DIAGNOSTIC YIELD OF STRESS ECHOCARDIOGRAPHY IN CORONARY ARTERY DISEASE PATIENTS

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ABSTRACT

Objective: *To find out the sensitivity and specificity of dobutamine stress echocardiography in comparison to the angiographic findings.*

Methodology: *This Cross-Sectional study was conducted at cardiology department, Lady Reading Hospital Peshawar, from January to December 2007. Data was collected by non probability purposive sampling technique. Study patients underwent both dobutamine stress echo and coronary angiography, after taking an informed consent. Dobutamine stress echo was performed according to standard protocol.*

Results: *Total of 50 patients, whose mean age was 51.6+/-9.7, were studied. Men were 35 (70%) and women were 15 (30%). Dobutamine was infused (10 to 40 micrograms/kg/min) in 3 minutes intervals. The inducible ischemia was detected in total 33(66%) patients. Seven patients (14%) had only resting wall motion abnormalities with no change by dobutamine stress. These patients were also taken as positive for ischemia. Coronary angiography showed 43/50 (86%) patients had > 50% stenosis in at least one coronary artery. Compared with coronary angiography, the sensitivity, specificity, positive and negative predictive values and accuracy of dobutamine stress echo for detection of coronary artery disease were 91%, 86%, 97%, 60%and 90% respectively. The sensitivities for SVD, DVD and TVD were 76%, 89% and 100% respectively.*

Conclusion: *Dobutamine stress echo is a sensitive and specific method in non invasive diagnosis of suspected CAD. It is highly sensitive for multivessel disease as compared to single vessel disease.*

Key Words: *Dobutamine stress echo, Coronary artery disease, Coronary angiography.*

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INTRODUCTION

Coronary artery disease remains a major public health problem[1]. It is the leading cause of death worldwide[2]. Based on data from the Framingham Heart Study the lifetime risk of developing symptomatic CAD after the age 40 is 45% for men and 32% for women[3].

The prevalence of chronic stable angina in European countries is 2-4%[4]. Several studies have shown that mortality on average is approximately 2-3% per annum and a further 2-3% each year will sustain a non-fatal myocardial infarction[5-7]. By this sharp increase in the prevalence of CAD the emphasis needs to be shifted from the treatment to prevention and early diagnosis.

The non invasive diagnosis of CAD is still a frequent and important clinical challenge in the contemporary cardiology. Numerous stress methods have been introduced for the induction of myocardial ischemia. Although coronary angiography remains the gold standard for the diagnosis of CAD but it can not be applied as a screening test, because it is invasive, costly and needs definite cardiac catheterization laboratory.

By comparison stress echocardiography is a widely available, safe reliable and cost effective

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test for the non invasive diagnosis of CAD[8]. Echocardiography has been used in combination with different drugs including dobutamine, dipyridamole and adenosine[9]. Dobutamine is probably the single most studied drug for stress. Dobutamine when combined with echocardiography fulfils all the prerequisites of a good diagnostic test. Today it has been the subject of increasing interest and use in different clinical setting such as detection of CAD[10] assessing the results of various revascularization procedure[11] and for risk stratification[12].

Dobutamine increases myocardial oxygen demand through positive inotropic and chronotropic effects. Thus escalating doses of dobutamine often are administered in conjunction with echocardiography to determine whether significant coronary artery disease is present particularly in patients unable to perform adequate exercise[13]. It is particularly useful in patients with atypical chest pain and do not have significant ECG changes[14] as well as in patients with LBBB, LVH or echocardiographic re-polarization changes.

Stress echocardiography is relatively less frequently used test for the diagnosis of coronary artery disease. So this study was conducted to know about the effectiveness of this diagnostic modality in our local setup.

It aids selection for coronary angiography and intervention at a very low cost. Thus in the era of emphasis on cost containment and universal health care access the lower cost, portability and easy availability of DSE will probably make this test modality extremely appealing in the near future.

METHODOLOGY

This cross sectional study was conducted in Cardiology department, Postgraduate Medical Institute, Lady Reading Hospital, Peshawar, from January 2007 to December 2007.

Non probability purposive sampling was used. Using WHO sample size estimating software, 50 stable angina patients at 95% confidence level with 5% margin of error was needed to find out the sensitivity and specificity of dobutamine stress echocardiography in comparison to the angiographic findings. The expected prevalence of patients with stable angina was 3.5%.

All patients with stable angina and undergoing coronary angiography with or without past history of myocardial infarction were included in the study. Patients with acute coronary syndrome, acute myocardial infarction, valvular heart diseases, congestive heart failure uncontrolled hypertension (systolic BP>190mmHg, Diastolic BP >120) and uncontrolled arrhythmia were excluded from the study.

Patients were admitted to cardiology department for dobutamine stress testing and coronary angiography and they were given specific computer numbers. They were briefly explained about the procedure and its risks and benefits. Verbal and informed consents were taken about the procedure. Under resting condition i.e before administration of dobutamine, all standard echocardiographic views were recorded where possible. Patient was started dobutamine infusion at 10µg/Kg/min for 03 minutes, and dose was increased by 20, 30, and 40µg/Kg/min. in 03 minutes as per incremental dosing protocol. When patient failed to achieve 85% of age predictive maximum heart rate and had no symptoms and signs of ischemia, atropine in a dose of 1mg was added after the last stage. End points for test termination included limiting symptoms, 85% age predicted heart rate, maximum dose of dobutamine, ST- segment depression of > 2mm on ECG, severe hypertension(systolic B.P>220 and diastolic B.P >120mmHg), or a drop in systolic B.P of > 40mmHg from the previous stage or any significant arrhythmia. B.P, heart rate and ECG were recorded at the end of each stage.

Echocardiographic Image Analysis:

For semiquantitative assessment, the LV was divided into 16 segments model recommended by the American Society of Echocardiography. Left ventricular wall motion was assessed qualitatively and graded as normal, hypokinetic, akinetic or dyskinetic according to 4 point scale. A score of 1(normal) to 4(dyskinetic) was assigned to each segment under resting conditions and during the test. A wall motion score index was derived by summation of individual segment score divided by the total number of segments.

A test was considered positive if new wall motion or worsening of previous wall motion abnormality developed in $\geq$ 1 segment and score increased by $\geq$ 1 grade. The resting wall motion abnormality was also considered positive in this study.

Coronary Angiography:

Coronary angiography was performed in all patients the next day after completion of DSE test. Judkin's technique was used via right femoral artery approach. Coronary angiogram was

evaluated by two independent observers, unaware of the DSE results. A coronary stenosis was considered significant if the vessel diameter was narrowed by≥ 50% in a major epicardial coronary artery or a major branch vessel. Visual estimation of percent diameter stenosis was performed in all the patients. The view demonstrating the maximum stenosis was considered for analysis.

Statistical Analysis:

Data was presented as means and frequencies along with standard deviation. Sensitivity, specificity, positive predictive values, negative predictive value and accuracy were calculated according to standard definitions. Student t test was used for analysis of continuous data i.e heart rate,systolic blood pressure, and wall motion score index in resting and peak stress test. P value of less than 0.05 was considered significant. Data was analysed in SPSS version 11.

RESULTS

A total of 50 patients aged 29 to 70 years presenting with chest pain of myocardial ischemic origin were enrolled in the study. Out of these 7 (14%) patients were having history of myocardial infarction and rest of the patients were having history suggestive of angina but no evidence of myocardial infarction. There were 35 males (70%) and 15 females (30%). The mean age was 51.6± 9.7years.

Stress Echocardiographic Characteristics:

The mean resting heart rate was 72.6± 11.9, peak heart rate was 136.9 ± 14.5, resting systolic B.P 128.3 ± 20.8, peak systolic B.P 143.9 ± 32.1, mean resting wall motion score index and peak wall motion score index were 1.2 ± 0.24 and 1.4 ± 0.3 respectively.

Wall motion score index increased significantly from rest to peak stress (1.2 ± 0.24 vs 1.4 ± 0.3 P< 0.0001). Similarly there was a significant increase in the heart rate and systolic blood pressure by dobutamine atropine stress test from resting to peak stress i.e. (72.6 ± 11.9 vs 136.9 ± 14.5 P<0.002) and (128.3 ± 20.8 vs 143.9 ± 32.1 P<0.0001) respectively Table 1.

Wall motion abnormalities as noted in different left ventricular segments, denoting the segmental arterial supply were LAD segments in 38 patients (76%), RCA segments in 26 patients (52%) and left circumflex segments in 14 patients (28%).

Dobutamine stress test was interpreted as normal in 10 patients (20%). Resting wall motion abnormality with no change with dobutamine stress was noted in 7 patients (14%). Inducible ischemia i.e new wall motion abnormalities with normal resting images was observed in 9 patients (18%). Resting wall motion abnormalities that worsened with dobutamine stress were present in 24 patients (48%).

Dobutamine dose required to achieve target heart rate was 20µg in 3 patients (6%), 30µg in 17 patients (34%) and 40 µg in 30 patients (60%).

A total of 9 patients needed atropine (18%) out of which 0.5mg was used in 6 patients (12%) and 1mg was used in 3 patients (6%).The reasons for test termination were completion of

Table 1: Peak Physiologic Response to Dobutamine

Parameters	Resting	Peak	p-value
Heart rate (Beats/min)	72.58 ±11.90	136.90 ±14.52	0.002
Systolic BP(mmHg)	128.30 ±20.79	143.86 ±32.05	0.0001
WMS	19.62 ±3.77	22.62 ±4.63	0.0001
WMSI	1.22 ± 0.23	1.41 ± 0.28	0.0001

maximum dose of 40µg /kg/min, in 17 patients (34%), chest pain in 4 patients (8%), 85% of the age predicted heart rate in 28 patients (56%) and supraventricular tachycardia in 1 patient (2%). The test was not stopped because of minor side effects like palpitation, sweating or nausea.

Overall Efficacy of DSE for Detection of CAD:

Out of 40 patients, detected as positive by DSE, 39 patients were true positive, 1 patient was false positive. Among 10 patients detected as negative 6 were true negative and 4 were false negative (Table 2). Out of 4 patients who were false negative, three had single vessel, one double and no patient had triple or left main stem disease.

The overall sensitivity, specificity, positive predictive value, negative predictive values and accuracy of dobutamine stress were 91%, 86%, 97%, 60% and 90% respectively with dobutamine stress echocardiography correctly identifying 39 patients with and 1 patient without disease (Table 3). The low negative predictive value in this study could be due to high pretest probability of study population.

Coronary angiography:

Significant CAD was detected in 43 patients (86%). Thirteen patients (26%) had single vessel disease, 9 (18%) had double vessel disease, 18 (36%) had triple vessel disease and 3 patients (6%) had multivessel and left main stem disease. The sensitivity of DSE for single and double vessel disease was 76% and 89% respectively while for triple vessel and left main stem disease it was 100% each (Table 3).

Table 2: DSE Versus Coronary Angiographic Results

DSE	Coronary angiography		Total No. of cases
	Disease Absent	Disease Present	
Positive	1	39	40
Negative	6	4	10
Total	7	43	50

Table 3: Sensitivity and Specificity of DSE

Sensitivity	91%
Specificity	86%
Positive predictive value	97%
Negative predictive value	60%
Accuracy	90%
Sensitivity for SVD	76%
Sensitivity for DVD	89%
Sensitivity for TVD	100%
Sensitivity for LMS	100%

DISCUSSION

The criteria used for positive test was resting wall motion abnormalities, as well as new wall motion abnormalities and worsening wall motion abnormalities. This criteria was also used in international studies . However in most of other studies resting wall motion abnormalities were not included in positive stress test result.

The overall sensitivity, specificity and accuracy reported in other studies are 80%, 84%, and 81% respectively. The sensitivity range is 71% to 94%. Similarly the specificity range is 64% to 90%[15].

In our data, the sensitivity was low for single vessel disease, i.e. 76% and high for double and triple vessel disease i.e. 89% and 100% respectively. In the literature the sensitivity of DSE in case of single vessel disease is low and for multivessel disease it is high[16,17].

The mean sensitivity was 74%, 86% and 92% for single double and triple vessel disease respectively. Sawada and associates[18] reported their experience in 103 patients who underwent dobutamine stress echocardiography and quantitative coronary angiography. Significant coronary artery disease, defined as 50% or more diameter stenosis, was present in 81 patients. Among these patients, the sensitivity and specificity of dobutamine-induced wall motion abnormalities for coronary artery disease were 89% (31 of 35) and 85% (17 of 20), respectively, and the sensitivity was 81% (17 of 21) in those with single-vessel disease and 100% (14 of 14) in those with multivessel disease.

In study done in Mayo Hospital Lahore the sensitivity, specificity, PPV and NPV of DSE compared with angiography were 87.5%, 95.2%, 87.5% and 82.35% respectively. For single, double and triple vessel disease the corresponding sensitivity for single, double and triple vessel disease were 77.5%, 85.7% and 100% respectively.

The diagnostic approach to coronary artery disease (CAD) using noninvasive methods still presents a challenge even today. The classically used methods such as treadmill stress testing have a rather low specificity and sensitivity especially in patients with one-vessel disease as well as methodological limitations such as in patients with mobility problems or left bundle branch block. In those patients drug myocardial scintigraphy with adenosine and dobutamine stress echocardiography provide a good alternative. Stress echocardiography has become a widely used examination, whose clinical utility, over the whole spectrum of CAD manifestations, has been well established by a large number of clinical studies.

Unfortunately in our country there are less number of studies that evaluated the efficacy of DSE, as a new possible diagnostic tool for the non invasive diagnosis of CAD. One such study was carried out in Mayo Hospital Lahore in which DSE was compared with exercise stress test and coronary angiography[19].

We used the same protocols for dobutamine stress i.e incremental doses of dobutamine from 10 to 40µ/kg/min with or without the addition of atropine at peak dose if the target heart rate was not achieved, as was used in previous studies. Reasons for test terminations were also same as in previous studies[15].

In this study the possible bias could be the patients with old myocardial infarction, and resting wall motion abnormalities. Seven patients were having only resting ischemia. This increased the sensitivity. If we exclude these patients then the sensitivity, specificity, PPV, NPV and accuracy of DSE would become 89%, 86%, 96%.,60%, and 76% respectively. All these 7 patients were true positive. In future studies we can select patients having history of angina and no history of myocardial infarction. But in our study it has only slightly increased the sensitivity but no effect on specificity as the population of MI patients was less.

Secondly majority of patients in our study were men (70%) in whom the prevalence of CAD is high, this could also have raised the sensitivity. Thirdly majority of our population (86%) had significant stenosis and out of these, majority had triple vessel disease (36%). This high prevalence of severe disease could also potentially raise sensitivity.

Another reason for high sensitivity may be referral bias. Most of these patients were being referred for angiography because of high pretest probability of CAD.

The major limitation of the present study is the subjective, non quantitative interpretation of echocardiographic images. Secondly quantitative coronary angiography for exact measurement of luminal diameter was not used. Only visual assessment was done.

Further studies are needed to use the quantitative techniques for the detection of ischemia like tissue Doppler imaging, strain and strain rate imaging, contrast echocardiography and 3D imaging. Also further studies are needed to evaluate the role of stress echo in risk stratification and to compare it with other non invasive investigations.

CONCLUSION

Dobutamine stress echo is highly sensitive, specific and accurate method for the non invasive diagnosis of CAD. The sensitivity of DSE is high for multivessel disease as compared to single vessel disease.

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CONTRIBUTORS

MA conducted, analyzed & wrote the manuscript. MH proposed & supervised the study. HT helped in the interpretation of stress echo cardiography results. MMP helped in final compilation. SQ helped in data collection and performing the stress echo cardiography .

GRANT SUPPORT, FINANCIAL DISCLOSURE AND CONFLICT OF INTEREST

None Declared