
DOBUTAMINE AND EXERCISE ECHOCARDIOGRAPHY IN THE EVALUATION OF KNOWN OR SUSPECTED CORONARY ARTERY DISEASE

AN OBSERVATIONAL STUDY FROM SINGLE CENTRE

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ABSTRACT

Background: Stress echocardiography has emerged as an important tool for non-invasive assessment of coronary artery disease (CAD). Exercise and dobutamine stress echocardiography (DSE) are frequently used modalities with distinct clinical indications and procedural variations. We report our findings on these two tests comparing various aspects and outcomes.

Methods: Four hundred seventy one consecutive patients underwent SE at Sheikh Zayed Hospital Rahim Yar Khan. Exercise Echo (Ex.E) was performed on treadmill using Bruce's protocol. DSE performed in standard method. SE was considered as positive with the appearance of new or worsening wall motion abnormality.

Results: Ex.E performed by 300 patients and DSE 171 with mean age of 48.09 and 54.92 respectively. Males were dominant in both groups. The risk factors were almost same in both groups. Ex.E was more performed for diagnosis of CAD than DSE (59% vs 25%). Viability testing was exclusively done by DSE. Post revascularization status was assessed in 10% and pre operative assessment for non cardiac surgery in only 2%. Incidence of side effects was 26% in DSE and none in Ex.E. The double product was greater in Ex.E. Positive tests were reported in 43% and 33% in DSE and Ex.E respectively. Stress induced LV dysfunction was more common in DSE. Comparing available coronary angiograms, single vessel disease was better detected by DSE (60% vs 46%). Double vessel disease was relatively higher in Ex.E (35% vs 28%).

Conclusion: Ex.E is safer and better non invasive diagnostic imaging modality in patients who can perform physical exercise, however DSE is more useful for viability, pre operative evaluation and patients physically disabled for treadmill or ergometer exercise test.

Keywords: Exercise Echocardiography, Dobutamine Stress Echocardiography, Coronary Artery Disease.

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INTRODUCTION

Stress Echocardiography (SE) is an extremely useful non invasive modern diagnostic tool for the evaluation of known or suspected coronary artery disease (CAD patients).^{1,2,3} The most common types of SE performed in clinical practice are Exercise Treadmill Echocardiography Ex.E and Dobutamine Stress Echo (DSE). The indications and techniques are different in both tests. The published data on SE is scarce in our country and moreover the comparative study between these two sisters modalities has never been reported from Pakistan. In this descriptive study, we will look into the indications, feasibility, outcomes and clinical implications of these two tests.

METHODS

PATIENTS:

Four hundred and seventy one consecutive patients underwent SE from March 1999 to October 2003 at Sheikh Zayed Medical College/Hospital, Rahim Yar Khan. Inclusion criteria was all those patients referred for evaluation of suspected or known ischemic heart disease. The patients having physical disability or inability to perform exercise were subjected to dobutamine stress echo. All other patients were included for treadmill exercise echo. Exclusion criteria was known contraindication to dobutamine / exercise echo.

Patients reported for SE with overnight fast or minimum 2½ hour fasting before the procedure. Medications were omitted 48 hour prior to the test in stable patients while unstable patients were tested on treatment. Clinical data regarding risk factors, prior ischemic heart disease, revascularization and cardiac drugs were recorded on pre-designed proforma. History and short physical examination was performed to rule out known contraindications to exercise/dobutamine SE.

EQUIPMENT:

We performed our studies using Toshiba's power vision digital echocardiographic machine model SSA 380A and TomTech^{pro} integrated operating system for stress and a multi frequency probe (2.5, 3.7 and 5 MHz). Studies recorded simultaneously on videotapes, magnetic optic disk (MOD's) and hard

disk. An echocardiographic bed with cutout window was used to facilitate imaging from cardiac apex. 12-lead ECG recorded at rest and end of each stage and during recovery. 1 mm down sloping or flat ST depression from J point considered positive for stress induced ischemia. Rhythm was continuously monitored to detect any arrhythmia. Dobutamine infusion administered through automatic infusion pump. BP and heart rate recorded at each stage. Fully equipped resuscitation trolley was available at bedside throughout the study. ETT was performed using standard treadmill machine.

PERSONALS:

**Author (SFH) himself performed all echocardiographic studies and their interpretation. Trained charge nurse took pulse and BP. An ECG technician recorded 12-lead ECG and looked after monitoring system. Clinical data collected by a trained computer assistant.

IMAGING:

EXERCISE TREADMILL ECHO:

Resting images obtained from standard imaging plain, digitized and stored. Chest electrodes were applied in a modified fashion i.e. one intercostal space above for V₂,V₃ and one space below for V₄,V₅,V₆ to facilitate the images from apex and parasternal area. In majority of patients Bruce protocol adopted and minority of patients were exercised on modified Bruce protocol. Exercise terminated according to recommended criteria. Patient laid down on imaging bed in the left lateral decubitus position immediately at the cessation of exercise (without cool down period). The post stress acquisition of images carried out within 60-90 seconds. The stress and rest images displayed side by side on quad screen format in cine loop. The study saved on hard disk and MOD's for future references.

DOBUTAMINE STRESS ECHO:

Resting echocardiographic images obtained from parasternal and apical windows. Four standard views 1= parasternal long axis, 2= parasternal short axis, 3= apical 4-chambers, 4= apical 2-chambers were obtained. In addition apical long axis and apical short axis views were also frequently recorded. Images recorded at the end of each stage (rest, low, mid and

peak dose). All images were digitized on-line and displayed side-by-side for comparison with resting images in a continuous cine loop. Four independent quad screens were used, 1 for all 4-chambers apical views, 1 quad screen for all 2-chamber apical view, and so on. The upper left quadrant of each quad screen showed base line images, the upper right quadrant for low dose and lower left quadrant for mid dose and lower right quadrant for peak dose images.

Echocardiographic Interpretation: 16 segments model recommended by the American Society of Echocardiography⁴ was used for analysis and each segment was scored on the basis of its motion and systolic thickening. 1= normal 2= hypokinetic 3= akinetic 4= dyskinetic 5= aneurysm. Wall motion score index (WMSI) was calculated dividing the sum of scores by total number of segments visualized. WMSI derived both for rest and stress. Positive test was labeled when a new wall motion abnormality noted or worsening of existing abnormality (hypokinesia to akinesia) appeared. Lack of hyperdynamic response to adequate level of stress was also considered as hypokinesia.⁵ For viability, biphasic response (improvement at low dose and worsening at high dose) was considered as the most positive indicator.

However persistent improvement in regional function till peak dose was also considered for viable myocardium or cardiomyopathy. Global LV function was assessed by EF and end systolic volume (ESV). Normally EF increases and ESV decreases during stress if it happens otherwise test is considered positive for exercise induced LV dysfunction.

RESULTS

Total 471 patients underwent SE (300 Ex.E & 171 DSE). Majority of patients in Ex.E were of younger age groups than DSE (Mean age 48.09 Vs 54.92). Males were dominant and almost equally distributed in both groups; however females were more in DSE than Ex.E. The risk factors were similarly present in both groups except hypertension and smoking which were more frequently noted in males (Table 1).

The diagnostic indications for CAD were 59.3% Vs 25% in Ex.E and DSE respectively. Evaluation of known CAD was the second most frequent indication

for SE. The viability assessment was performed by DSE in 24% and none in Ex.E. The post revascularization status in CABG / PCI were studied in about 10% of all cases. Only 2% patients were tested for pre-operative assessment for non cardiac surgery. In Ex.E the test was terminated due to fatigue/dyspnoea in 86% and angina/ECG changes in 14%. In DSE test stopped due to new regional wall motion abnormality in almost half of the patients, 22% achieved target heart rate, 10% developed hypertension, 10% peak dose of dobutamine was administered. Only 7% complained of angina and 3% tests were terminated because of ventricular arrhythmias.

Table 1 - Patients characteristics

	Ex.E	DSE
Mean Age	48.09	54.92
Male.	205(68%)	106(62%)
Diabetes Mellitus	22%	26%
Hypertension	54%	31%
Smoking	33%	19%
Hypercholesterolemia	20%	22%
Family History of CAD	19%	25%
Diagnostic of chest pain, dyspnoea or LV dysfunction	178(59.33%)	43 (25%)
Evaluation of known CAD	107(35.67%)	73 (43%)
Assessment of viable myocardium	0 (0%)	42 (24%)
Follow up after CABG	9 (3%)	8 (5%)
Follow up after angioplasty/atherectomy	3(1%)	2(1%)
Preoperative assessment for non-cardiac surgery	2(0.67%)	3(2%)
Rehab study after MI	1(0.33%)	0(0%)
No of patients	300	171

The incidence of side effects in DSE was 26% and their frequency was light headedness, chest pain, palpitation, tremor or shivering in descending order. One patient developed VF who was successfully resuscitated. (Table 2)

Table 2 - Frequency of Side Effects in DSE

Side Effects	Percentage
Headache	4
Palpitations	14
Chest Pain	33
Lightheadedness	36
Tremor or chills	7
Others	4

Complications

Complications	Percentage
Sustained V-Tachycardia	2

The majority of patients in both groups had satisfactory image quality except 10% cases had inadequate post exercise images in Ex.E. Average maximum heart rate was more in Ex.E than DSE (148 Vs 102 mmHg). Maximum average systolic blood pressure was almost same (145 Vs 140 mmHg). Patients obtained better workload in the form of heart rate and systolic blood pressure in Ex.E than DSE. (Double product 21460 Ex.E vs 14280 DSE). The acquisition time defined as the time from the termination of exercise and completion of acquiring post stress images was 60 – 90 seconds in 248 patients (83%) and within 60 seconds in 42 patients (14%). Only 10 patients (3%) were imaged in more than 90 seconds.

The overall results revealed negative tests as 61% & 53% in Ex.E and DSE respectively, wherein the positive percentage was more in DSE (47.3%) comparing Ex.E (33.6%). Inconclusive tests were only 5.3% in Ex.E and none in DSE. Post stress increase in end systolic volume (ESV) and decrease in EF occurred more in DSE than Ex.E. The coronary angiograms of 14 patients were available for comparison. There was 100% correlation with SE. The single vessel disease was more detected by DSE than Ex.E(60% Vs 46%). The double vessel disease was relatively high in Ex.E (35%) comparing DSE (28%). The correlation of lesions in different coronary artery territories on stress echo was almost similar to coronary angiography except left circumflex distribution. LAD lesions were equally detected on both modalities wherein RCA and LCx disease were diagnosed significantly higher in DSE than Ex.E. (Table 4)

Table 4 - Correlation with Coronary Angiography

Positive Stress Echo	Positive Coronary Angio	Correlation
14	14	100%

Distribution of lesions by individual coronary arteries

Vessels	No. of Lesions detected by SE	No. of Lesions detected by Cor. Angio.
LAD.	12	12
RCA.	12	13
LCx.	9	13
Total Lesion	33	38

P. Value = 0.193

Table 5 - Comparison of detection of lesions by DSE vs Ex. E

No. of lesions detected by	LAD	RCA	LCx.
DSE	7(88%)	8(100%)	7 (88%)
Ex. E	5 (83%)	4(67%)	2(33%)
p. value	0.108	0.02	0.009

LAD = Left Anterior Descending; RCA = Right Coronary Artery; Left Cx. = Left Circumflex Artery.

DISCUSSION

From the study cohort of 471 patients, 300 (64%) underwent treadmill exercise echo and 171 (36%) underwent dobutamine stress echo. Patients who underwent dobutamine stress were older and more often had a history of previous MI and bypass surgery, more cardiac risk factors (hyperlipidemia, hypertension, diabetes, smoking, and family history of premature (CAD), more frequent abnormal resting ECGs, a higher peak WMSI, a greater number of new reversible wall motion abnormalities, worse LV systolic function.

In this series of patients 61% and 53% were negative tests for diagnosis of CAD in DSE and Ex.E respectively and therefore these patients were not recommended for coronary angiography. With limited resources a test with high predictive value is very useful to restrict expensive invasive procedure like coronary angiography. Predictive value and diagnostic accuracy of dobutamine stress echocardiography is superior than simple exercise ECG.^{5,6} The diagnostic sensitivity and accuracy directly comparing exercise echocardiography with DSE in the same 334 patients revealed higher values in favor of exercise echo (sensitivity 85% vs 75% p < 0.01) and (accuracy 86% vs 79% p < 0.05).^{7,8,9,10,11} In our study majority of patients underwent Ex.E (64% vs 36%). Exercise echocardiography is superior to DSE because it is more physiological, better hemodynamic profile, reproduction of symptoms and less side effects. In current study 26% patients develop some sort of side effects with DSE and none in Ex.E.

However exercise echo is technically more demanding due to hyperventilation, excessive chest wall motion and tachycardia. DSE is less demanding because the patient is lying comfortably in a good

ultrasound imaging position, no hyperventilation or marked tachycardia and ample time for imaging.

The low annual risk of 0.4-0.9% have been reported with a normal stress echocardiography in number of studies, one of them enrolled 9000 patients.¹²⁻¹⁷ Contrarily a positive stress echocardiography and extent of regional wall motion abnormalities is directly associated with higher risk of events.^{11,18} In our series almost half of patients in DSE and 61% in Ex.E have normal stress echo. They were reassured and advised for risk factor modification and no further invasive test was suggested.

We performed DSE for viability studies in 24 % of all patients. DSE is a valuable test for detection of hibernating myocardium (84% sensitivity, 81% specificity).^{19,20} Increase in end systolic volume and decrease in EF was noted more in DSE than Ex.E and it was perhaps due to high number of resting LV dysfunction studied for viability purpose in DSE group. Only 2% patients underwent preoperative evaluation wherein DSE is considered as one of the most important test for the evaluation of cardiac risk in patients undergoing major non cardiac surgery. It is perhaps due to lack of awareness on the part of surgeons/anesthetists and non availability of trained personals to perform DSE in our country. 10% of the patients were studied for the assessment of revisualization procedures. Our acquisition time was almost the same as recommended, 83% within 60-90 seconds and 14% within 60 seconds. Almost all patients have good imaging quality except 10% have inadequate post stress images in Ex.E. Image quality and expertise of the person performing the test are two major determinants for a good quality stress echo.

100% correlation of stress echo with coronary angiograms was observed and coronary vessel distribution was almost same as detected on stress echo in LAD and RCA territory, however left circumflex disease was diagnosed relatively low and it is consistent with many studies. However, DSE was superior to Ex.E in the diagnosis of left circumflex disease (p.value 0.009). The mean sensitivities of DSE for the diagnosis of LAD, LCx and RCA are 72%, 55% and 76% and mean specificities were 88%, 93% and 89% respectively.^{21,22,23} The sensitivity for the diagnosis of left circumflex was less than for

LAD ($p < 0.02$) and RCA ($p < 0.005$). The lower sensitivity of LCx may be due to anatomic variation and problems with resolution of lateral wall endocardium.

Non cardiac side effects like lightheadedness was frequently encountered in DSE followed by tremor or chills. Chest pain was complained by 33% of patients which is higher than reported elsewhere (20%)^{25,26}. However severe angina leading to termination of test was occurred in 4% in DSE and 9% Ex.E. None of the patient developed dobutamine stress induced hypotension in our series which is reported 20% in certain studies^{23,24}. Reason may be relatively less peak dose of dobutamine given in our series and very limited use of atropine (only in 8 patients). Only 2.3% patients developed ventricular arrhythmias in DSE and these are not uncommon 10% of the patients developed premature atrial or ventricular ectopy and 4% had runs of SVT or VT.^{24,25} The pooled data from various studies revealed ventricular fibrillation or MI in 1 in 2000 patients. Usually these arrhythmias appears in patients with resting wall motion abnormalities or previous history of arrhythmias. One of our patient developed ventricular fibrillation and was successfully resuscitated. He had previous anterior wall MI.

Limitations: Very few coronary angiograms¹⁴ were available for comparison the reason was the study was conducted at district hospital lacking facility of coronary angiography, financial constraints, traveling long distance to tertiary care centers, and uneducated rural population with dominant traditional taboos. However our data is quite insufficient for a true validation study. The study was conducted by a single investigator (SFH) who was trained as observer in stress echo at Mayo clinic Rochester MN, USA and therefore lacking intra-observer variability. One quarter of the patients in DSE group was studied for viable myocardium, hence not a true representative matching group for comparison with Ex.E patients mostly tested for diagnosis and evaluation of coronary artery disease.

CONCLUSION

Stress echocardiography has emerged as a valuable, non invasive, reproducible and cost effective tool for the assessment of coronary artery disease. However,

exercise echo is dependent on patient motivation and their ability to perform exercise. Dobutamine echocardiography is an alternative to exercise in patients who are physically handicapped or poorly motivated to exercise. Currently these investigational tools are not only underutilized in our country, but also, for the main part, remains unacknowledged by the health care providers. By the optimal use of stress echo in suspected or known cases of coronary artery disease can prevent significant number of coronary angiographies unnecessarily performed

Acknowledgment

We wish to acknowledge Dr. Ghulam Mustafa for his contribution in data analysis. Special thanks for Mr. Muhammad Ilyas for his secretarial assistance and Dr. Daniyeh for review of manuscript.

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