Dobutamine Stress Echocardiography - Need for a Better Gold Standard?

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Introduction

Dobutamine stress echocardiography (DSE) has come a long way as establishing itself as a feasible, safe, effective, relatively cheaper non-invasive technique to detect population suffering from coronary artery disease (CAD) and following up patients post revascularization. Besides these DSE is commonly used to diagnose low gradient, low flow true severe aortic stenosis (AS); differentiating it from pseudo-AS and to follow up patients with dilated cardiomyopathy (DCMP).

Various non-invasive techniques have different sensitivity and specificity to accurately judge a viable myocardium and to accurately detect the improvement in regional wall motion abnormality (RWMA) post-revascularization, leading to an overall increase in left ventricular ejection fraction (LVEF). The comparison of various modalities, role of DSE in intermediate coronary lesions (75%) and other important uses and controversies surrounding DSE are discussed; suggesting the incremental value of DSE as a indispensable and versatile a diagnostic technique.

Response of Heart to Stress

Exercise and inotropic stress leads to generalized increase in systolic wall thickening, a reduction in systolic dimensions of heart and an increment in LVEF.

Indications

DSE is reserved for patients who cannot exercise or exercise submaximally may be due to orthopedic problems, neurological disease etc. It is commonly used to identify viable myocardium, to diagnose ischemia, to assess severity of AS in patients with LV dysfunction and evaluation of patients with DCMP. Apart from above, DSE is being used in post cardiac transplant patients with reimplanted coronaries to look for ischemia as intimal hyperplasia is noted in these subset of patients which is angiographically difficulty to quantify but causes significantly high one year mortality.1 DSE has proven itself as a novel and efficient technique to detect ischemia in patients with a implanted pacemaker and patients with left bundle branch block (LBBB).

Contraindications

Patient selection is an important aspect both for a referring physician and the non-invasive cardiologist doing the procedure. Contraindications include myocardial infarction (MI) less than 72 hours, unstable angina, hemodynamic instability, symptomatic ventricular arrhythmia, acute myocarditis / pericarditis, presence of intracardiac thrombus, uncontrolled hypertension, pregnancy and acutely ill patients. It is important to be aware of the contraindications to avoid landing up into any complication.

Methodology

DSE can be done both on outpatient (OPD) or inpatient (IPD) basis after making a clinical diagnosis and physical assessment of the patient. Medications that reduce chronotropic response (beta blockers, calcium channel blockers) are withheld ideally 48 hours before the procedure. patient needs to be fasting for 4-6 hours before the procedure. An informed consent is taken and vitals (heart rate, blood pressure, ECG) are monitored throughout the procedure. Images are acquired at baseline i.e. parasternal long axis (PLAX), short axis (SAX), four chamber view (4c), two chamber view (2c) (Figure 1). Dobutamine infusion is started at 5 mcg/kg/min and increased till 40 mcg/kg/min, each stage lasting for three minutes (Tables 1 and 2).

The end-points being:

- Target heart rate (85% of maximum predicted heart rate (MPHR))
- New wall motion abnormality.
- Peak dose (atropine 0.2-1 mg if heart rate not within 10% target heart rate)
- Ventricular tachycardia/supraventricular tachycardia
- Blood pressure (BP) >220/110 mmHg.
- Decrease in systolic BP from previous level.
- Intolerable symptoms.

Interpretation

Different Characteristics of Viable Tissue Versus Different Techniques to Assess Viable Myocardium2

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Table 1: Interpretation of dobutamine stress echocardiogram (DSE) at baseline, low dose and peak dose

<table>
<thead>
<tr>
<th>Nature of tissue</th>
<th>Rest function</th>
<th>Low dose</th>
<th>Peak dose</th>
</tr>
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<tbody>
<tr>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Ischemic</td>
<td>Normal</td>
<td>Normal (may worsen)</td>
<td>Worsen</td>
</tr>
<tr>
<td>Viable, ischemic</td>
<td>RWMA</td>
<td>Improves</td>
<td>Worsen (biphasic response)</td>
</tr>
<tr>
<td>Non-viable, nonischemic</td>
<td>RWMA</td>
<td>Improves</td>
<td>Sustained improvement</td>
</tr>
<tr>
<td>Infarct</td>
<td>No change</td>
<td>No change</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Reliability of dobutamine stress echo in predicting coronary artery disease in various territories.4 (LM-left main, LAD-left anterior descending, LCX-left circumflex artery, RCA-right coronary artery, SVD-single vessel disease, DVD-double vessel disease and TVD-triple vessel disease)

<table>
<thead>
<tr>
<th>Region</th>
<th>%</th>
<th>Sensitivity</th>
<th>Specificity</th>
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<tbody>
<tr>
<td>LM</td>
<td>100</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>LAD</td>
<td>88</td>
<td>80</td>
<td></td>
</tr>
<tr>
<td>LCX</td>
<td>65</td>
<td>85</td>
<td></td>
</tr>
<tr>
<td>RCA</td>
<td>75</td>
<td>86</td>
<td></td>
</tr>
<tr>
<td>i. SVD</td>
<td>65</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ii. DVD</td>
<td>82</td>
<td></td>
<td></td>
</tr>
<tr>
<td>iii. TVD</td>
<td>85</td>
<td></td>
<td></td>
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Intermediate Coronary Lesions

This is where results of stress echo and coronary angiogram were directly compared for intermediate coronary lesions (75%) for presence or absence of ischemia and as it can be understood, the results were very misleading. Firstly, the past data was not in terms of what we see today as quantitative angiogram (QCA). The major limitation of data with stress echo is that it was either compared with severity of stenosis on coronary angiogram or to perfusion defects on radionucleotide scans. Radionucleotide imaging has a high false positive results in borderline lesions and hence considered to be less specific then stress echocardiography in assessment of coronary stenosis.5 The majority of work was done in an era when QCA was not done and limitation of a diagnostic angiogram was not well understood (Table 3).

There is lack of data on comparison of stress echocardiography as a whole with functional assessment of coronary stenosis. So, stress echocardiography needs to be compared with coronary stenosis assessed by coronary flow reserve.6

DSE with Strain Rate for Contractile Reserve

Regional deformation using strain rate during DSE detects ischemia with sensitivity of 89% and specificity of 86%.7 Peak systolic strain rate only increases during DSE peak stress in patients with normal flow reserve. Increase in peak systolic strain rate of <0.6 s\(^{-1}\) correlates well with fractional flow reserve (FFR) of <0.75.7

The limitations are that data of DSE with strain rate is small and only with intermediate single vessel disease. The complex lesions and also low dose DSE in this aspect needs to be evaluated further, but whatever small data has been published shows promising results.

Table 3: Different techniques to assess viable myocardium. The first three characteristics are evaluated by scintigraphic techniques while preserved contractile reserve can be probed by DSE

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Technique</th>
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<tbody>
<tr>
<td>a. Myocardial</td>
<td>Fluorine -18 -</td>
</tr>
<tr>
<td>glucose utilization</td>
<td>fluorodeoxyglucose</td>
</tr>
<tr>
<td>b. Cell membrane integrity</td>
<td>Thallium-201</td>
</tr>
<tr>
<td>c. Intact mitochondria</td>
<td>Technetium -99m sestamibi/ tetrofosmin</td>
</tr>
<tr>
<td>d. Contractile reserve</td>
<td>Dobutamine-echocardiography/ MRI</td>
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Safety and Prognosis

DSE is a safe and well tolerated non-invasive technique. It can cause hypotension, hypertension and bradycardia in some cases. Ventricular tachycardia (VT) is infrequent and cardiac mortality is 1%/year. DSE is well being used before non cardiac surgeries prior to giving a cardiac clearance by the treating physician and carries a negative predictive value of 93-100%.

Role in Dilated Cardiomyopathy (DCM)

Low dose DSE is used to
assess myocardial contractile reserve. Poor prognosis is seen in male patients with LV end systolic volume (ESV)>150 ml, no decrease in LV end diastolic volume (EDV) and in patients with atrial fibrillation (AF). Response of systolic sphericity index (systolic long axis/minor axis) is an index of functional status of congestive heart failure (CHF).

Low Flow, Low Gradient Aortic Stenosis

DSE is used to differentiate between true AS versus pseudo-AS in patients with poor ejection fraction (EF). The aortic valve area (AVA) remains fixed in cases with true AS with increase in pressure gradients (PG), cardiac output (CO) and contractile reserve (CR) while in pseudo-AS there is increase in AVA with no increase in PG with increase in CR and CO (Table 4).

Limitations

The probability of a positive stress test or DSE depends upon Bayesian pretest probability for presence of CAD dividing the patient population into low, intermediate and high risk depending upon the presence or absence of factors like diabetes mellitus, positive family history of premature CAD, smoking, dyslipidemia etc. Therefore, it is important before a DSE, that a detailed history is taken into account to avoid a referral bias.

Echocardiography is all aspects is an operator dependent technique which is not so with other imaging techniques like MRI or radionuclide scan. This is one major reason that inspite of better accuracy of DSE than other techniques, the study and data may become misleading in inexperienced hands. The false negative results may be seen for LCx territory lesions and single vessel disease as the sensitivity dips down to as low as 65%.

Poor echo window may be seen in 15-40% of cases referred for transthoracic DSE where the role for transesophageal DSE or dobutamine MRI comes into play.

References


Table 4: Showing parameters of low dose DSE in true AS versus pseudo-AS in patients with low ejection fraction

<table>
<thead>
<tr>
<th></th>
<th>CO</th>
<th>PG</th>
<th>AVA</th>
<th>CR</th>
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<tbody>
<tr>
<td>Fixed AS</td>
<td>↑</td>
<td>↑</td>
<td>−</td>
<td>↑</td>
</tr>
<tr>
<td>Relative AS</td>
<td>↑</td>
<td>−</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Intermediate</td>
<td>−</td>
<td>±</td>
<td>±</td>
<td>−</td>
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