test probability of coronary artery disease adopted for ESC guidelines on the diagnosis and management of chronic coronary syndromes (nuuti, J., et al. (2020). "2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes." Eur Heart J 41(3): 407-477.).

DISCUSSION

CAD is the most common cause of cardiovascular death worldwide. The current guidelines recommend non-invasive stress cardiac imaging for patients with pretest probability ≥ 5% for having coronary artery disease [5]. Among the non-invasive tests, dobutamine ECHO and exercise ECG are widely available with fair sensitivity and specificity. However, both tests have limitations including poor Echo window and being subjective and many artifacts for exercise ECG [4, 6].

The present study aimed to evaluate the diagnostic accuracy of dobutamine ECHO alone and in combination with ECG for detecting obstructive CAD in a cohort of 50 patients with a pretest probability of more than 5%. The study population had a mean age of 42.3 ± 10.7 years, with 52% being male. Utilizing CA as the gold standard, our findings shed light on the effectiveness of these diagnostic modalities in clinical practice.

The results revealed that 37 out of 50 patients demonstrated more than 50% stenosis in one or more epicardial coronary arteries according to CA, confirming the presence of obstructive CAD. When dobutamine ECHO was employed as a standalone diagnostic tool, it exhibited a sensitivity of 78.4% and a specificity of 84.6%, showcasing its capability to identify true positive cases while minimizing false positives.

Our study explored the augmentation of diagnostic accuracy by incorporating ECG alongside dobutamine ECHO. The combined approach demonstrated a notable enhancement, with sensitivity increasing to 89.2% and specificity reaching 92.3%. This suggests that the integration of ECG complements dobutamine ECHO, providing a more comprehensive and accurate assessment of obstructive CAD.

The mean age of the study population (42.3 ± 10.7 years) suggests a relatively younger cohort compared to some studies where patients with suspected CAD might be older on average. For example, the mean age of the large ISCHEMIA trial, Initial Invasive or Conservative Strategy for Stable Coronary Disease, study population was around 64 years old [7]. This could indicate that our study is capturing a broader age range, possibly including individuals with early-onset CAD or those with risk factors at a younger age. The gender distribution in our study (52% male, 48% female) appears to be relatively balanced. Discordant with our results, males were the most affected with CAD in most of the studies. The percentages of males in the ISCHEMIA trial, the Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX) were around 75% [7, 8]. However, gender distribution in our study aligns with the understanding that CAD affects both men and women, and recent research emphasizes the importance of considering gender-specific risk factors.

In line with previous studies [7, 8], the prevalence of cardiovascular risk factors, including diabetes mellitus (DM), hypertension (HTN), obesity, smoking, and hyperlipidemia, aligns with expectations for a population with suspected CAD. The high prevalence of hyperlipidemia (78%) emphasizes the importance of lipid management in this patient group. The incidence of a family history of CAD (44%) is in line with the recognition that a familial predisposition contributes to the development of CAD. This reinforces the importance of considering family history as a significant risk factor in risk assessment and management.

Stress echocardiography is a widely accepted method for determining the degree and severity of coronary artery disease. This diagnostic approach involves applying physical, pharmacological, or electrical stress in combination with echocardiography, providing a highly accurate diagnosis of myocardial ischemia. One notable characteristic of inducible ischemia is a brief deterioration of localized function during stress. In comparison to other imaging methods like magnetic resonance or radionuclide stress perfusion imaging, stress echocardiography stands out for its cost-effectiveness, lack of negative environmental impact, and absence of biohazards to both patients and healthcare providers [9].In pharmacological stress testing for diagnosing coronary artery disease with echocardiography, dipyridamole and dobutamine are commonly used stressors, suggested over 20 years ago [10, 11]. Naser *et al*. conducted a study utilizing DSE in 86 individuals, demonstrating high sensitivity (97%), specificity (83%), and accuracy (95%) compared to invasive diagnostics like coronary angiography. They concluded that DSE has significantly advanced as a non-invasive diagnostic tool for identifying coronary artery disorders, myocardial ischemia, viability, and prognostics [12].In the broader context of stress echocardiography, the reported accuracy of stress echocardiography varies, with sensitivity values for ischemia detection ranging from 40 to 92% for dipyridamole, 68 to 96% for dobutamine, and 75 to 93% for pacing. Specificity, on the other hand, ranges from 93 to 100%, 66 to 100%, and 76 to 100% for the respective stress modalities [13]. However, the accuracy is influenced not only by the physician's expertise in performing and interpreting echocardiographic images but also by various clinical, anatomical, and physiological factors. These factors include patient heterogeneity, variability of stress protocols, severity and location of coronary disease, significance of diseased vessels, presence of collateral circulation, and degree of ventricular hypertrophy [14].

In terms of standalone exercise ECG analyzing eight separate investigations, Froelicher found a sensitivity of 64% (range 33 to 82%) for exercise ECG [15], while a

meta-analysis by Gianrossi*et al*. involving 147 trials calculated the mean specificity of the exercise test to be 77% [16]. Despite these figures, exercise ECG may suffer from motion artifacts and hyperpnea during exercise, potentially affecting image quality. Advances in imaging and recording methods have helped overcome these challenges [4].Dobutamine ECG as standalone test was used in the past. Canella *etal*. illustrated that continuous ECG monitoring, though improbable, could offer supplementary insights compared to the ECG obtained after each dobutamine dosage. The study encompassed a varied patient cohort, including individuals in the post-myocardial infarction phase, presenting challenges such as Q waves and repolarization issues that complicate the analysis of dobutamine-induced electrocardiographic changes. Nevertheless, the outcomes were positive.[17] Comparisons between dobutamine stress echocardiography and other methods, such as dobutamine ECG, reveal notable differences in sensitivity. Cohen *et al*. found ECG to have less than 10% sensitivity in 51 patients with coronary artery disease, compared to 86% for dobutamine echocardiography [18]. Similarly, Mzeikd*et al*. reported a sensitivity of 47% vs. 78% for ECG and dobutamine echocardiography, respectively, using the same ECG criteria but different dobutamine protocols [19]. In the context of pharmacological stress testing, the role of ECG data versus imaging becomes evident. Typically, ECG data is overlooked, and the image is the primary determinant of a positive or negative test result. Even in cases where the ECG does not exhibit exercise-induced alterations, patients are diagnosed with ischemia based on imaging findings. In contrast, a patient with normal pictures and ECG abnormalities indicative of ischemia is often considered an electrocardiographic false positive [20].

Our study results, in comparison to others, underscore the robust correlation and effectiveness of combined dobutamine ECHO and ECG in diagnosing and assessing coronary artery disease. In our investigation, we observed a significant correlation (P value <0.001) between dobutamine ECG, dobutamine ECHO, and coronary angiography. Combined dobutamine ECHO and ECG demonstrated impressive metrics with 90% accuracy, 90% sensitivity, 75% specificity, 89.19% positive predictive value (PPV), and 92.31% negative predictive value (NPV). Our study delved into the initial research that evaluated this combination in cases of myocardial ischemia.Discordant with our study, authors comparing ECG and imaging data for the same patient in pharmacological stress testing with dobutamine have concluded that imaging is more reliable and informative than ECG [21]. However, sensitivity and specificity of pharmacological stress tests using dobutamine-ECG depend on the interpretability of the baseline ECG and the patient's likelihood of having coronary artery disease. Individuals with a reduced risk of coronary artery lesions may exhibit lower sensitivity [22].

The utilization of dobutamine testing in conjunction with continuous ECG recording for identifying coronary lesions has been explored in previous studies. While some studies employ electrocardiographic control with recordings made every three minutes and constant echocardiographic monitoring, others collect the ECG at specific intervals after dobutamine infusion. Results from these studies suggest that continuous ECG monitoring may provide additional information, particularly in diverse patient populations, including those in the post-myocardial infarction phase [22].

Our study, assessing dobutamine ECHO and ECG separately, stands out for its strengths. All patients underwent gold standard coronary angiography, regardless of DSE results. Blinded assessments by two separate physicians and declarations after coronary angiography enhance the reliability of our findings.

Limitations:

A relatively small sample size, potential variations in operator expertise and equipment qualityneed acknowledgment. Larger cohorts and standardized protocols in future research are essential to validate and build upon our results.

CONCLUSION

Our study supports the diagnostic superiority of combined dobutamine ECHO and ECG, offering a simple, cost-effective, and widely available non-invasive test for diagnosing chronic coronary syndrome with improved accuracy.

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