Dobutamine Stress Echocardiography – Methodology, Clinical Applications and Current Perspectives

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Abstract

Dobutamine stress echocardiography is often used as a non-invasive diagnostic modality for detection of coronary artery disease. In terms of accuracy it rivals SPECT scintigraphy. Application of non-coronary artery disease has made it an attractive diagnostic tool. However, like all diagnostic modalities it has its inherent limitations. Quantitation of stress echocardiography can resolve most of the problems surrounding its use.

INDICATIONS

The principal indications of DSE are:

1. Patients who cannot exercise or exercise submaximally.
2. Patients with uninterpretable ECG caused by repolarisation abnormalities, pre-excitation, depression of ST segment at baseline, left bundle branch block.
3. Identification of viable myocardium.
4. Evaluation of severity of aortic stenosis with LV dysfunction.
5. Evaluation of patients of dilated cardiomyopathy.

Its role for evaluation of prosthetic valve function, severity of valvular regurgitation, provocation of outflow tract gradients in hypertrophic cardiomyopathy are yet to be validated for clinical use.

METHODOLOGY

DSE may be performed as an in–patient or out–patient procedure. A complete request with clinical diagnosis, reason for study and brief history is required. Any patient meeting any of the conditions of absolute contraindications (myocardial infarction less than 72 hours, unstable angina, hemodynamic instability, symptomatic ventricular arrhythmias, acute myocarditis/pericarditis, intracardiac thrombus, uncontrolled hypertension, pregnancy, acutely ill patients) are excluded. The minimum personnel in attendance are a nurse, a technician and the physician who is to perform the test.

Any medication that can reduce the chronotropic response of the heart should be withheld in the morning. The subject should be fasting for a period of not less than 4 hours. To ensure patient safety an emergency cart which is fully equipped with emergency medications, defibrillator etc. is kept ready. Upon arrival, physical assessment is done and an informed consent is obtained. Patient education before
The test is of paramount importance.

The vital parameters of the patient (heart rate, blood pressure, ECG, oxygen saturation) are monitored throughout the procedure. The patient is positioned properly (usually left lateral decubitus) for proper image acquisition. At baseline the resting images are acquired (parasternal long-axis and short-axis, apical two and four chamber views) which are digitised and stored. Dobutamine infusion is then begun at 5µg/kg/min and increased every 3 minutes to 10,20,30,40,50 µg/kg/min till an end point is reached.

The end points are
- 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 abnormality (RWMA).
- Peak dose (If heart rate is not within 10% of target heart rate with 40 µg/kg/min of dobutamine, atropine 0.2 to 1 mg I.V. is given to increase heart rate).
- Ventricular tachycardia or sustained supraventricular tachycardia.
- Severe hypertension (systolic B.P. > 220 mmHg or diastolic B.P > 110 mmHg).
- Decrease in systolic B.P. from previous level (Amount depends on the judgement of person monitoring the test).
- Intolerable symptoms.

The images are digitised and stored during low dose, peak dose and after peak dose. The images are compared in a quad screen format. The videotape is kept on during imaging. Review of video tape is necessary after review of digitised cine–loop images.

**INTERPRETATION**

As seen in Table 1, with dobutamine infusion in a normal tissue, left ventricular (LV) wall motion becomes hyperdynamic. Worsening of wall motion or the development of new ones is typical of stress–induced myocardial ischemia. Although less specific, the lack of hyperdynamic motion may indicate ischemia particularly if confined to a specific segment. Other adjunctive diagnostic criteria for positive DSE include LV cavity dilatation, a decrease in EF, diastolic dysfunction and new or worsening MR. These criteria for detecting coronary artery disease (CAD) are more specific, but less sensitive. Despite severe CAD, dilatation of LV cavity may not be observed during DSE.

Akinetic segments may harbour viable tissue. It is therefore imperative to recognize reversible dysfunction. Coronary revascularisation leads to improved LV function and hence has a direct bearing on survival. A biphasic response, i.e. improvement of RWMA at low dose with worsening at peak dose, identifies viable and ischemic myocardium.

This particular response best predicts recovery of myocardial function after revascularisation. A non-ischemic but viable myocardium shows sustained improvement at peak dose. Infarcted tissue on the other hand shows no change during any of the DSE stages.

Dobutamine infusion at low dose (10–20 µg/kg/min) increases coronary blood flow, which improves contractility. With an increase in dose, myocardial oxygen consumption increases without any increase in coronary blood flow due to coronary stenosis. The resultant ischemia is responsible for worsening wall motion.

**SAFETY**

DSE is relatively safe and well tolerated. Mild side effects like chest pain, palpitation, headache, light headedness, nausea, breathlessness are frequently observed. Hypertension, hypotension and paradoxical bradycardia (mediated by Bezold Jarisch Reflex) are also known. Ventricular tachycardia is the most feared but infrequent complication of DSE. Serious cardiac arrhythmias are more frequent in patients of aortic stenosis with severe LV dysfunction. After atropine administration, tachycardia is prolonged. But there is no significant increase in side effects.

**PROGNOSTIC EVALUATION**

The predictive power of clinical data is strengthened by the addition of Duke score, resting LV function, results of exercise echo. In subjects with a normal exercise echocardiography, the cardiac event rate is 0.9 to 1% per year at follow up. In subjects unable to exercise, DSE may have a comparable predictive value. A normal DSE predicts cardiac mortality of 1% per year. Together with age, heart failure, ischemia, the extent of abnormal wall motion is important predictors of cardiac death. Angiographic data adds little to the prognostic power. The prognostic power of DSE has also been compared with vasodilator stressors. Compared to dipyridamole, dobutamine has similar negative as well as positive predictive value. However, when cardiac death is considered, dipyridamole has a marginal edge over dobutamine.

**PREDICTION OF IMPROVEMENT IN LVEF AFTER ACUTE MYOCARDIAL INFARCTION**

LVEF is the most powerful predictor of mortality after myocardial infarction (MI). The final value achieved and the
degree of improvement is more important predictors of mortality than the value of EF at the time of acute event. An increment in EF ≥ 5% is predicted by i) non Q wave MI ii) anterior location iii) myocardial viability in ≥ 2 segments. Amongst all the independent predictors of increment in EF ≥ 5%, myocardial viability is the best.15

Microvascular integrity is a pre-requisite for myocardial viability. But low dose DSE is a more accurate predictor of reversible dysfunction than contrast echocardiography after reperfusion.16 Similarly, metabolically active myocardium detected by PET is viable. But it may not necessarily predict contractile reserve with late functional recovery. Moreover, viable myocardium detected by PET may not contain enough contractile elements that translates into an increment in contractile force after reperfusion.17

Dobutamine responsive wall motion is specific (90 to 93%) during all stages of DSE, but low dose dobutamine alone is sensitive (86%) for identifying reversible dysfunction.18

**CARDIAC RISK STRATIFICATION IN PATIENTS UNDERGOING NON-CARDIAC SURGERY**

Clinical variables alone (diabetes mellitus, angina, q waves in ECG, Age > 70 years, symptomatic ventricular arrhythmias) may identify 1/3rd of patients at very low risk for preoperative complication of vascular surgery. Absence of any of the clinical risk factors identifies a low risk group with a cardiac event rate of 1%. DSE can identify a high risk and an intermediate risk group based on ischemia threshold.19

The ACC/AHA task force has approved DSE for preoperative evaluation of noncardiac surgery. For preoperative risk assessment the positive predictive value for MI or death has been 7 to 23%. The negative predictive valve has been 93% to 100%.20 Clinical assessment in combination with DSE has the potential to facilitate clinical decision-making.

**ROLE IN DILATED CARDIOMYOPATHY**

Idiopathic dilated cardiomyopathy is characterised by dilated ventricles and decreased systolic function. Downregulation of myocardial β receptor density and hence contractile reserve is predictive of clinical outcome. Myocardial contractile reserve assessed by low–dose DSE (5 – 20 µg/kg/min) is a useful marker to predict the outcome of LV systolic function in patients of DCM.21 Low–dose DSE in patients with DCM have identified, LV end–systolic volume > 150 ml, no decrease of LV end–diastolic volume, atrial fibrillation and male gender as factors related to fatal outcome.22 The response of systolic sphericity index (systolic long axis/minor axis dimension ratio) to low-dose DSE is an alternative index of the functional status of chronic heart failure in patients with DCM.22 In patients of heart failure, peak exercise oxygen consumption (VO₂ max) carries prognostic and therapeutic importance. At borderline VO₂ max (10 – 14 ml/kg/min), low-dose DSE based upon LV end–systolic diameter and end–systolic wall stress, is a valuable prognostic indicator in patients of heart failure and DCM.24

DSE is useful for non invasive differentiation of ischemic from idiopathic DCM.25,26

Improvement of wall motion score index at low-dose and deterioration at peak dose is characteristic of ischemic cardiomyopathy. In non-ischemic cardiomyopathy, sustained improvement at low and peak dose is seen.

**EVALUATION OF AORTIC STENOSIS**

It is possible to identify three distinct hemodynamic subjects in patients with severe aortic stenosis (AS), low gradients and LV dysfunction with low dose DSE.27

1. Patients with fixed AS have an increased cardiac output, transvalvular gradient, with no change in aortic valve area and preserved contractile reserve. This group of patients is more likely to benefit form surgery.

2. Patients with relative AS have an increased valve area but no change in gradient and preserved contractile reserve. These patients are considered to have LV dysfunction unrelated to aortic valve disease and should be treated conservatively.

3. Patients without contractile reserve are unable to increase their cardiac output. They are said to have AS of indeterminate severity. This group may have a very poor prognosis.

The increment in aortic valve area with low dose DSE is determined by three important factors. The most important variable being amount of flow augmentation induced by dobutamine. The two other variables are calcific etiology (rather than rheumatic) and the baseline flow rate.28 The anatomic valve area assessed by planimetry during transoesophageal echocardiography is the maximal area measured at systole. The effective valve area is the pansystolic functional area, averaged throughout the complete ejection period. Thus dobutamine-induced changes in effective valve area may be due to a change in the timing of maximal leaflet opening because leaflet inertia may be overcome earlier when flow is augmented. Absence of commissural fusion in calcific etiology is responsible for increase in valve area with flow augmentation.

**ACCURACY**

The accuracy of any diagnostic stress testing is expressed as the sensitivity and specificity of the technique for detection of angiographically detected stenosis. It does not take into consideration the prevalence of disease in the study population. Therefore these parameters have their limitations. Referral bias is also known to influence accuracy.

In case of DSE, image quality, LV morphology and observer discordance influence accuracy. It is limited by several causes of false negative results – inadequate stress, antianginal treatment (especially beta blockers), mild stenosis, left circumflex disease, poor image quality and delayed post-stress images. Similarly it is known to produce false positive results in female sex, basal segments in posterior myocardial circulation, intermediate grade coronary stenosis, poor
endocardial visualization, abnormal motion due to tethering to the fibrous skeleton of heart. 29

A meta-analysis suggested that sensitivity and specificity of DSE are 86% and 85% respectively. Bicycle stress echo is more sensitive than DSE at the cost of specificity. Treadmill exercise echo has the highest specificity. DSE is more specific than perfusion scintigraphy. 30

LIMITATIONS 31

Discordance between observers has been the greatest problem. Each observer may have a different threshold for identifying abnormal wall motion. Recognition of mild ischemia and worsening of wall motion with resting RWMA pose a problem in the absence of a means of quantitation.

Image quality and image acquisition are critically important issues. Studies are uninterpretable if the same imaging planes are not compared or if the LV is insufficiently visualised.

Small LV size poses a problem because of the smaller endocardial circumference over which a wall motion abnormality can be detected.

An ischemia based technique has its inherent limitations to diagnose single vessel disease, recognise multivessel disease and recognise ischemia within areas of abnormal resting wall motion.

QUANTITATION

A truly quantitative approach could overcome the most important limiting factor of stress echocardiography, i.e. observer discordance. Such an approach should be feasible in most patients, obtained with minimal incremental time to standard imaging, a reasonable interpretation time, consistent between and within observers, limited test – retest variation, definable normal range suitable for most candidates.

Measuring endocardial motion from 2D-images might serve in quantitation. Better definition of the endocardial border with harmonic and contrast imaging are already in practice. However tissue Doppler imaging (TDI) seems to have great potential of quantitation of stress echocardiography. The fundamental principle behind TDI lies in the fact that velocity increment seen in normal tissues is blunted in ischemic tissues.32

However TDI has its own limitations. The feasibility of apical measurement is limited as it is relatively fixed and velocities are low. Besides normal adjacent tissue may augment the velocity of normal segments. It is likely that TDI may be superseded by the more sophisticated strain and strain – rate imaging.33

CONCLUSION

As a diagnostic tool, DSE has come a long way from detection of myocardial ischemia; viability; prognostication; to issues beyond coronary artery disease. Compared to other forms of stress testing, it has a comparable accuracy in terms of sensitivity and specificity. With new techniques, quantitation of stress echocardiography will resolve many of its limitations. As a diagnostic procedure, its safety and cost effectiveness is established. However the need for specialised training and a learning curve has made it accessible in a relatively fewer centres and remains under–utilised in general practice.

REFERENCES

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