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Echocardiographic diastolic stress test

Echokardiograficzna rozkurczowa próba wysiłkowa

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Abstract

Diastolic dysfunction can lead to heart failure symptoms if it causes elevated left atrial pressure. Diastolic function changes dynamically for example during physical exercise. That is why echocardiography at rest may not detect signs of left atrial pressure elevation. In this article, we present an outline of diastolic function assessment at rest, and indications for a diastolic stress test, its protocols and interpretation.

Key words: echocardiography, diastole, stress test, diastolic dysfunction, heart failure

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Introduction

Correct myocardial diastolic function is the basis for hemodynamically effective heart activity. Among other things, the left ventricular filling and, consequently, the left ventricular ejection volume depends on it. Please note that the diastolic function is a parameter that can vary dynamically over time, depending on preload, afterload and the heart rate. Diastolic dysfunction may be of a transient nature, when it is more functional, as it happens in acute ischemia, or it may be perpetuated when it results from completed heart muscle remodeling [1]. Abnormalities of mechanisms determining normal left ventricular diastole result in increased ventricular pressure and impairment of normal blood flow from the left atrium and pulmonary circulation. It is worth mentioning at this point that if there is no significant obstacle to the inflow of blood from the left atrium to the left ventricle (as in the case of significant mitral stenosis or left atrial myxoma entering the mitral outlet), then during the left ventricular diastolic period the left atrial pressure is closely related to the left ventricular pressure. In this case we can assume that elevated left ventricular filling pressure leads to elevated left atrial pressure and left atrial and pulmonary circulation pressure reflects left ventricular filling pressure [2].

The aim of diastolic stress echocardiography test is to detect a left ventricle diastolic reserve impairment, which leads to an increase in left ventricular filling pressure during exercise. Most heart failure patients experience symptoms during exercise, and functional diastolic disorders can explain them. In such cases, it is the increase in left ventricular inflation pressure correlates to an increase in pressure in the left atrium and pulmonary circulation, which is associated with dyspnea during physical activity and worse tolerance of exercise. For this reason, the assessment of left ventricular filling pressure is becoming more and more important in the diagnosis of heart failure, especially in patients with preserved left ventricular ejection fraction. Echocardiography enables a non-invasive evaluation of these pressures [3].

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Evaluation of left ventricular diastolic function in resting echocardiography

Before discussing the most important aspects of diastolic stress echocardiography, the basics of left ventricular diastolic function evaluation in resting transthoracic echocardiography are presented below.

In 2016, there was a consensus on the evaluation of the diastolic function of the American Society of Echocardiography and the European Association of Cardiovascular Imaging. There are a number of echocardiographic parameters that should be evaluated in order to answer the question about the presence and severity of left ventricular diastolic dysfunction. It is worth emphasizing that diastolic function evaluation in the resting exam is an integral part of routine echocardiographic examination, especially in patients with dyspnea and suspected heart failure [4]. In the guidelines on heart failure published in 2016, abnormal diastolic function is one of the important parameters in the diagnosis of heart failure in patients with left ventricular ejection fraction ≥ 40% [5].

The guidelines for diastolic function evaluation listed 18 parameters that are useful in the evaluation of left ventricular diastolic function. The multitude of these parameters indicates the lack of one ideal parameter evaluating left ventricular diastolic dysfunction, and thus the difficulties in diagnosing and assessing its severity. Despite the variety of available parameters and diagnostic difficulties, the authors have selected several of them to be assessed in a mandatory rest test.

The first step in the evaluation of left ventricular diastolic function is the morphological evaluation of the heart and the systolic function of the left ventricular muscle. In the morphological evaluation of the heart, the presence of thickened myocardium and the size of the left atrium is an important clue for the possibility of diastolic dysfunction. In the assessment of left ventricular systolic function, the most important parameter is the ejection fraction measured by Simpson's method. The left ventricular ejection fraction ≥ 50% is considered normal. The guidelines provide separate algorithms for people with a morphologically normal heart and normal left ventricular ejection fraction and for those with reduced left ventricular ejection fraction (< 50%) or myocardial disease with preserved left ventricular ejection fraction, taking into account clinical and heart structure data.

In the first group of patients, our task is first to detect the presence of diastolic dysfunction, and then to assess their severity. The authors of the guidelines assume that in patients with abnormal left ventricular ejection fraction or abnormal left ventricular muscle structure, diastolic dysfunction always coexist, and echocardiographic evaluation should be directed to the detection of elevated pressure in the left atrium.

The general left ventricular diastolic function evaluation scheme (Figure 1) is presented below, however, it should be remembered that in some pathologies some of these parameters are impossible to be measured or useless, because their abnormal value results from other pathologies and does not indicate diastolic function disorders.

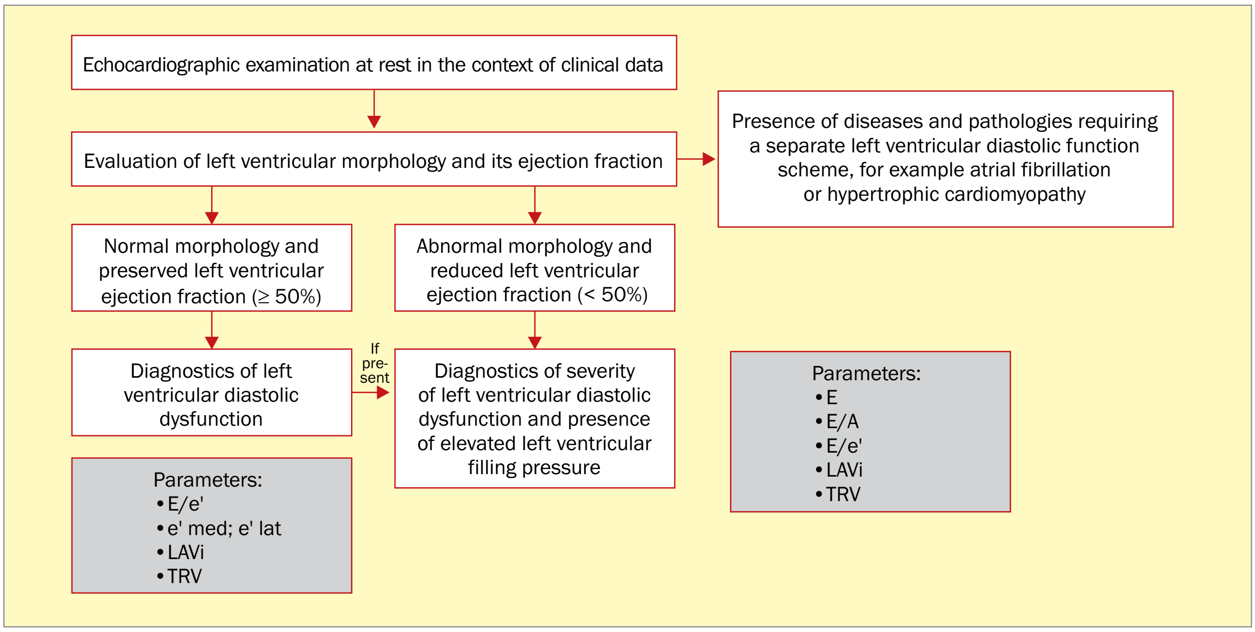


Figure 1. Diagram of evaluation of diastolic function in resting echocardiography; A — late-diastolic wave velocity of left ventricular filling caused by atrial systole E — early diastolic mitral inflow velocity; e' — mean value of early diastolic lateral and medial mitral ring velocity; e' med — value of early diastolic mitral ring medial velocity expressed in centimeters per second; e' lat — early diastolic lateral velocity of the mitral annulus expressed in centimeters per second; LAVi — left atrial volume expressed in milliliters per square meter indexed to the body area; TRV — maximum tricuspid regurgitation wave velocity expressed in meters per second

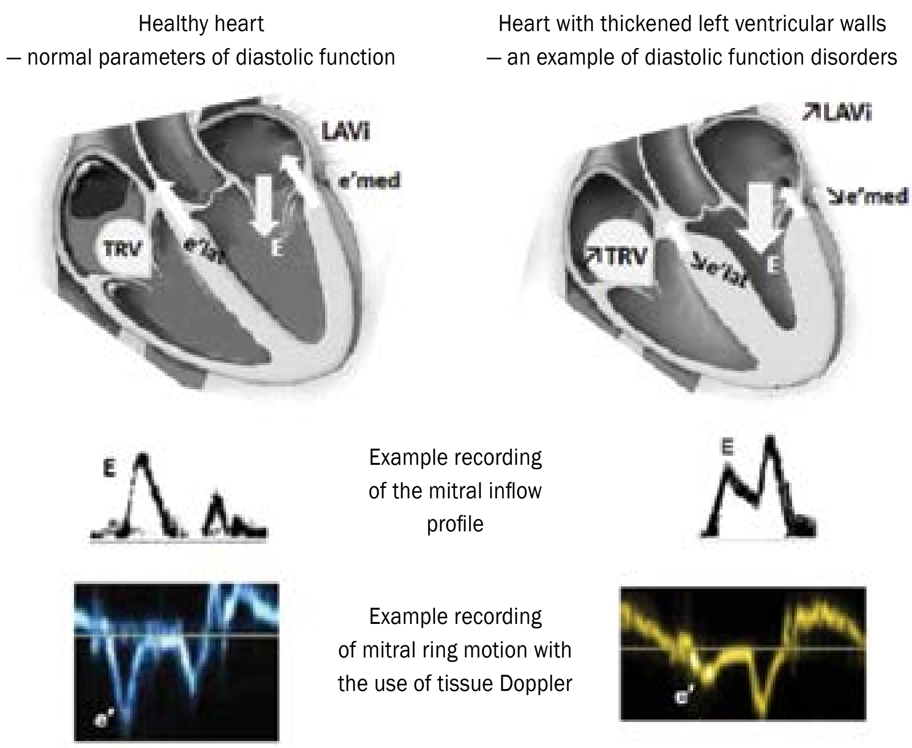


Figure 2. Changes in parameters used to detect diastolic dysfunction on the example of a patient with thickened left ventricular walls; E — early diastolic velocity of mitral inflow wave; e' — value of early diastolic lateral or medial mitral ring velocity; e' med — value of early diastolic lateral mitral ring velocity; e' lat — value of early diastolic lateral mitral ring velocity; LAVi — left atrial volume indexed to body surface area; TRV — maximum tricuspid regurgitation wave velocity

The 2016 guidelines discuss in detail the differences in the evaluation of diastolic function in selected clinical situations, such as hypertrophic cardiomyopathy, significant mitral regurgitation or atrial fibrillation.

Assessment of left ventricular diastolic dysfunction

To assess the presence of left ventricular diastolic dysfunction we evaluate four groups of parameters (Figure 2):

- parameters related to left ventricular filling represented by the ratio of early diastolic mitral inflow wave velocity (E-wave) and average value of early diastolic lateral and medial mitral ring velocity (e');
- parameters related to the myocardial function represented by the values of e' lateral and medial part of the mitral ring separately (e' lat i e' med);
- parameters related to secondary remodeling of the heart muscle represented by the left atrial volume indexed to the body surface area (LAVi);
- parameters related to hemodynamic effects on pulmonary circulation and right cardiac cavities represented by the maximum tricuspid regurgitation wave velocity (TRV).

Table 1 shows the cut-off points for incorrect values of the above parameters. If it is technically impossible to measure e'; in both parts of the mitral ring, the cut-off point for the parameter E/e' lat is > 13 and for E/e' med > 15. In the 2016 guidelines for heart failure, the authors suggest a slightly lower cut-off point for abnormal E/e' ≥ 13 [5]. In addition, an incorrect value for average e', which is < 9 cm/s, is also given.

It is worth noting that for the detection of diastolic dysfunction disorders, the new guidelines do not recommend the use of the ratio of E and A waves, but still, as will be discussed later, it is a key parameter in grading the severity of diastolic dysfunction.

Next, it is necessary to assess how many of the above groups of parameters is fulfilled by the tested person. If none or only one of the parameters is met, the diastolic function should be considered correct. If two parameters have exceeded the cut-off points for normal values, the presence of diastolic dysfunction cannot be decided on the basis of this test. However, if the patient has 3 or 4 of the above abnormalities, we find an abnormal diastolic function and we can proceed to the assessment of its severity.

Table 1. Cut-off points for abnormal parameter values used to assess the presence of left ventricular diastolic dysfunction

Meaning of the parameter	Parameter	Values that may indicate diastolic dysfunction
Left ventricular filling pressure	E/e'	> 14
Myocardium function (fulfillment of one of them is enough)	e' lat	< 10 cm/s
	e' med	< 7 cm/s
Secondary reconstruction	LAVi	> 34 ml/m^2
Hemodynamic impact on pulmonary circulation	TRV	> 2,8 m/s

E — early diastolic mitral inflow wave velocity; e' — average value of early diastolic lateral and medial mitral ring velocities; e' med — the value of early diastolic velocity of the medial part of the mitral ring expressed in centimeters per second; e' lat — early diastolic lateral velocity of the mitral ring expressed in centimeters per second; LAVi — left atrial volume expressed in milliliters per square meter indexed to the body area; TRV — maximum tricuspid regurgitation wave velocity expressed in meters per second

Evaluation of the severity of left ventricular diastolic dysfunction

The aim of the assessment of left ventricular diastolic function abnormalities is first of all to assess the presence of elevated pressure in the left atrium. The severity of diastolic dysfunction is assessed in all patients:
- with abnormal diastolic function (diagnosed according to the criteria described in the "Assessment of the presence of left ventricular diastolic dysfunction disorders") section;
- abnormal left ventricular ejection fraction (< 50%);
- abnormal myocardium (*e.g.* thickening) with preserved left ventricular ejection fraction (≥ 50%).

In the beginning we evaluate two parameters of mitral inflow - the previously mentioned E-wave, which is the early diastolic mitral inflow wave velocity and its relation to the late diastolic left ventricular filling wave velocity caused by atrial contraction (E/A).

If the E/A ratio is ≤ 0. 8 and if the E-wave velocity is ≤ 50 cm/s, then it should be assumed that at rest the blood pressure in the left ventricle and left atrium is not elevated and first-degree diastolic function disorders should be recognized.

If the E/A ratio ≥ 2 then we recognize III degree left ventricular diastolic dysfunction and the presence of elevated pressures in the left atrium.

The greatest diagnostic challenge is in patients with an E/A ratio ≤ 0. 8 at a simultaneous E wave > 50 cm/s or with an E/A ratio between 0.8 and 2. In these patients we analyze additional parameters: E/e' (averaged) ratio, TRV and indexed left atrial volume. We use the same points as in determining the presence of diastolic function disorders, *i.e.* E/e' ratio > 14, for TRV > 2.8 m/s and for LAVi > 34 ml/m^2. If at least two of the above criteria are met, we recognize second degree diastolic dysfunction and the presence of elevated pressure in the left atrium. If only one criterion or the results of all three parameters are below the cut-off points, the first degree of diastolic dysfunction is recognized, without the coexistence of elevated pressure in the left atrium (Table 2) [4].

Indications for echocardiographic diastolic stress test

Diastolic stress test should be performed in patients with first-degree diastolic dysfunction, without elevated left ventricular filling pressures at rest, if there are symptoms suggestive of heart failure, in particular exercise dyspnea, to answer the question whether the symptoms experienced by the patient result from diastolic reserve impairment [4]. Diagnostic guidelines for heart failure suggest wider indications for diastolic stress echocardiography. In this document, experts suggest a diastolic stress test in all suspected heart failure patients with preserved left ventricular ejection fraction, in whom other examinations, such as resting echocardiographic examination or measurement of natriuretic peptides, did not allow such a diagnosis to be confirmed, and the patients feel dyspnea, especially exertional dyspnea. The risk factors of developing heart failure with preserved ejection fraction of the left ventricle, such as age, hypertension, diabetes mellitus, sedentary lifestyle, overweight and obesity, should be borne in mind [6].

Diastolic stress echocardiography should not be performed for diagnostic purposes in patients in whom the resting examination allows to detect elevated pressures in the left atrium, *i.e.* in the second and third degree of diastolic dysfunction. Perhaps such an attempt could have prognostic significance, but this requires further research and a prospective assessment.

Therefore, the main aim of diastolic echocardiographic stress test is to determine the development of elevated left ventricular filling pressure during exercise in patients with normal left ventricular filling pressure and, consequently, normal left atrial pressure at rest. This is particularly important if there are signs of heart failure during exercise. Of course, other cardiac and extra-cardiac causes of dyspnea and exercise intolerance such as coronary disease, significant valve abnormalities, anemia or respiratory diseases should be excluded.

Table 2. Criteria for recognition of different degrees of left ventricular diastolic dysfunction

Level of diastolic dysfunction	Criteria	Left atrial pressure increased at rest
I*	E/A ≤ 0.8 and E wave velocity ≤ 50 cm/s	Absent
	E/A ≤ 0.8 and E wave velocity > 50 cm/s **and the absence** of two or all additional criteria (E/e' > 14; TRV > 2.8 m/s; LAVi > 34 ml/m^2)	
	E/A above 0.8 and below 2 **and the absence** of two or all additional criteria (E/e' > 14; TRV > 2.8 m/s; LAVi > 34 ml/m^2)	
II*	E/A ≤ 0.8 and E wave velocity > 50 cm/s **and the presence** of two or all additional criteria (E/e' > 14; TRV > 2.8 m/s; LAVi > 34 ml/m^2)	Present
	E/A above 0.8 and below 2 **and the presence** of two or all additional criteria (E/e' > 14; TRV > 2.8 m/s; LAVi > 34 ml/m^2)	
III	E/A ≥ 2	Present

*If only two of the three additional criteria are available and one of them is met and the other one is not then we cannot determine the degree of diastolic dysfunction. If both are not met, we recognize the first degree of diastolic dysfunction, and if both are met, we recognize the second degree of diastolic dysfunction; A — late-diastolic wave velocity of left ventricular filling caused by atrial systole; E — early diastolic mitral inflow velocity; e' — averaged value of early diastolic lateral and medial mitral ring velocity; LAVi — volume of the left atrium expressed in milliliters per square meter indexed to the body surface area; TRV — maximum tricuspid regurgitation wave velocity expressed in meters per second

Selected technical aspects of diastolic echocardiographic stress test

The most common diastolic stress test is performed using cycle-ergometer. We cannot replace physical exercise with other stress methods such as dobutamine or quick heart stimulation, because the use of these methods in itself affects the diastolic function.

During echocardiographic stress test for evaluation of diastolic function we evaluate mitral inflow, myocardial velocities of the medial and lateral part of the mitral ring and peak velocity of the TRV. Acquisition of images should be performed at rest, at each stage of the physical exercise and during the relaxation. The limitation of evaluation of diastolic function during exercise is the fusion of the E and A-wave of mitral inflow in the case of high heart rate, usually above 110 bpm.

In this case, the E-wave should not be measured, but further changes in the TRV can be evaluated. There are a number of different protocols for stress echocardiographic diastolic echocardiography, one of which will be discussed in more detail below [7].

The EU-FP7 MEDIA Group, after analyzing 38 studies assessing diastolic function in during exercise, proposed a clinically useful shortened protocol for testing with the use of a cyclo-ergometer (*Cardiff*-MEDIA protocol). It assumes echocardiographic evaluation at a minimum of three time points — at the beginning of the examination before the beginning of the exercise, when symptoms appear or when the heart rate reaches 100–110 bpm and during rest when the mitral inflow wave separates or after 2 minutes. The initial load on the cyclo-ergometer is 15 W, then increased by 5 W per minute. The pedaling speed should be maintained at 55–65 times per minute. This protocol is presented in Figure 2 [6].

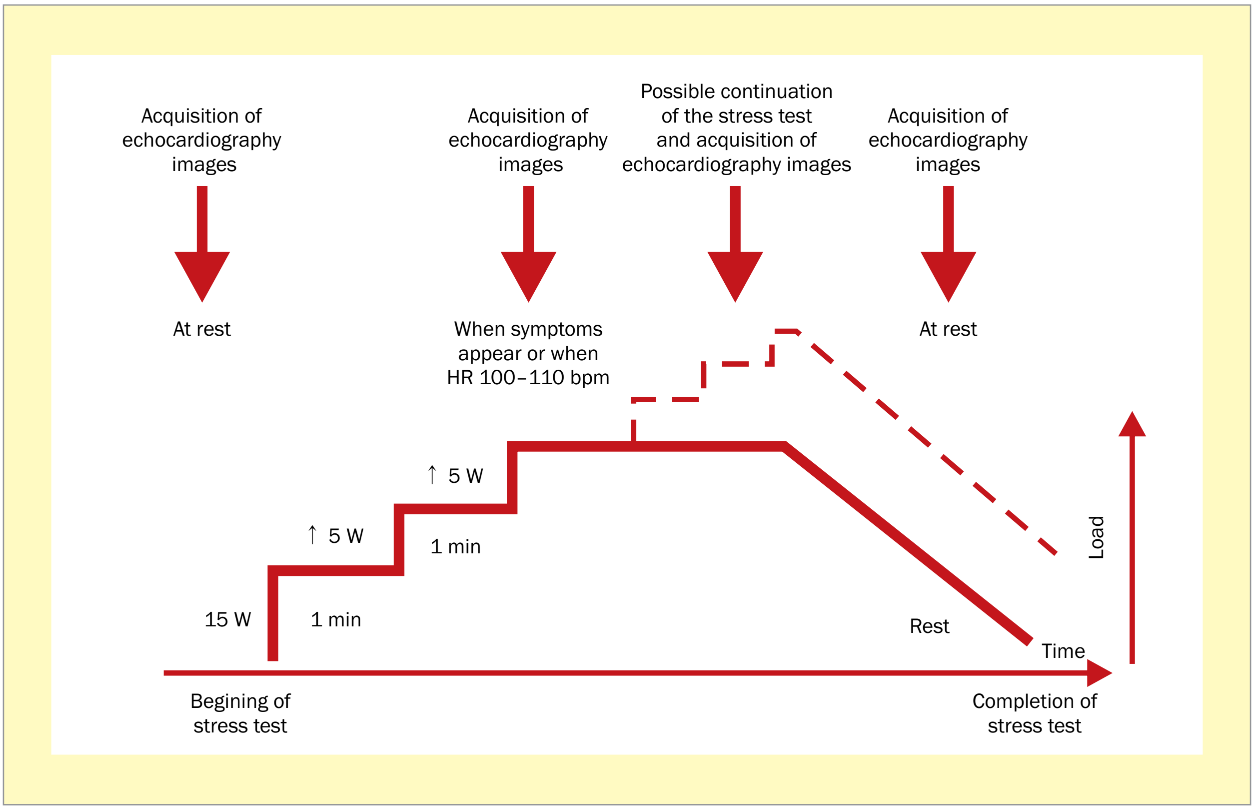
An alternative to the cyclo-ergometer can be a treadmill stress test. Then we acquire echocardiographic images before and after the exercise, during the rest period, after appropriate decrease pulse when the measurement of E wave becomes possible.

Of course, the evaluation of changes in diastolic function parameters during exercise may be a part of an echocardiographic stress test aimed at evaluating other parameters, for example, segmental contractility disorders in the case of suspected coronary artery disease.

Interpretation of echocardiographic diastolic stress test results

When evaluating the results of diastolic exercise echocardiography, we primarily evaluate the E/e' ratio and TRV, *i.e.* the parameters that tell us about the left ventricular filling pressure and its effect on pulmonary circulation, in the when symptoms appear or at the peak of effort and during rest.

According to the American Society for Echocardiography and the European Cardiovascular Imaging Association guidelines from 2016, an abnormal result indicating stress impairment of the diastolic reserve is considered to be an increase in the ratio of the E wave to the mean value of the e' > 14 wave or an increase in the ratio of E wave to e' med wave > 15 with an increase in TRV > 2.8 m/s, if reduced myocardial velocities were detected at rest (e' med value < 7 cm/s or e' wavelengths < 10 cm/s). E/e' (averaged or medial) < 10 with peak rate of tricuspid regurgitation < 2.8 m/s in the effort is considered to be a normal result. In other cases, the test result is undiagnostic. In such cases, the authors of the guidelines suggest possible invasive tests to assess the left ventricular filling pressure. The interpretation of echocardiography diastolic stress test is summarized in Table 3.



Rycina 3. Cardiff-MEDIA echocardiographic diastolic stress test protocol

Table 3. The way of interpreting results of diastolic exercise echocardiography proposed by the American Society of Echocardiography and the European Association of Cardiovascular Imaging from 2016

Parameter	Normal result (both conditions must be fulfilled together)	Undiagnostic result	Abnormal result* (both conditions must be fulfilled together)
E/e' (or E/e' med)	< 10 (10)	10–14 (15)	> 14 (15)
TRV [m/s]	< 2.8	Any	> 2.8

*In addition, in a resting test, the speed of e' med < 7 cm/s or, if only e' lat has been registered, it must be < 10 cm/s; E — early diastolic velocity of mitral inflow wave; e' — averaged value of early diastolic lateral and medial mitral ring velocity; e' med — value of early diastolic velocity of the medial part of the mitral ring (used for interpretation when the velocity of both parts of the mitral ring cannot be measured); e' lat — value of early diastolic lateral velocity of the mitral ring; TRV — maximum tricuspid regurgitation wave velocity expressed in meters per second

It is worth mentioning that the above interpretation of the results and the proposed cut-off points were not widely validated. Some studies have shown that the E/e' ratio above 13 is associated with worse exercise tolerance and has a high prognostic value for the detection of ischemic heart disease [8, 4]. Perhaps, the heart failure guidelines consider E/e' ratio ≥13 [5] to be abnormal.

Summary

The evaluation of left ventricular diastolic function at rest is an integral part of echocardiography. If first degree of diastolic dysfunction is found in the resting examination, or if there is a large clinical suspicion of heart failure and the previous examination does not give us the final diagnosis, it is worth to refer the patient to the echocardiographic diastolic stress test. This is usually done on a cyclo-ergometer, less frequently with the use of a treadmill. There are many possible test protocols. Cardiff-MEDIA protocol with at least 3 echocardiographic image acquisitions is one of the easier and more useful ones and is discussed above. In the exercise we evaluate the E/e' ratio, which indicates the pressure in the left ventricle during exercise and the maximum velocity of the return wave passing through the tricuspid valve, which indirectly tells us about the influence of elevation of this pressure on pulmonary circulation pressure. Abnormal values of both of these parameters at lowered myocardial velocities at rest indicate diastolic dysfunction with increased left ventricular filling pressure and increased left atrial pressure during the exercise.

Streszczenie

Zaburzenia funkcji rozkurczowej lewej komory mogą tłumaczyć objawy niewydolności serca, jeśli prowadzą do podwyższonego ciśnienia w lewym przedsionku. Funkcja rozkurczowa zmienia się dynamicznie między innymi pod wpływem wysiłku fizycznego. Z tego powodu w spoczynkowym badaniu echokardiograficznym możemy nie stwierdzić zaburzeń funkcji rozkurczowej tłumaczącej objawy niewydolności serca. W artykule zostały zaprezentowane metody oceny funkcji rozkurczowej w spoczynkowym badaniu echokardiograficznym, wskazania do echokardiograficznej rozkurczowej próby wysiłkowej, protokoły jej wykonania i sposób interpretacji wyników

Słowa kluczowe: echokardiografia, rozkurcz, próba wysiłkowa, dysfunkcja rozkurczowa, niewydolność serca

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