**2 DETERMINATION OF LESION SEVERITY BY DOBUTAMINE STRESS ECHOCARDIOGRAPHY WHEN COMPARED WITH QUANTITATIVE CORONARY ANGIOGRAPHY: A RETROSPECTIVE COHORT STUDY.**

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**ABSTRACT**

**Background:**

Exercise stress testing is done commonly for the detection of coronary artery disease (CAD). It is a non-invasive method for CAD detection. In certain patients where exercise testing is not possible, some other form of non-invasive stress testing is required. Out of various techniques which can induce ischemia, traditionally dobutamine stress echocardiography (DSE) has been relied up on. DSE can be done for detection and localization of CAD.

**Methods and results:**

In this study, a retrospective cohort study **was done** in the patients who underwent both DSE and quantitative coronary angiogram (CAG). The study was carried out on various parameters: a) severity of CAD was correlated with the heart rate at which a positive DSE test is obtained; b) ability of DSE to detect coronary artery stenosis with a minimal lumen diameter <1 mm was evaluated; c) a new model of coronary artery distribution was utilized to determine the ability of dobutamine stress echocardiography (DSE) in detecting stenosis in individual coronary arteries.
A total number of 104 patients were identified who underwent both DSE and CAG. All of these patients were evaluated on the above mentioned parameters. Interpretation of echocardiograms was done using a modified 16-segment model. Incremental infusion of dobutamine was given in all these patients. Two-dimensional echocardiograms were obtained: at rest, during low stress (low dose dobutamine), peak stress (peak dose dobutamine) and after stress (recovery). The data obtained was then analyzed for an overall sensitivity, specificity and accuracy of this technique in detection of CAD (diameter stenosis ≥50%).

**Conclusion:**

DSE was found to have a high sensitivity and specificity for the detection and localization of CAD when compared with CAG. Dobutamine stress echocardiography is equally sensitive in detecting CAD in all the three major coronary artery distributions, especially by using the modified 16-segment model with areas of coronary artery distribution. Lesions where the minimal lumen diameter is <1 mm are more likely to be correctly identified by DSE. A multivessel CAD is more likely to be present when a DSE becomes positive at a heart rate ≤125 beats/min.

Key words: Dobutamine stress echocardiography, Coronary angiography, Coronary artery disease.

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## INTRODUCTION

Exercise stress testing is done commonly for the detection of coronary artery disease (CAD). It is a non-invasive method for CAD detection. In certain patients where exercise testing is not possible, some other form of non-invasive stress testing is required. Out of various techniques which can induce ischemia, traditionally dobutamine stress echocardiography (DSE) has been relied up on for this. DSE can be done for detection as well as localization of CAD.

Some earlier studies have reported the role of DSE in providing information regarding the localization and severity of CAD in a patient. These studies focused up on the correlation between echocardiographic wall motion and coronary artery anomaly. A few of these studies[1] however managed to demonstrate such a relationship but many other were imprecise in their association regarding the same. Many of the earlier studies have used various pharmacological agents to induce cardiac stress in a patient in order to detect CAD.[2-7]Our study focused precisely to demonstrate the ability of dobutamine to induce the pharmacological cardiac stress in order to find out a correlation between the echo cardiographic wall motion abnormality and the associated coronary artery anomaly. The standard 16-segment model developed by Bourdillon *et al.*[8]for correlating myocardial segment with the coronary artery perfusing those segments was used in our study with slight modifications. These modifications were done in order to accommodate an overlap in coronary artery distribution to apical lateral and apical inferior myocardial segments. Many studies done previously have relied on qualitative assessment of the degree of coronary artery stenosis while comparing DSE with CAG.[2-7] However better accuracy in estimating coronary artery narrowing can be done by quantitative CAG.[8,9] The ability of DSE to accurately detect the significant stenosis in individual coronary arteries has varied widely.[1] Quantitative angiographic techniques can measure the percent diameter stenosis and the minimal lumen diameter of a specific lesion. DSE offers a better advantage over many other forms of standard exercise testing as the amount of cardiac stress can be controlled without much efforts. This helps to avert any side effects or complications that may be associated with exercise testing. Since the degree of cardiac stress can be controlled, DSE may provide a better accuracy regarding physiological significance of a coronary artery lesion.

After keeping all the benefits of DSE, certain aims and objectives were shortlisted for our study :a) to correlate severity of CAD with the heart rate at which a positive DSE test will be obtained; b) to look and evaluate the ability of DSE to detect coronary artery stenosis with a minimal lumen diameter <1 mm; c) to correlate the heart rate at which a positive test result occurs with the severity of coronary artery disease.

## MATERIALS AND METHODS

### Study design:

In this study, a retrospective cohort study. It consists of all cases that underwent DSE and CAG in Dhiraj General Hospital, Vadodara, Gujarat.Correlation between the echocardiographic wall motion abnormality and CAG findings was carried out. This study consists of data of patients who underwent both DSE and CAG in our cardiology department over one year i.e. December 2013 to November 2015. A total number of 104 such patients were identified and enrolled in our study. Patients were subjected to DSE only where exercise stress testing was not possible. This included the patients who had suffered prior stroke, or had claudication, severe arthritis or other conditions that prevented exercise stress testing. The patients who had undergone a prior coronary artery bypass grafting were excluded from our study group.

A total of 104 patients were selected. Out of these 68 were males and 36 were females. Then mean age of the patients was 56.6 years (range 24 to 76). The study protocol was approved by the institutional review board. An informed, written consent was obtained from all the study patients.

**Dobutamine infusion protocol:**

Dobutamine was started at 10 mcg/kg/min and increased every 3 minutes to 20, 30 and 40 mcg/kg/min. Infusion was started at a lower dose (5mcg/kg/min) if baseline LV function was abnormal. Images, electrocardiogram (ECG) and blood pressure were recorded at rest, at low dose (5 to 10 mcg/kg/min), at peak dose (30 to 40 mcg/kg/min) and the recovery (5 min. after termination of infusion). The dobutamine infusion was discontinued when any of the following end points were reached: a) a new regional wall motion abnormality or wall thickening noted in two or more contiguous segments; b) ≥2 mm ST segment depression on the ECG; c) >15 mm Hg decrease in systolic blood pressure from the baseline value; d) any significant side effects or arrhythmia; e) maximal dose of 30-40 mcg/kg/min; and f) achievement of 85% of the age predicted maximum heart rate (APMHR).

**QuantitativeCoronary Angiography:**

Judkins' technique was used to obtain single-plane coronary angiograms involving a standard cineangiographic system. This system was interfaced to a digital radiographic computer system (Xcelera r3.1L1).An investigator was assigned to report quantitative angiographic measurements of percent diameter stenosis and minimal lumen diameter. This investigator howsoever had no knowledge of the clinical history of the patient, ECG and DSE findings. Single cine images that best demonstrated the most severe narrowing were chosen for quantification. An automatic edge detection method was used for quantification of the luminal diameter and stenosis . The catheter shaft of known diameter was used as a reference to obtain a calibration factor. A centerline was automatically derived by positioning a circular region of interest over the catheter shaft. Calibration was achieved by entering the known catheter diameter resulting in a calibration factor (mm/pixel) for quantitative analysis. In a similar fashion, a circular region of interest was positioned over each stenotic segment. Quantification of the stenosis severity was then done by the designated operator. DSE wall motion abnormalities were then correlated with the location of stenosis in the individual coronary arteries. The stenotic location was determined by the geometric diameter percent stenosis and minimal lumen diameter. In a case if there was stenosis in the branch vessel, it was assigned to the main contributing vessel. Single vessel disease (SVD) was designated in the presence of ≥50% diameter stenosis in only one vessel. Multi-vessel disease (MVD) was designated in the presence of ≥50% diameter stenosis in more than one epicardial coronary artery. There was no separation done on the basis of left or right dominant circulation.

**Dobutamine Stress Echocardiography:**

Two-dimensional (2-D) echocardiograms (ECHO) were obtained with the GE S6 echocardiography machine using a 3 MHz transducer. Two-dimensional ECHO was done after placing the patient in left lateral decubitus position. Four views were taken in each case comprising of parasternal long-axis, parasternal short-axis at the papillary muscle level, apical four-chamber and apical two-chamber. All the four views were taken each during the stress ECHO at rest, at low dose dobutamine (5-10 mcg/kg/min), peak dose dobutamine (30-40 mcg/kg/min) and at recovery (5 min. after termination of infusion). Dobutamine dose was increased every 3 mins. All the ECHO cine loop images that were obtained were arranged in a quad screen display. This was done so that all images obtained in each stage could be directly compared during playback in a continuous loop format.

**Echocardiographic analysis:**

All the images were interpreted by two investigators who had no idea about the patients' clinical history, ECG or coronary angiograms. In case of disagreement between the two investigators, all the images were reviewed by a third investigator in blinded manner.

If there was a progressive increase in myocardial thickening or wall motion or both, it was designated as a normal response. In case there was a reduction in systolic thickening or wall motion at any stage in the protocol as compared to the previous stage, it was designated as an abnormal response. A lack of increase in the wall motion or systolic thickening, or both, with incremental dobutamine infusion was considered abnormal.

**Left ventricle segmental model:**

A modified scheme from that proposed by the Bourdillon*et al.*[8]was used (Figure 1.) to locate and correlate the segmental wall motion abnormalities with the coronary artery distribution. The apical lateral and apicalinferior segments were designated as overlap areas. The apicallateral segment was taken to be a part of the LAD coronary artery distribution in case there were associated additional septal or anterior wall motion abnormalities. The same segment was taken to be a part of theLCx artery distribution in case there were associated posterior or posterolateral wall motion abnormalities.The apical inferior segment was taken as part of the RCA distribution in case there were additionalinferior wall motion abnormalities. It was taken as a part of the LAD region in case there were additional anterior or anteroseptalwall motion abnormalities.Segmental wall motion was graded as previously reported.[1]

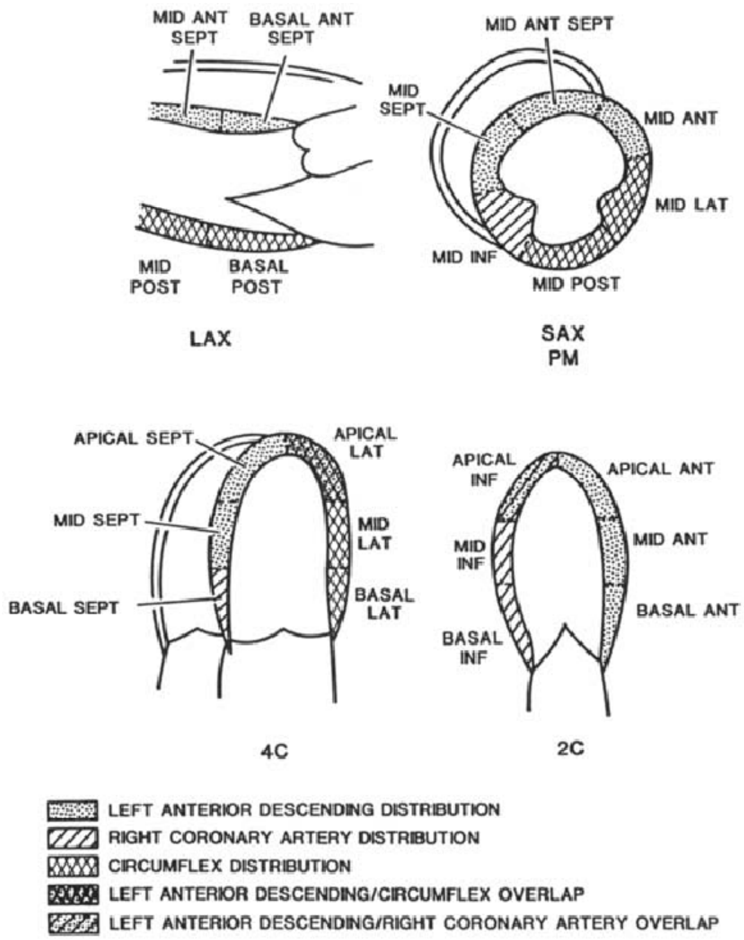


**Figure 1.** Diagram of the modified 16-segment model with areas of coronary artery distribution shown as areas of stippling or cross hatching. The overlap areas are represented as a combination of the graphics in the overlap territory. ANT = anterior; 4C = four chamber; INF = inferior; LAT = lateral; LAX = long axis; POST = posterior; SAX PM = short axis at the papillary muscle level;

**Statistical Analyses:**

Continuous variables were expressed as mean value ± SD ormedian with interquartile range.Data was analyzed using statistical variant analysis or SPSS after applying tests like chi square test. A *p* value of $<0.05$ was considered significant for the purpose of this study.

**RESULTS**

**Overall findings:**

Out of the total 104 patients 88 had abnormal coronary artery findings as defined by ≥50% luminal narrowing. DSE yielded abnormal results in 85 of the 88 patients. This led to an overall sensitivity of 96%. The test correctly identified normal status (stenosis of <50%) in 13 patients. This gave an overall specificity of 81% (13 of 16).

**Individual coronary artery stenosis:** (Table 1.)

A total of 138 coronary artery lesions were identified with a stenosis of ≥50% in diameter. Of 51 stenosis in the LAD coronary artery, 40 (78%) were identified on the basis of a wall motion abnormality in a region supplied by that vessel. Of the eleven stenosis that could not be detected, eight had <70% lumen narrowing and a minimal lumen diameter >1 mm and two lesions were in diagonal vessels.

A total of 34 lesions were identified in the LCx artery distribution. Out of these 34 lesions, 26 (76%) were detected by DSE. Of the eight lesions that were not attributed to LCx distribution, the DSE identified five in the right coronary artery distribution.

A total of 53 RCA lesions were identified. DSE was able to detect 42 (79%) out of the total 53 RCA lesions. Of the 11 lesions that were not detected, 9 were interpreted as an LCx coronary artery lesion or were supplied by collateral flow.

**Table 1. Individual coronary artery stenosis**

| Coronary artery | Total no. of lesions | No. detected* |
|---|---|---|
| LAD | 51 | 40 (79%) |
| LCx | 34 | 26 (76%) |
| RCA | 53 | 42 (79%) |

*There were no significant differences (p > 0 .051) among the percent of lesions detected in the three coronary arteries. LAD = left anterior descending coronary artery. LCx = left circumflex coronary artery. RCA = right coronary artery.

**Patients with minimal lumen diameter <1 mm:**

Fifty-six patients had a stenosis with a minimal lumen diameter <1 mm. DSE yield was abnormal in 50 (89%) of these 56 patients. Of the six stenosis missed, one was in a diagonal branch of the LAD coronary artery, two were in patients with MVD whose study was stopped before the target heart rate was reached, two lesions were in LCx coronary artery and one was in a heavily collateralized LAD coronary artery . There was no significant difference in the percent of positive study results among the three coronary artery distributions.

**Effect of Heart Rate on Accuracy:**

1. Normal wall motion at rest: The results became positive in 50% of the patients at a heart rate ≤125 beats/min. who had normal wall motion at rest. In the other half, the test results became positive at a heart rate of >125 beats/min. The patients who's DSE test was positive at a heart rate of ≤125 beats/min. had a likelihood of harboring MVD (p <0.05).
2. Abnormal wall motion at rest: In majority of the patients having abnormal wall motion at rest the test became positive at a heart rate ≤125 beats/min. Most of these patients with positive results at a heart rate ≤125 beats/min. had MVD and rest few had significant SVD.
   Heart rate was not found to be statistically significant discriminator for the presence of MVD in patients with wall motion abnormalities at rest.

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## DISCUSSION

A clinically useful non-invasive, non-exercise test for evaluating coronary artery disease in a patient if available is a very good tool. Dobutamine stress echocardiography been proposed as a very useful tool for this purpose.[3-7] It serves the purpose well in evaluating CAD in a patient with a very good sensitivity, specificity and accuracy. The other benefits of DSE are that it carries it carries minimum risks and due to the short duration of action, its effects can be easily monitored and controlled. DSE is also easy to perform and can be done with ease in patients where exercise testing is not possible. Also DSE carries a better yield in terms of results as compared to exercise testing. In this study we have reported our clinical experience, effects, evaluation of DSE in terms of detecting CAD and preoperative risk assessment. The results of our study were good in highlighting and consolidating the role of DSE for the same purpose. The overall sensitivity of the test was 96% and specificity of 81%. These findings are very similar to those previously which have been previously reported.[7]

In our study there was no statistical significant difference in the DSE test's ability to detect to detect coronary artery lesions in three vascular territories. According to some previous studies, the LCx artery territory lesions are less accurately detected than the lesions in LAD and RCA artery territories.[1,11] The reason for this difficulty is perhaps the overlap in perfusion areas between the RCA and LCx arteries. This showed earlier that DSE testing had more sensitivity, specificity and accuracy for the LAD and RCA artery lesions than the LCx artery lesions. However there was improved accuracy for the LCx artery lesion in our study. This improvement in accuracy can be attributed to the use of an overlap method for determining the proper coronary distribution of wall motion abnormalities. Our method takes into consideration the overlap in perfusion that is possible between the LCx and RCA coronary arteries as well as the overlap between the LAD and RCA coronary arteries.

There is a well established notion that an "early positive" stress test result identifies a patient with more severe CAD. This notion was very well supported by our observations. Multi-vessel disease was more frequently found in patients was seen who had normal wall motion at rest and a positive DSE test result at a heart rate ≤125 beats/min. Whereas, in patients with normal wall motion at rest, a single vessel disease was seen more common if the DSE test result was positive at a heart rate >125 beats/min.

However, in our study heart rate did not have much difference among the patients with wall motion abnormalities at rest.

## CONCLUSIONS

Dobutamine stress echocardiography is equally sensitive in detecting CAD in all the three major coronary artery distributions, especially by using the modified 16-segment model with areas of coronary artery distribution. Lesions where the minimal lumen diameter is <I mm are more likely to

be correctly identified by DSE. A multivessel CAD is more likely to be present when a DSE becomes positive at a heart rate ≤125 beats/min.

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