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## Stress echocardiography. Part I: Stress echocardiography in coronary heart disease

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### Abstract

Stress echocardiography (stress echo) is a method in which various stimuli are used to elicit myocardial contractility or provoke cardiac ischemia with simultaneous echocardiographic image acquisition of left ventricular function and valvular flow, if needed. The technique is a well-recognized, safe and widely available stress test used for the diagnosis and assessment of prognosis in coronary heart disease, but may also prove valuable in valvular heart disease. The stressors used include physical exercise, pharmacological agents (dobutamine, vasodilators) and pacing stress, most often with the use of a permanent pacemaker. Two operators should perform the test: a physician experienced in stress echocardiography (at least 100 tests completed under supervision of an expert) and a trained nurse or another doctor. The laboratory should feature a defibrillator and a resuscitation kit with a set of pharmaceuticals, an intubation kit and an AMBU bag. Pacing stress echo requires an external programmer for the implanted permanent pacemaker. Exercise should be the preferred stressor for the diagnosis of ischemic heart disease with alternative of high-dose dobutamine test in cases of contraindications to physical stress. Pacing stress echo is recommended for patients with pacemakers, and dipyridamole test for the assessment of coronary flow reserve. Chest pain in patients with intermediate probability of coronary artery disease, inability to perform physical exercise and non-diagnostic resting or exercise electrocardiography are indications for stress echo. The test is also used in symptomatic patients after revascularization or patients qualified for revascularization for functional assessment of coronary artery stenosis. Low-dose dobutamine test is usually performed in patients after myocardial infarction or with moderate-to-severe left ventricular dysfunction to assess myocardial viability before potential revascularization.

## Introduction

Stress echocardiography (stress echo, SE) is a method in which various stimuli are used to elicit myocardial contractility or provoke cardiac ischemia with simultaneous echocardiographic recording of left ventricular function and valvular flow, if needed<sup>(1-7)</sup>. SE is used for the diagnosis of coronary heart disease and valvular heart defects. The stressors used include physical exercise, pharmacological agents (dobutamine, vasodilators) and pacing stress, most often with the use of a permanent pacemaker.

## Methods

Qualifications of medical personnel performing stress echo and laboratory equipment

The test should be performed by two operators: a physician experienced in stress echocardiography (at least 100 tests performed under supervision of an expert) and a trained nurse or another doctor. The laboratory should feature a defibrillator and a resuscitation kit with a set of pharmaceuticals, an intubation kit and an AMBU bag. Pacing stress echo requires an external programmer for the implanted permanent pacemaker.

## Stress echo protocols

### Exercise tests

Stress test may be performed on a treadmill or a cycle ergometer in a sitting or semi-recumbent position on the left side. Bruce protocol is used for treadmill: step increments by 25 W every 3 minutes until termination criteria are reached (85% of max heart rate, contractility disorders, severe anginal pain, ST elevation in ECG, and maximum stress load).

### Pharmacological stress echo

#### *Dobutamine tests*

**Dobutamine** is a synthetic catecholamine increasing left ventricular contractility, reducing ventricular afterload and, at higher doses, increasing heart rate. Dobutamine is administered in intravenous infusion, with doses increased every 3 minutes to 5, 10, 20, 30, 40  $\mu\text{g}/\text{kg}/\text{min}$ . If no clear increase in heart rate is observed, atropine is administered with a starting dose of 30  $\mu\text{g}/\text{kg}/\text{min}$ , at a maximum of 4 doses 0.25 mg each at 1-minute intervals until target submaximal heart rate is reached. Intravenous metoprolol at a dose of 2.5–5 mg should be used in the event of major myocardial ischemia with side effects.

#### *Vasodilator tests*

**Adenosine** is an endogenous purine nucleoside. Under normal conditions, stimulation of adenosine receptors causes a

4–5-fold increase in the coronary flow. In the case of coronary stenosis, a steal phenomenon is observed.

**Dipyridamole** inhibits metabolism and increases the levels of endogenous adenosine, which results in the effects similar to those after intravenous adenosine. Patients should refrain from caffeine 12 hours and theophylline derivatives for 24 hours before the test.

**Dipyridamole stress test** involves an intravenous administration of a total dose of 0.84 mg/kg within 6 minutes (or divided doses – 0.56 mg/kg within 3 minutes, followed by 0.28 mg/kg for the next 3 minutes after a 4-minute interval). Regardless of test results, intravenous aminophylline at 240 mg should be administered after test completion to reverse the effects of dipyridamole. In the adenosine test, the drug should be administered in an intravenous infusion at a maximum dose of 140  $\mu\text{g}/\text{kg}/\text{min}$  for 6 minutes.

Tests using vasodilators additionally allow for the measurement of coronary reserve in the anterior descending left coronary artery.

### Pacing stress echo

**Stress-pacing echocardiography** can be performed in patients with a permanently implanted pacemaker. The pacemaker is externally programmed at 100–110 impulses/min and then increased by 10 impulses/min every 3 minutes until 85% of maximum age predicted heart rate is reached, or a target rate of 150 impulses/min or maximum rate for a given pacemaker is reached. A rapid stress-testing protocol includes two stages: 3 minutes of stimulation at 100 impulses/min and 3 to 5 minutes of 85% of maximum age predicted heart rate. In the case of grade II or III AV block, particularly during atrial stimulation, atropine (a total dose of 2 mg) may be used until 1:1 conduction is reached. The accuracy of the test in the assessment of coronary heart disease is very high, comparable to other stress echo tests. This is a non-invasive, safe and well-tolerated test that may be discontinued at any time. This technique should be considered in every patient with a pacemaker.

### The use of contrast agents during stress echo

Contrast agents used in stress echocardiography are suspensions of encapsulated, gas-filled microbubbles. Following intravenous administration they pass through the pulmonary circulation and cause strong opacification of left cardiac chambers. They are administered intravenously either as boluses or as constant rate continuous infusions with the ultrasound imaging set in harmonic mode. As their use improves visualization of endocardial border, a suboptimal ultrasound window resulting in poor quality of images is the primary indication for the use of contrast agent. Attempts are also made to use contrast agents for the assessment of myocardial perfusion at rest and during stress (in Poland only for the purposes of research). Although contrast agents are safe, there are

some limitations in clinically instable patients (including acute coronary syndrome).

### Three-dimensional echocardiography

Matrix-array transducers used in three-dimensional echocardiography enable real-time recording of spatial data for the entire left ventricle. Simultaneous recording of several projections significantly reduces data acquisition time both at rest and during stress.

### Quantitative analysis of regional systolic function

Quantitative analysis of regional myocardial function may be performed using tissue Doppler or acoustic marker tracking techniques. Muscle movement speed and strain, as well as strain rate are analyzed. Although quantitative analysis allows for objective assessment of regional myocardial contractile function, it has not been included in stress echocardiography standards so far.

### The use of stress echo in coronary heart disease

Stress echo is performed for diagnostic purposes and/or prognosis estimation.

### Diagnosis of myocardial ischemia

Unfeasibility or non-diagnostic result of stress ECG (failure to reach target heart rate during the test, left bundle branch block, stimulatory rhythm, resting repolarization abnormalities, skeletal diseases, lower limb atherosclerosis) is the most common indication for stress echocardiography. Stress and pharmacological tests show similar diagnostic sensitivity, specificity and accuracy in ischemia. The choice of stressor depends on limitations and contraindications, as well as preferences and experience in a given facility. According to guidelines, stress echocardiography has priority over stress electrocardiography, and exercise stress test is the first-choice option in patients able to exercise. Pharmacological or pacing stress test is performed in other patients. Coronary drugs (including beta-blockers) should be discontinued before the test unless contraindicated. Image acquisition in at least three basic projections, i.e. parasternal in the long and short axis, apical four-chamber, two-chamber, and long axis, is performed at each stage with simultaneous recording of heart rate and arterial blood pressure. Doppler parameters are recorded as part of simultaneous valvular assessment. Recording standardized cardiac cross-sections that are identical throughout the entire test is important for comparative analysis.

Segmental contractility analysis is based on left ventricular division into 17 or 16 segments. Each segment is scored between 1 and 4 (1 – normokinesia, 2 – hypokinesia,

3 – akinesia, 4 – dyskinesia), which allows calculation of the left ventricular contractility index at each stage (wall motion score index, WMSI – total score for segments visualized/number of segments visualized). Reduced contractility in at least two segments is considered a positive result, indicative of ischemia. This does not apply to dyskinesia of a segment that is akinetic at rest as this segment may be passively 'pushed out' as a result of hyperkinesia of other ventricular elements. Contractility assessment should include centripetal movement and, most of all, systolic thickening of segments. A large number of segments with poor contractility, contractility disorders in areas supplied by more than one coronary artery (multivessel disease), significant deterioration of contractility (e.g. transition from normokinesia to akinesia or dyskinesia), short time between test onset and ischemia, long-lasting regression of contractility disorders at rest, and left ventricular dilation during exercise are indicative of very severe ischemia. Absence of provoked contractility disorders using the full protocol indicates a negative result. The absence of new contractility disorders in the event of premature test discontinuation due to serious arrhythmia, excess increase in blood pressure above 220/120 mm Hg, a decrease in blood pressure below 90 mm Hg (or by 30 mm Hg below baseline) and patient's request are considered a non-diagnostic result.

### Assessment of myocardial viability

Patients with significant ischemic left ventricular systolic dysfunction and reversible contractility disorders (involving at least four left ventricular segments) present with lower perioperative mortality, higher improvement of regional and general contractile function after invasive treatment, a lower number of heart failure symptoms and lower mortality compared to patients with irreversible contractility disorders. An intravenous infusion of low-dose dobutamine (usually 5 and 10  $\mu\text{g}/\text{kg}/\text{min}$ , 20  $\mu\text{g}/\text{kg}/\text{min}$ , or 2.5, 5, 7.5, 15, 20  $\mu\text{g}/\text{kg}/\text{min}$ ) administered at 3-minute (or 5-minute) stages, is used for the assessment of myocardial viability. Improved contractility of a given segment during dobutamine infusion indicates its viability. Continuation of dobutamine infusion in accordance with the protocol at doses of up to 40  $\mu\text{g}/\text{kg}/\text{min}$  is recommended. A two-phase response including initial contractility improvement (at low dobutamine doses), followed by impairment (at higher doses) is specific for preserved viability of myocardial segment supplied by a stenotic coronary artery and is considered to be the most precise prognostic indicator of improved left ventricular contractility after revascularization.

### The role of stress echo in the diagnosis of coronary artery disease

Stress echo is recommended for the diagnosis of ischemic heart disease: high-dose dobutamine test in the case of contraindications, pacing stress echo in patients with pacemaker, and dipyridamole test for the assessment of coronary flow reserve. Chest pain in patients with intermediate

probability of coronary artery disease, inability to perform physical exercise and non-diagnostic resting or exercise electrocardiography are indications for stress echo. The test is also used in symptomatic patients after revascularization or patients qualified for revascularization for functional assessment of coronary artery stenosis. Low-dose dobutamine test is usually performed in patients after myocardial infarction or with moderate-to-severe left ventricular dysfunction to assess myocardial viability before potential revascularization.

### Possible complications of stress echo

Death, cardiac arrest due to ventricular fibrillation or asystole, myocardial infarction, shock, and pulmonary edema are the most severe, yet very rare complications of stress echo. Ventricular and supraventricular tachyarrhythmia, especially during dobutamine stress echo, are slightly more common. Anxiety, tremor, dyspnea, headache, palpitations, nausea, flushing, paresthesia, excess blood pressure elevation or drop may be experienced during dobutamine stress

echo. Excess reduction of blood pressure or atrioventricular block may occur during dipyridamole or adenosine stress echo. Pacing stress echo is the best-tolerated test. Pacing stress echo and stress echo are the safest tests.

### Contraindications to stress echo

Contraindications to stress echo include, among other conditions, unstable coronary heart disease, decompensated heart failure, uncontrolled high blood pressure, severe ventricular arrhythmias, endocarditis, myocarditis and pericarditis, as well as lack of patient's consent.

### Conflict of interest

*The authors do not report any financial or personal connections with other persons or organizations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.*

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