Stress echocardiography in conditions other than coronary heart disease

Edyta Płońska-Gościniak¹, Tomasz Kukulski², Jarosław D. Kasprzak³, Zbigniew Gąsior⁴, Andrzej Szyszka⁵, Andrzej Gackowski⁶, Wojciech Braksator⁷, Piotr Gościniak⁸, Piotr Pysz⁹, Szymon Olędzki¹, Wojciech Kosmala¹¹

¹ Department of Cardiology Pomeranian Medical University, Szczecin, Poland
² Department of Cardiology, Congenital Heart Diseases and Electrotherapy, The Silesian Center for Heart Diseases in Zabrze, Medical University of Silesia, Zabrze, Poland
³ Department of Cardiology, Medical University of Lodz, Lodz, Poland
⁴ Department of Cardiology, Medical University of Silesia in Katowice, Katowice, Poland
⁵ Department of Cardiology, Poznan University of Medical Sciences, Poznań, Poland
⁶ Department of Coronary Disease and Heart Failure of Jagiellonian University, Medical College, Noninvasive Cardiovascular Laboratory, Specialist Hospital in Cracow, Cracow, Poland
⁷ Department of Sports Cardiology and Noninvasive Cardiac Diagnosis, Medical University of Warsaw, Warsaw, Poland
⁸ Independent Laboratory of Non-Invasive Heart Diagnostics for Children and Adults, Independent Public Clinical Hospital No. 1, Pomeranian Medical University in Szczecin, Szczecin, Poland
⁹ Department of Cardiology and Structural Heart Diseases, Medical University of Silesia, School of Medicine in Katowice, Poland
¹⁰ Cardiac Rehabilitation Department Treatment and Rehabilitation Center, Long-Term Care Hospital, Jaworzê, Poland
¹¹ Department of Cardiology, Medical University of Wroclaw, Wroclaw, Poland

Correspondence: Prof. Edyta Płońska-Gościniak, ul. Poniatowskiego 33c, 71-111 Szczecin; e-mail: edytaplonska@life.pl

DOI: 10.15557/JoU.2019.0007

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

![BP, ECG, monitoring of clinical symptoms](image1)

**Fig. 1. Dobutamine stress echo protocol and parameters recorded at each test stage**[2]. LV – left ventricle, SV – stroke volume, AVA – aortic valve area, BP – blood pressure

![BP, ECG, monitoring of clinical symptoms](image2)

**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**[3]
Stress echocardiography. Part II: Stress echocardiography in conditions other than coronary heart disease

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 mm² 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 wysiłkowy, 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 cm², AVA <1.0 cm²) 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 cm²) 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 cm² 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/m², 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 cm², 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.
dynamic mitral regurgitation, pulmonary hypertension or left ventricular diastolic dysfunction (Fig. 3).

**Mitral regurgitation**

Increasing MR (≥ grade 1), 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 mm² 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

---

| Defect stage (MR, MS, AR) inconsistent with clinical symptoms | Asymptomatic moderate-to-severe defect (MR, MS, AR) |
|---------------------------------------------------------------|---------------------------------------------------|
| Symptoms, Δ BP, exercise tolerance |

- Δ 18–20 mm Hg MP in AS
- Δ MPG >15–18 mm Hg in MS
- Δ >10–13 mm² EROA in MR

- Δ <5% LVEF (no contractile reserve)
- Δ <2% GLS (no contractile reserve)
- Δ SV <20% (no flow reserve)
- Δ WMSI (ischemia)
- LV dyssynchrony
- RV dysfunction (TAPSE <19 mm)

**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
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(7,8).

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.

References
1. Sicari R, Nihoyannopoulos P, Evangelista A, Kasprzak J, Lancellotti P, Poldermans D et al.: Stress echocardiography expert consensus statement: European Association of Echocardiography (EAE) (a registered branch of the ESC). Eur J Echocardiogr 2008; 9: 415–437.
2. Płońska-Gościniak E, Gackowski A, Gąsior Z: Rekomendacje 2011 Sekcji Echokardiografii Polskiego Towarzystwa Kardiologicznego dotyczące zastosowania echokardiografii obciążeniowej w praktyce klinicznej. Kardiol Pol 2011; 69: 642–648.
3. Lancellotti P, Pellikka P, Budts W, Chaudhry FA, Donal E, Dulgheru R et al.: The clinical use of stress echocardiography in non-ischaemic heart disease: recommendations from the European Association of Cardiovascular Imaging and the American Society of Echocardiography. Eur Heart J Cardiovasc Imaging 2016; 17: 1191–1229.
4. Vahanian A, Alfieri O, Andreotti F, Antunes MJ, Barón-Esquivias G, Baumgartner H et al.: Guidelines on the management of valvular heart disease (version 2012): the Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). Eur J Cardiothorac Surg 2012; 42: S1–S44.
5. Clavel MA, Ennezat PV, Maréchaux S, Dumesnil JG, Capoulade R, Hachicha Z et al.: Stress echocardiography to assess stenosis severity and predict outcome in patients with paradoxical low-flow, low-gradient aortic stenosis and preserved LVEF. JACC Cardiovasc Imaging 2013; 6: 175–183.
6. Ypenburg C, Sieders A, Bleeker GB, Holman ER, van der Wall EE, Schalji MJ et al.: Myocardial contractile reserve predicts improvement in left ventricular function after cardiac resynchronization therapy. Am Heart J 2007; 154: 1160–1165.
7. Płońska-Gościniak E, Kasprzak JD, Kukulski T, Mizia-Stec K, Nowalany-Koziełska E, Gąsior Z et al.: Role of lowdose dobutamine echocardiography in predicting response to biventricular pacing. Results from the multicenter Viability in Cardiac Resynchronisation Therapy (ViaCRT) study. Pol Arch Med Wewn 2016; 126: 989–994.
8. Płońska-Gościniak E, Gościniak P: Echokardiografia obciążeniowa. In: Lipiec P, Hoffman P (eds.): Echokardiografia kliniczna. Podręcznik Sekcji Echokardiografii Polskiego Towarzystwa Kardiologicznego. Medica Total Project, Warszawa 2017, p. 40–49.
9. Płońska-Gościniak E, Kasprzak JD, Ołędzki S, Rzucidło-Resil J, Gościniak P, Kukulski T et al.: Polish Stress Echocardiography Registry (Pol-STRESS registry) – a multicenter study. Stress echocardiography in Poland: numbers, settings, results, and complications. Kardiol Pol 2017; 75: 922–930.