Original Article

Initial Experience of Dobutamine Stress Echocardiography in Ibn Al-Bitar Hospital for Cardiac Surgery

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Summary:

Background: Dobutamine stress echocardiography (DSE) is a well established non invasive test for the diagnosis and risk stratification of patients with coronary artery disease. Aim of the study was to conduct a pilot study in order to establish the basis for the future routine practice of DSE in our center (Ibn Al-Bitar Hospital for Cardiac Surgery).

Patients and Methods: Fifty consecutive patients who were referred from the outpatient of our center, from August 2007 to July 2008, were included. The age range was 39 – 70 years with an average of 57.18 years. Fifty-eight percent were males. Patients were enrolled in the study in accordance with the American Heart Association/ American College of Cardiology guidelines, including mainly those who are unable to exercise due to an orthopedic problem (26%) or limited functional capacity (30%). Some Patients with resting electrocardiographic changes (20%) and non diagnostic exercise test (14%) were also included as well as five patients (10%) for the assessment of myocardial viability. The baseline echocardiogram was normal in 44 % of cases. Others had resting wall motion abnormalities due to previous myocardial infarction (50%) or left bundle branch block (6%). Dobutamine was given by a syringe or an infusion pump at incremental doses (every three minutes) of 5,10,20,30, and finally 40 µg/kg/min. Atropine was needed at peak test in 36% of cases to increase the proportion of patients who reach the target heart rate.

Results: The test was positive in 5 patients (10%); negative in 34(68%), non diagnostic in 2(4%), aborted due to intolerable symptoms in 3(6%) and stopped due to arrhythmias in 3(6%) patients. Side effects included chest tightness and irritability in 40%, headache in 12%, nausea and vomiting in 10%, and postural hypotension in 4%. Infrequent ventricular/atrial ectopics occurred in 13%, supraventricular tachycardia in one patient, and complex multiple ventricular ectopics in 3 patients; no incidence of sustained ventricular tachycardia or ventricular fibrillation occurred. There was no incidence of myocardial infarction or death.

Conclusions: DSE is a safe and practical test provided it is used according to the recommended protocols. A special unit for DSE in our centre is recommended.

Keywords: Dobutamine, echocardiography, imagining stress test.

Fac Med Baghdad 2009; Vol. 51, No.3
Received Dec. 2008
Accepted Jan. 2009

Introduction:

In seeking an imaging solution to the limitations of standard exercise stress testing, echocardiography is attractive on practical grounds. It is the most widely disseminated and inexpensive technique for non-invasive imaging of the heart. It is "patient friendly" because it is rapidly performed, and is highly versatile, being usable in a variety of environments. In combination with various stressors, echocardiography provides a means of identifying myocardial ischemia by detection of stress induced wall motion abnormalities (1).

In 1979, Mason and colleagues demonstrated the proof of concept using M-mode echocardiography. In the late 1980s stress echocardiography started to be more practical and widely studied after improvement in image quality and digital acquisition[2]. The accuracy of stress echocardiography for detection of significant coronary stenosis ranges from 80–90% exceeding that of the exercise ECG (especially in women and patients with left ventricular hypertrophy) and being comparable to that of stress myocardial perfusion scintigraphy. Stress echocardiography is a powerful prognostic tool in chronic coronary disease, after myocardial infarction, and in evaluation of patients

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before major non-cardiac surgery. It is an accurate test for prediction of functional recovery of dyssynergic zones after revascularization, and also provides valuable physiologic information in patients under consideration for valve surgery. (1, 3-6)

There are two main modalities for stress echocardiography:

Exercise echocardiography. This is usually done with the use of the traditional treadmill test, or using supine or sitting bicycle exercise.

Pharmacological stress echocardiography. Dobutamine stress echocardiography is the most widely use test. Vasodilator stressors (adenosine and dipyridamole) are also used, mainly in Europe.

Pathophysiology:

Exercise and inotropic stress normally provoke a generalized increase of regional wall motion and thickening, with an increment of ejection fraction mainly caused by a reduction of systolic dimensions. Regional systolic dysfunction is usually caused by coronary artery disease, but cardiomyopathies may also show regional variation in function (1, 7). In the absence of hemodynamically significant coronary stenosis, an increase in systolic wall thickening should be observed in all coronary territories with a decrease in the size of the left ventricular cavity (7). In the setting of significant coronary artery disease, regional myocardial thickening will decrease as a result of oxygen supply–demand mismatch. The area supplied by the stenosed coronary artery will, therefore, display a change in contraction, enabling the identification and extent of underlying coronary ischemic disease7.Ischemia is typically manifest as new or worsening wall motion abnormalities, delayed contraction, or (if severe) the development of left ventricular enlargement or a decrease in ejection fraction(1,2,7). Dobutamine stress testing is used for diagnosing coronary artery disease, risk assessment (e.g., pre-operative patients or post myocardial infarction), or viability study. Our aim was to conduct a pilot study in order to establish the basis for the future routine practice of Dobutamine Stress Echocardiography DSE in our center (Ibn Al-Bitar Hospital for Cardiac Surgery)

Patients and methods:

The study was conducted between August 2007 and July 2008. The total number of examinations was 50 consecutive patients. All these patients were referred for DSE from the outpatient clinic of our center in accordance with the published guidelines of American Heart Association/American College of Cardiology (AHA/ACC). Before starting our routine testing of patients, we conducted 10 pilot examinations on patients referred for treadmill exercise test with normal electrocardiogram (ECG) and low or moderate pretest probability with normal baseline echocardiography and no previous history of ischemic heart disease to build up initial experience. These 10 patients are not included in the 50 patients mentioned in this study. All these 10 patients had negative both dobutamine stress echocardiography and routine treadmill exercise testing. We conducted our tests in the unit of treadmill exercise testing in our center, making use of available resuscitation equipments and ECG monitoring devices. The 12 leads of the ECG are placed on the chest in a modified way to allow for echocardiographic examination. The protocols used for DSE has been published in many references (1, 2, 7, 8). Generally the test needs a two dimensional echocardiographic Doppler machine. Modern machines are supplied with optional software optimized for the different modalities of stress echocardiography that are easy to use and provide possibility for reviewing the images taken in different stages of stress side by side in a quad screen format (figure).

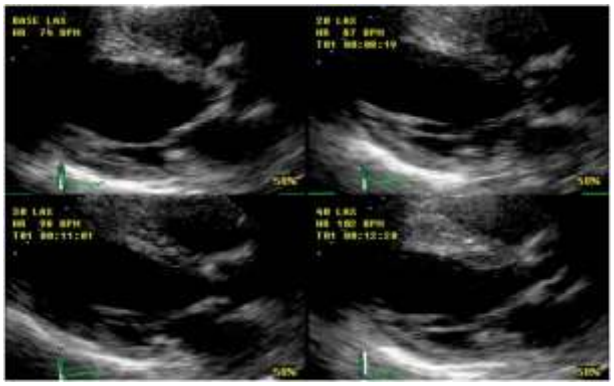

Figure 1: Quad screen format for reviewing stored views.

We used the iE 33 machine (Phillips iE33, Holland) First of all the baseline images in four standard views are taken. Then images are taken during low dose, peak dose when target reached or wall motion abnormalities develop, then after recovery. The software provided will aid the operator in organizing the sequence of image acquisition and also displaying the loops in a quad screen format for easier comparison. In addition a tape recorder or another digital device like a personal computer is usually used to store the whole study for further revision if necessary. Analysis and interpretation of stress echocardiography is made visually and is a qualitative one and is based on analysis of thickening (rather than motion, which may be influenced by translation or tethering) before, during, and after stress. Echocardiographic evidence of ischemia was identified if regional function worsened in any segment, except if the basal inferior (or septal) walls were involved, in which case an adjacent abnormal segment was required [9,10]. An increase in end-systolic volume at peak stress as compared with low dose is also regarded as abnormal. For the purpose of analysis and scoring of different myocardial regions the American Society of Echocardiography proposed a 16

segment model. Each segment is analyzed and given a score and the average score calculated. Patients were instructed about stopping beta blockers or calcium channel blockers the target heart rate is determined according to patient's age (85% of the maximum predicted heart rate).In all cases the drug was given by a syringe pump or an infusion pump. The drug dilution and calculation of infusion rates were carefully done. Resuscitation equipments and necessary drugs (B-blockers, atropine, lidocain) are ensured to be readily available. The infusion rates for dobutamine are predetermined for each stage according to patient's body weight and the dilution of dobutamine used, and then the protocol is started. Dobutamine infusion started at a rate of 5 µg/kg/min, with increments to 10, 20, 30, then 40 µg/kg/min. at 3 minutes intervals. If the target heart rate not reached then atropine is given each minute in a dose of 0.3 – 06 mg, while keeping the dobutamine infusion, to a maximum of 2 mg. During the infusion of dobutamine a 12 lead ECG monitoring for rhythm and ST changes is ensured, and the ECG recorded every 3 minutes. Blood pressure is measured at end of each stage. Throughout the infusion of dobutamine we keep viewing different segments of myocardium for early detection of any new wall motion abnormality. Any symptoms from patients are reported as a predetermined routine, the software organizes the sequence of obtaining the four standard views which are normally taken in four sets:

The baseline images, Low dose infusion (usually 10µg/ kg/minute), Peak dose images when the target heart rate is reached, and finally the recovery images after stopping the infusion and the heart rate is decreased

Protocol endpoints: Target heart rate(85% of age-predicted maximal heart rate or, if soon after myocardial infarction, 70% of age predicted maximal heart rate), Development of new regional wall motion abnormalities of at least moderate severity, Peak dose, Ventricular tachycardia or sustained supraventricular tachycardia, Severe hypertension (systolic blood pressure >220 mm Hg or diastolic blood pressure >110 mm Hg), Sustained decrease in systolic blood pressure (a decrease of 20 mm Hg from previous level of infusion may be used as a guideline for terminating the test, but amounts depends on baseline blood pressure and judgment of the person monitoring the test), Intolerable symptoms

At the end of the protocol the infusion is stopped and recovery images taken when the heart rate is less than 110/ min (usually 5 minutes after stopping infusion). At the end of the study the images stored from the four stages are reviewed carefully for any evidence of induced new wall motion abnormality.

The whole procedure takes about 45 minute for each patient

Results:

The study included 50 consecutive patients, 29 patients were males and 21 were females. The age ranged from 39-70 years, with an average of 57.18 years. The baseline characteristics of the study population are summarized in table 1. The indications for dobutamine stress echocardiography are summarized in table 2.

Table1: Baseline characteristics of the Study population

	No. of patients
Total number	50
Male	29 (58%)
Female	21 (42%)
Diabetes mellitus	11 (22%)
Hypertension	25 (50%)
β- blockers used (stopped before test)	15 (30%)
β- blockers used (not stopped)	7 (14%)
Calcium channel blockers (diltiazem)	5 (10%)
Baseline heart rate	
<50	1 (2%)
50-59	1 (2%)
60-69	12 (24%)
70- 79	25 (50%)
80-89	9 (18%)
> 90	2 (4%)
Echocardiographic image quality	
Patients with good/ acceptable image quality	45 (90%)
Patients with difficult echocardiographic window	5 (10%)

Table 2: Indications for dobutamine stress testing

Indication	No of patients
Limited functional capacity	15 (30%)
Orthopedic limitation (lower limbs, spine disease)	13 (26%)
Patients already had a treadmill exercise testing but with failure to reach the target heart rate, or with equivocal test results	7 (14%)
Resting ECG changes (e.g., LBBB, ST depression > 1mm)	10 (20%)
For assessment of viability	5 (10%)

The test objective: Diagnosis of coronary artery disease was the objective of the test in 23(46%) patient, Pre-operative assessment of patients for non cardiac surgery3 (6%), Risk stratification of patients with known coronary artery disease19 (32%) and viability testing in 5 (10%).

Target heart rate: Of the 50 patients studied, it was possible to reach the target heart rate in 39 patients (78%). It was necessary to add atropine at peak dobutamine dose in 18 patients (36%).

Side effects: The test in general was fairly tolerated by most patients. The majority of patients described a feeling of palpitations and feeling of strong rapid heartbeats, and this was well tolerated by most patients. Table 3 shows the frequency of side effects

Table 3.: Side effects during the test

Headache	6 (12%)
Nausea / vomiting	6 (10%)
Irritability, anxiety, fear, tremor	12 (24%)
Postural hypotension after the test	2 (4%)
Chest/ neck discomfort or tightness	8 (16%)
Shortness of breath	2 (4%)

Arrhythmias: No patient developed VT/VF, one patient had SVT, AND 13 (26%) had few atrial/ventricular ectopics and 3(3%) had frequent pvcs
Final Test results are given in table 4

Table 4: Final test results

Positive test	5 (10%)
Negative test	34 (68%)
Non diagnostic (target heart rate not reached)	2 (4%)
Test aborted due to intolerable symptoms	3 (6%)
Test stopped due to significant arrhythmias	3 (6%)
Test stopped due to increased blood pressure (>200/110)	3 (6%)

Conclusions:
The dobutamine stress test is a safe and accurate test when practiced in skilled hands according to the recommended protocol. However significant side effects and arrhythmias are reported and these should be anticipated and treated promptly. Every effort should be made to ensure accurate dosage calculation and continuous monitoring of the echocardiogram and the rhythm. The drug must be given by carefully monitored infusion pump or syringe pump. A special training for dobutamine stress echocardiography both regarding obtaining proper and adequate image quality and the interpretation of the test is very important. Trained medical personnel is also important the test represents an important solution for patients who are unable to exercise and those who have base line ECG changes. We recommend that a specialized unit be established for stress echocardiography to increase the options of non invasive evaluation of patients. Due to the small population of the study, it was not possible to compare the test results with coronary angiography. We recommend, after having a special unit for dobutamine stress echocardiography, that a further study comparing the test results with coronary angiography be done

Discussion:
Patient population: We included in this study the first 50 consecutive patients with dobutamine stress testing. The selection of patients was from the outpatient clinic and in accordance with the practice guideline and represented an everyday practice and included many patients with previous myocardial infarction and abnormal resting echocardiogram. While it was the first experience in dobutamine stress testing, we enrolled in the test patients unable to exercise who were managed subsequently according to the test results (for example pre-operative risk assessment).
Learning curve and the need for training and experience:
Achieving the target heart rate is a key goal in the test. We did not use atropine in the initial 7 patients. After performing about 25 tests we were more confident in reaching maximum dobutamine dose and following it by atropine administration up to 1.5 mg. This helps to achieve the target heart rate in a greater proportion of patients. In one 62 year-old female patient with normal resting ECG and echocardiogram, who was continuing her beta blockers (Atenolol 100 mg daily) we reached 50 µg/kg/min dobutamine infusion followed by atropine up to 1.5 mg but the heart rate did not reach beyond 127 beats per minutes. There is no agreement upon whether to stop or continue β-blockers (8, 9), but our impression is that these drugs are better stopped or at least the dose decreased before the test. We followed a policy to instruct patients to stop beta blockers 2 days before the test. Diltiazem or other non dihydropyridine calcium channel blockers were stopped 1 day before the test. The test requires the operator to have a good experience in obtaining the proper sections of myocardium in the best resolution possible. The interpretation of the test is not always easy. While a normal test with a normal baseline echocardiogram is relatively easy to interpret, the presence of resting wall motion abnormalities makes the interpretation more difficult. Experience is needed for both the normal and abnormal response to dobutamine stress. Such experience needs to be preceded by a good experience in performing and interpreting the echocardiograms of patients with ischemic heart disease at rest. All researchers refer to this as the most important skill (11). Being operator dependant to this extent is at the same time a limitation of dobutamine stress echocardiography. To minimize this limitation, it has been recommended that the whole study recorded on a video tape or another digital format and interpreted by a second person who is blinded to the first interpreter's conclusions (9).
Safety of the test
This was a major concern. In more than 9 series (8, 12-17) that included more than 3000 patients, no mortality was recorded. One patient had ventricular fibrillation that was resuscitated successfully. In our study there was no mortality or myocardial infarction. Also no event that required direct current (DC) cardioverion

occurred. There was one instance of a supraventricular tachycardia. This event occurred in a 70 year old female who was on a beta-blocker that was stopped before the test. The infusion of dobutamine was at 20 µg/kg/min and was stopped immediately. The rhythm returned to sinus after about 2 minutes. The test was cancelled. In two patients the test stopped due to frequent complex ventricular ectopics (ventricular bigemini and couplets). Both patients had abnormal resting echocardiograms due to previous myocardial infarction. One study pooled data from three hundred centers in the world, that included 85,997 patients for whom different forms of stress echocardiography were done between 1998 and 2004 (18). Dobutamine stress echocardiography was done in 35,103 patients. Life-threatening events occurred in a rate of 1 in 557 studies of DSE. Of the 35,103 studies, five patients died (two ventricular fibrillation and three cardiac rupture).The test is generally safe when practice by skilled personnel. We made every effort to ensure safety of the test. This includes the following points:

The proper selection of patients and exclusion of contraindiactions to stress testing and the drugs used during the test , The strict adherence to the established protocol and administration of the drug according to body weight using controlled infusion pump or syringe pump , The continuous monitoring of the echocardiogram and the heart rhythm for any new wall motion abnormality or arrhythmias.

Side effects: Headache, nausea and vomiting, and chest discomfort and irritability are the most bothering symptoms but these were fairly tolerated by the majority of patients. Nausea and vomiting occurred at higher doses of dobutamine. It is thus necessary that patients be fasting for at least three hours before the test 12. Postural hypotension occurred in two patients. The patient's blood pressure should be checked before the patient leaves the examination couch gradually and the patient should not be left alone when he first sits up off the couch.

Test final results: The test was considered positive in five patients: The first patient was a 61 year-old male, hypertensive, non diabetic, who had his beta blockers stopped 2 days before the test. He is known to have ischemic heart disease, with history or percutaneous coronary intervention (PCI) to the right coronary artery two years before the test. The patient was able to exercise but his resting ECG had ST / T changes in the inferior and lateral leads. The resting echocardiogram was abnormal (anteroseptal MI). At the peak dose and maximal target heart rate, induced wall motion abnormality noted in the apical and inferior regions. The function recovered to baseline after 5 minutes. There was mild chest pain. The second patient was a 55 year-old male, diabetic and hypertensive. The resting ECG showed left bundle branch block, and the resting echocardiogram showed LV dysfunction with an ejection fraction of 40%. At peak dose, a global deterioration of contractility was noted. The third patient is a 51 year-old male, hypertensive, non diabetic, with history of renal disease. The test was for pre-operative risk assessment. His ECG had resting ST/T wave changes. At peak test and maximal heart rate, induced hypokinesia of the anteroseptal region was observed. There was only mild chest pain The fourth patient is a 42 year-old male, diabetic, hypertensive, with history of inferior myocardial infarction 2 months before the test. The patient was unable to exercise (artificial limb). The resting echocardiogram showed inferior myocardial infarction. At peak test dose there was an increase in the end systolic volume (global hypokinesia). There was mild-moderate chest and neck tightness. The fifth patient was a 45 year-old female, with left bundle branch block and Preserved LV systolic function. At the peak dose there was anteroseptal hypokinesia with mild chest pain. The test considered positive. However, there is a possibility of a false positive test. Currently the first line test is a radionuclide imaging with vasodilator agents like adenosine or dipyridamole (19).

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