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Stress echocardiography. Part II: Stress echocardiography in conditions other than coronary heart disease

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Keywords

stress echocardiography, dobutamine, exercise, cardiac valvular defects

Abstract

Stress echocardiography (stress echo), with use of both old and new ultrasonographic cardiac function imaging techniques, has nowadays become a widely available, safe and inexpensive diagnostic method. Cardiac stress, such as exercise or an inotropic agent, allows for dynamic assessment of a wide range of functional parameters describing ventricles, heart valves and pulmonary circulation. In addition to diagnosis of ischemic heart disease, stress echocardiography is also used in patients with acquired and congenital valvular defects, hypertrophic cardiomyopathy, dilated cardiomyopathy as well as diastolic and systolic heart failure. Physical exercise is the recommended stressor in patients with aortic and especially mitral valvular disease. Nevertheless, dobutamine stress echo is useful for the assessment of contractile and flow reserve in aortic stenosis with reduced left ventricular ejection fraction. Stress echo should always be performed by an appropriately trained cardiologist assisted by a nurse or another doctor, in the settings of an adequately equipped echocardiographic laboratory and with compliance to safety requirements. Moreover, continuous education of cardiologists performing stress echo is needed.

Introduction

Stress echocardiography (stress echo, SE), with use of both old and new ultrasonographic cardiac function imaging techniques, has nowadays become a widely available, safe and inexpensive diagnostic method. Cardiac stress, such as exercise or an inotropic agent, allows for dynamic assessment of a wide array of ventricles, heart valves and pulmonary circulation functional parameters. The registration of dynamic cardiac response provides completely new insight important from both diagnostic and prognostic point of view. In addition to diagnosis of ischemic heart disease, stress echocardiography is also used in patients with valvular defects, hypertrophic cardiomyopathy, dilated cardiomyopathy as well as diastolic and systolic heart failure[1]. The protocol for dobutamine stress echo is shown in Fig. 1. Low-dose dobutamine stress echo (up to 20 μg/kg/min) is recommended for patients with low-gradient and low-flow aortic stenosis and reduced ejection fraction (EF). High-dose dobutamine stress echo (up to 40 μg/kg/min) is often needed in patients with heart failure treated with beta-blockers. Fig. 2 shows stress echo protocol for cycle ergometer (examination usually performed in the left lateral recumbent position) or treadmill.

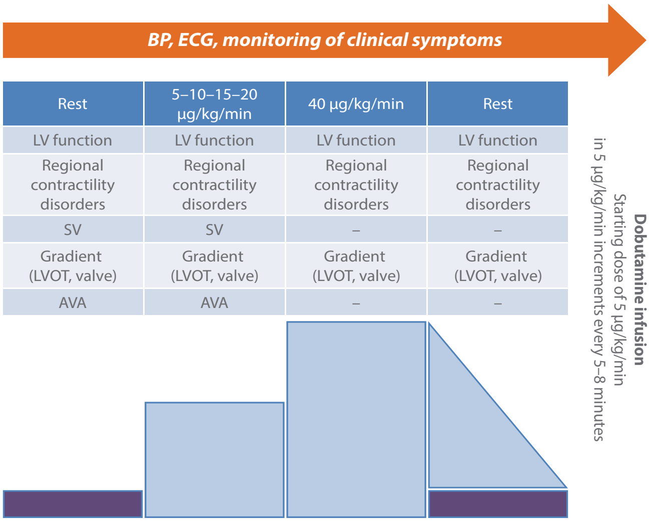
A number of echocardiographic parameters may be registered during the stress echo; in practice, however, the assessment is limited to those most important for given clinical problem (Tab. 1). The choice of stressor depends on clinical scenario (e.g. an evaluation of flow and contractile reserve only in dobutamine test) and patient's physical fitness. Cycle ergometer should be recommended for the less fit and elderly patients. Furthermore, it is easier to record Doppler parameters using a cycle ergometer than a treadmill. Diagnostic end-points, reasons for stress echo interruption, and criteria for an abnormal stress echo are shown in Tab. 2.

Acquired cardiac valvular diseases

Physical exercise is the recommended stressor in patients with aortic (regurgitation, stenosis) and mitral valvular defects (regurgitation, stenosis). One should bear in mind that especially in the latter ones, where the dynamic influence of momentarily left ventricular function on the defect is of particular significance, the use of dobutamine, which is LV function dependent, can alter loading conditions and this way may cause difficulty in test results interpretation. On the contrary, for the assessment of contractile and flow reserve in aortic stenosis, where an increase in the left ventricular stroke volume is of key importance, dobutamine stress echo is tremendously useful. The benefits of exercise stress in patients with valvular defects along with the basic assessment criteria are summarized in Fig. 3.

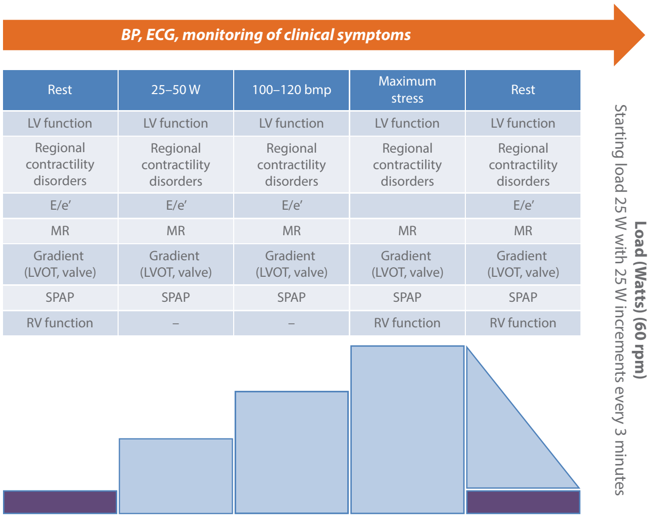
Aortic stenosis

In the case of severe aortic valve stenosis, progressive LV pressure overload and/or coexisting ischemic/postinfarction myocardial damage inevitably lead to reduced LV stroke volume and, consequently, reduced flow velocity and transvalvular gradient. In this subgroup of patients with the so-called classical low-flow low-flow aortic stenosis (defined as EF <50%; mean gradient <40 mm Hg; maximum transvalvular flow velocity V_{max} <4.0 m/s; aortic valve area, AVA <1.0 cm²), differentiation between severe (true severe) and moderate (pseudo-severe) aortic stenosis, as well as an estimation of LV contractile reserve are feasible during dobutamine stress echo. In accordance with the protocol, dobutamine dose should be gradually increased from 10 to 30 μg/kg/min at 3–5-minute intervals, under continuous monitoring of blood pressure, ECG and clinical symptoms (dyspnea, angina pectoris, ventricular arrhythmia). Patients with >20% increase



Rest	5–10–15–20 μg/kg/min	40 μg/kg/min	Rest
LV function	LV function	LV function	LV function
Regional contractility disorders	Regional contractility disorders	Regional contractility disorders	Regional contractility disorders
SV	SV	–	–
Gradient (LVOT, valve)	Gradient (LVOT, valve)	Gradient (LVOT, valve)	Gradient (LVOT, valve)
AVA	AVA	–	–

Fig. 1. *Dobutamine stress echo protocol and parameters recorded at each test stage[1]. LV – left ventricle, SV – stroke volume, AVA – aortic valve area, BP – blood pressure*



Rest	25–50 W	100–120 bmp	Maximum stress	Rest
LV function	LV function	LV function	LV function	LV function
Regional contractility disorders	Regional contractility disorders	Regional contractility disorders	Regional contractility disorders	Regional contractility disorders
E/e'	E/e'	E/e'		E/e'
MR	MR	MR	MR	MR
Gradient (LVOT, valve)	Gradient (LVOT, valve)	Gradient (LVOT, valve)	Gradient (LVOT, valve)	Gradient (LVOT, valve)
SPAP	SPAP	SPAP	SPAP	SPAP
RV function	–	–	RV function	RV function

Fig. 2. *Protocol for stress echo (SE) using cycle ergometer or treadmill. Parameters recorded at each test stage are shown: MR – mitral regurgitation, RV – right ventricle, LV – left ventricle, LVOT – left ventricular outflow tract, PB – blood pressure, SPAP – systolic pulmonary artery pressure[1]*

Tab. 1. *Threshold values of stress echo parameters associated with prognosis and treatment response. DE – dobutamine stress echo, SE- exercise stress echo, EF – ejection fraction, SV - stroke volume, WMSI – contractility index*

Parameters	Threshold values
Left intraventricular obstruction	LVOT gradient >50 mm Hg
Impaired functional reserve	Δ WMSI <0.25 in ectatic cardiomyopathy (SE, DE) Δ EF <7.5% in NS and CRT patients (SE, DE) Δ EF <4.5% in primary MR and AR (SE) Δ Global longitudinal strain <2% in organic MR (SE)
Impaired flow reserve	Δ SV <20% (DE)
Dynamic mitral regurgitation	Δ EROA >13 mm^2 in functional MR (SE)
Systolic pulmonary hypertension	SPAP >60 mm Hg (SE)
Limited valvular compliance	Mean diastolic gradient in mitral stenosis >15 mm Hg (SE); >18 mm Hg (DE) Systolic gradient in aortic stenosis >18 mm Hg (SE)
Prosthetic malfunction	Mean diastolic gradient in mitral position >10 mm Hg (SE, DE) Mean systolic gradient in aortic position >20 mm Hg (SE, DE)
Functional stenosis after mitral ring plasty	Mean diastolic gradient >7 mm Hg
RV dysfunction	TAPSE <19 mm in limited MR (SE)
DE – stres echo z dobutaminą, SE – stres echo wysiłkowe, EF – frakcja wyrzutowa, SV – objętość wyrzutowa, WMSI – wskaźnik kurczliwości	

in left ventricular stroke volume (LV SV) due to inotropic stimulation and a simultaneous increase in both the flow through the aortic orifice and transvalvular gradient (>40 mm Hg) without significant increase in aortic valve area (change in AVA by <0.2 cm^2, AVA <1,0 cm^2) should be diagnosed with severe aortic stenosis with preserved flow reserve. Alternatively, if the dobutamine-induced SV increase (>20% of resting SV) is accompanied by significant AVA increase (AVA >1.0 cm^2) without simultaneous rise of the gradient (mean gradient <40 mm Hg), moderate aortic stenosis with preserved flow reserve should be diagnosed. Patients with severe stenosis and no flow reserve present persistent AVA <1.0 cm^2 and lack of SV increase (or <20% increase from the resting value) despite higher doses (up to 30 μg/kg/min). This subgroup is characterized by worse prognosis compared to patients with preserved flow reserve regardless of treatment (conservative or surgical). Doppler technique should be used for calculations of both aortic orifice area and LV stroke volume. Although the role of dobutamine stress echo in the diagnosis and the prognosis estimation in patients with the so-called paradoxical low-gradient severe stenosis (SV <35 mL/m^2, EF >50%, mean gradient <40 mm Hg) is currently not precisely defined, it may help differentiate between true severe and pseudo-severe stenosis[2–4].

Cycle ergometer stress testing may help determine the time of surgical/percutaneous intervention (AVR/TAVI) in asymptomatic patients with severe aortic stenosis (AVA <1.0 cm^2, mean transvalvular gradient <40 mm Hg, EF >50%). Increased exercise gradient (by >18–20 mm Hg), reduced LV contractility, no LV contractile reserve and exercise-induced systolic pulmonary artery pressure (SPAP) >60 mm Hg may indicate the need for earlier surgical intervention (Fig. 3).

Aortic regurgitation

Cycle ergometer stress test, which is performed to elicit clinical symptoms (exercise dyspnea), as well as to assess exercise tolerance (the level of exercise load) and LV contractile reserve, is recommended for patients with asymptomatic aortic regurgitation. Defect staging based on exercise and dobutamine stress echo is not recommended as increased heart rate and reduced diastolic time limit the accuracy of quantitative measurement of aortic regurgitation wave. The lack of contractile reserve (Δ EF <5% at peak load) should preferably be accompanied with concurrent assessment of longitudinal LV strain (tissue Doppler). Thus revealed subclinical LV dysfunction has a documented prognostic value and is associated with worse postoperative prognosis. The test may help determine true cause of symptoms reported by patients with moderate aortic regurgitation as clinical manifestation may in fact be related to exercise-induced

Tab. 2. *Diagnostic end-points and reasons for stress echo interruption*

Diagnostic end-points	Reasons for test interruption	Improper test criteria (>1 criterion)
Maximum dobutamine dose/ maximum exercise	Intolerable symptoms	Symptoms: angina pectoris, dyspnea, syncope, fatigue at low stress level
Target heart rate	Muscular fatigue	Ischemia (ST drop by >2 mm vs baseline)
Typical changes in ECG	Hypertension (220/120 mm Hg)	New disorders of regional contractility
Typical changes in echocardiogram	Symptomatic hypotension (decrease by >40 mm Hg)	Arrhythmias (NSVT, SVT)
Retrosternal pain	Arrhythmias (SVT, AF, multiple ventricular ectopic beats)	Specific end-points*
* Specific end-points refer to threshold values for echo parameters, which are associated with worse prognosis, absence of treatment response (e.g. intraventricular gradient> 50 mmHg) – see Tab. 1.		

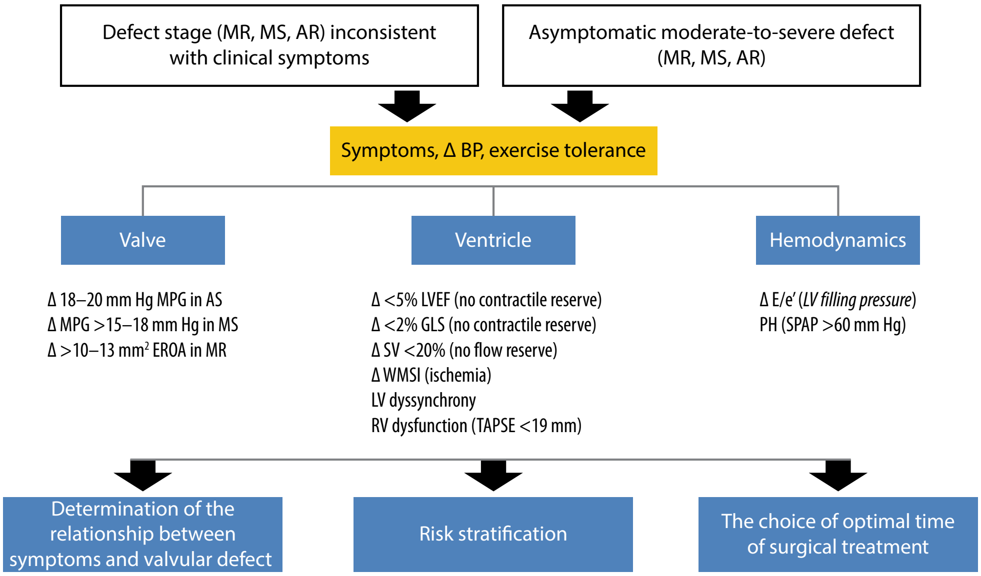


Fig. 3. *The usefulness of stress echo (SE) in the assessment of acquired valvular defects. The following parameters are individually assessed: valvular function alone, LV and RV function, and other hemodynamic consequences of the defect[1]. MR – mitral regurgitation, MS – mitral stenosis, AR – aortic regurgitation, AS – aortic stenosis, SV – stroke volume, MPG - mean pressure gradient, PH – pulmonary hypertension*

dynamic mitral regurgitation, pulmonary hypertension or left ventricular diastolic dysfunction (Fig. 3).

Mitral regurgitation

Increasing MR (≥ grade1), dynamic pulmonary hypertension (SPAP >60 mm Hg), lack of the LV contractile reserve (Δ EF <5%, Δ longitudinal LV strain <2%), and lack of the RV contractile reserve (Δ TAPSE <19 mm) imply poor prognosis in symptomatic patients with moderate **primary** mitral regurgitation. In case of patients with severe asymptomatic primary mitral regurgitation, stress echo should primarily focus on possible provocation of clinical symptoms (dyspnea), detection of dynamic pulmonary hypertension (SPAP >60 mm Hg) and assessment of LV contractile reserve while repeated grading of regurgitant flow is not required.

For **functional** regurgitation, exercise stress is needed when there is a large disproportion between the degree of regurgitation at rest and clinical symptoms (positional dyspnea, exercise intolerance, recurrent pulmonary edema). Cardiac stress test may help decide if planned revascularization (e.g. CABG) should be complemented with mitral repair. In these settings, exercise-induced increase in ERO by >13 mm^2 and exercise pulmonary hypertension >60 mm Hg indicate worse prognosis. On the other hand, exercise-induced reduction of regurgitation or even its full resolution, suggest presence of the contractile reserve and better prognosis (Fig. 3).

Mitral stenosis

Stress testing allows for simultaneous analysis of hemodynamic stage and symptoms associated with the defect, particularly in patients with disproportion between symptoms and resting measurement of orifice area and diastolic gradient. Exercise gradient >15 mm Hg (mean gradient) and SPAP >60 mm Hg (maximum gradient) signify severe mitral stenosis regardless of the area of mitral orifice (Fig. 3).

Prosthetic valves

In case of patients with implanted prosthetic valves and clinical symptoms, stress echo facilitates verification of relationship between reported symptoms and prosthetic malfunction. Cycle ergometer is the preferred option in most patients. Low-dose dobutamine test (up to 20 μg/kg/min) is performed in patients with moderate-to-severe symptoms.

Cycle ergometer testing allows for diagnosis of valvular stenosis or patient-prosthesis mismatch (PPM) in patients with mitral or aortic prostheses and mild-to-moderate increase in resting transvalvular gradients. Low-dose dobutamine (DE) stress echo allows for differentiation between true prosthetic malfunction, prosthetic pseudo-malfunction and mismatch in patients with low valvular flow, low resting effective orifice area (EOA) and decreased Doppler velocity index (DVI) (Tab. 1).

Hypertrophic cardiomyopathy

Exercise stress echo reveals clinical symptoms and allows for monitoring of response to treatment in patients with hypertrophic cardiomyopathy (HCM). Increased exercise gradient >50 mm Hg, abnormal blood pressure (BP) response to exercise, LV systolic and diastolic dysfunction (regional contractile disorders, increased E/e'), as well as increased dynamic mitral regurgitation are associated with worse exercise tolerance and poor prognosis. Exercise stress test is contraindicated in patients with gradient >50 mm Hg measured during rest or Valsalva maneuver (Tab. 1).

Dilated cardiomyopathy and cardiac resynchronization therapy

Low-dose dobutamine test is helpful for prediction of response to cardiac resynchronization therapy (CRT). The increase of LVEF by >7%, presence of contractile reserve (improved wall motion score index, WMSI) and reduction of mitral regurgitation during dobutamine test are the predictors of advantageous LV remodeling after CRT pacemaker implantation[5,6].

Stress echo should always be performed by an appropriately trained cardiologist assisted by a nurse or another doctor, in the settings of an adequately equipped echocardiographic laboratory and with compliance to safety requirements. Moreover, continuous education of cardiologists performing stress echo is needed[7–9].

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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