Serezhina E.K., Obrezan A.G.
International Medical Center "SOGAZ", St. Petersburg, Russia

The Valsalva load test and spectral tracking echocardiography effectiveness in the diagnosis of heart failure with preserved left ventricular ejection fraction

Aim To determine the applicability of speckle-tracking EchoCG (STE) and the Valsalva maneuver for diagnosis of heart failure with preserved left ventricular ejection fraction (CHFpEF).

Material and methods Transthoracic STE with simultaneous electrocardiogram (ECG) recording was performed for patients with CHFpEF and healthy sex- and age-matched subjects (control group) at rest and during the Valsalva maneuver. The study was conducted in compliance with standards of Good Clinical Practice and principles of the Helsinki Declaration. The study protocol was approved by the Ethical Committee of the St. Petersburg State University.

Results During the Valsalva maneuver, deviations of both global and segmental myocardial strain were more pronounced than at rest. In patients of the study group performing the Valsalva maneuver, LV end-diastolic volume and LV end-systolic volume (99%) were increased. Heart rate was considerably reduced (significance of difference >99%) in patients with CHFpEF during the Valsalva maneuver compared to the control group. The increased predictive value of these parameters during the Valsalva maneuver can justify the inclusion of this method in early detection and prognostic assessment of CHFpEF.

Conclusion Speckle-tracking EchoCG with the Valsalva maneuver is a noninvasive, generally available, and easily reproducible outpatient method for diagnosis of CHFpEF.

Keywords Heart failure; speckle-tracking echocardiography; dynamometric test; lead

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Corresponding author Serezhina E.K. E-mail: zlotnikova.elena.konst@gmail.com

Introduction

Considering the increasing incidence of heart failure (HF), particularly heart failure with preserved ejection fraction (HFpEF), it is vital to establish the diagnostic criteria for this disease. There is no agreement between the American and European cardiac communities on this subject. The American experts use only symptoms and signs of HF in patients with normal left ventricular ejection fraction (LVEF) and do not take into consideration echocardiography derived hemodynamically significant valve pathology and other HF triggers to confirm HF, and the European community insists on confirming left ventricular (LV) diastolic dysfunction to make the diagnosis [1, 2]. Catheterization of heart chambers is currently the gold standard for identifying this condition, however, this intervention can only be performed by highly experienced professionals using expensive equipment. Furthermore, the repeatability of the procedure is insufficient and risk-benefit ratio is high. The use of cardiac chamber catheterization is limited in the outpatient setting. Thus, it is vital to seek for novel diagnostic techniques and criteria easily reproducible in the outpatient setting for the assessment of cardiac function [3].

The active development of spectral tracking echocardiography (STE) in recent years has enabled quantitative and qualitative segmental evaluation of systolic and diastolic myocardial function. This diagnostic approach has several advantages, including good reproducibility, high accuracy, ease of outpatient use, non-invasiveness, and angular independence of the ultrasound window [4, 5].

Given that LV diastolic dysfunction in patients with HFpEF can only be identified during exercise stress tests, diagnosis of this condition in the outpatient setting is difficult [6]. These include frequent limited physical activity, the need for special expensive equipment, heart chamber artifacts on the echocardiography and electrocardiogram (ECG), which make assessing the obtained data difficult [4], and the absence of a trigger during the function testing.

A Valsalva maneuver, a stress test that displays compensatory elasticity of the myocardium necessary for the implementation of cardiac relaxation function, which defines the diastolic component of HF, may be used to overcome these constraints.

This test was first described by Antonio Maria Valsalva in 1704, who used it to increase the intrathoracic pressure to evaluate the hemodynamic response to changes in intrathoracic pressure. It was previously established that the effect of intrathoracic pressure on left and right ventricular functions was determined simultaneously, not separately. Modern invasive methods allow directly measuring the pressure in each ventricle individually, and emerging imaging techniques can detect changes in pressure indirectly in a particular heart chamber.

Let us analyze the natural changes in blood pressure (BP) and heart rate (HR) deviations from the initial levels during the Valsalva maneuver in accordance with the four clearly defined phases (I–IV).

Phase I takes place in the first 2–3 seconds of the test and is characterized by a short-term increase in blood pressure and mild bradycardia due to elevated intrathoracic pressure, which takes blood to the periphery.

Phase II is divided into early and late. During early phase II, blood pressure progressively decreases due to reduced venous return and lower cardiac output. This drop in pressure inhibits the baroreflex, which increases sympathetic activity and, as a result, causes tachycardia and blood vessel narrowing, leading to increased peripheral resistance and blood pressure. This response corresponds to late phase II and is highly dependent on the activation of alpha adrenoceptors.

Phase III begins at the end of exhalation and lasts 1–2 seconds with a simultaneous increase in venous return due to an acute decrease in intrathoracic pressure. Furthermore, BP drops due to dilatation of the chest vessels causing a reflex rise of HR.

Higher venous return leads to increased diastolic ventricular filling. According to the Frank-Starling law, a larger preload increases systolic volume and cardiac output. Since peripheral resistance remains high due to prolonged vasoconstriction, BP rises significantly, which characterizes phase IV. It depends on beta-adrenergic stimulation rather than vasoconstriction, which creates higher activation of baroreceptors resulting in substantial vagal bradycardia and vasodilation. Meanwhile, blood pressure progressively falls, although it remains elevated for some time, partly due to the release of circulating catecholamines [7].

Moreover, patients with diastolic dysfunction of the myocardium in phase I have larger stroke volume and elevated BP, which persists in phase II, then there is a drop in BP characteristic of phase III, but no excessive increase in phase IV. Relative tachycardia of phase II and bradycardia characteristic of phase IV are also not observed in this group. In this regard, the pressure curve has is of rectangular form [8].

Thus, the Valsalva maneuver is a safe, non-invasive, easy to use approach to the diagnosis of myocardial diastolic dysfunction, adjusted to human physiology and reproducible in the outpatient setting. Numerous studies completed since the 1980s have confirmed both the diagnostic and prognostic significance of this test in patients with HF [9–11].

It should be highlighted that this test is rather informative and useful during myocardial tissue Doppler imaging. The Valsalva maneuver reduces LV preload, which has a significant effect on the cardiovascular system. Our findings support the use of quantitative assessment of the LV myocardial strain properties under the effect of isometric load during the Valsalva test for the early detection of HFpEF.

Objective

Assess the applicability of spectral tracking echocardiography and the Valsalva maneuver for the diagnosis of HFpEF.

Material and Methods

The study group included 43 patients with HFpEF verified using the ESC criteria. Exclusion criteria were LVEF < 50%, atrial fibrillation and atrial flutter, atrioventricular conduction disorders, pacemaker or implanted cardioverter-defibrillator, valve abnormalities with stenosis and/or regurgitation higher than grade 1, minor cardiac abnormalities, prognostically significant comorbidities (thyroid dysfunction, musculoskeletal disorders of upper extremities).

The control group consisted of healthy individuals and comparable with the study group in the sex and age composition.

Data were collected after a 10-minute period of rest in the supine position. HR was monitored throughout the study using standard three-lead ECG on a VIVID IQ system (GE, USA). BP was measured at rest and in the first minute after stopping the exercise using a mechanical tonometer (Riester, Germany). The Valsalva maneuver was conducted using a clock-like pressure gauge calibrated with mercury sphygmomanometer, which could display positive pressure values and was connected to a disposable mouthpiece. The patient was instructed to maintain the pressure in the above-described system at 40 mm Hg. The test was performed at the indicated pressure (phase I and phase II) for 15 cardiac cycles (approximately 10 s), which was consistent with the tests applied in the previous studies [12–14]. After cycle 15 (at the beginning of phase III), the recording began after a signal to the subject and lasted until cardiac cycle 25. An independent observer recorded all cardiac cycles by counting the number of contractions on the echocardiography in real time. All subjects were instructed to perform each maneuver several times to get adjusted. Transthoracic echocardiography was performed on a Vivid IQ (GE, USA) device during the test. Three consecutive cardiac cycles were registered in four-, three-, and two-chamber views at rest and during the test. The same frame rate was used for each time for the subsequent analysis of STE findings. All data was stored in electronic version. All parameters were measured following the current guidelines [15]. Endocardial and epicardial boundaries were manually marked at the end systole and end diastole to calculate the strain parameters. The strain was calculated automatically for each myocardial segment, and the mean value was calculated for the three axes to determine LV global longitudinal strain (GLS). It should be reminded that myocardium shortens during systole, which produces negative strain values. Absolute strain values are used for the comparison. The levels of HF biomarkers in venous blood were determined in the subjects.

The data obtained were processed using Microsoft Office Exel. The hypothesis about the normality of distribution of the studied indicators was preliminary tested using Pearson's test to justify the possibility of using parametric criteria, such as the Student's t-test to verify the significance of differences between the means, and the Fisher's exact test used in a univariate analysis of variance (ANOVA). Continuous values are expressed as M ± SE, where M is the mean, and SE is the standard error, or M ± SD, where M is the mean and SD is the standard deviation. ANOVA was used to assess the significance of differences of quantitative parameters in patients with HFpEF and the control subjects. The differences were statistically significant with $p < 0.05$.

Results

Clinical characteristics of patients with HFpEF and the control subjects are presented in Table 1.

All patients underwent spectral tracking echocardiography at rest and during the Valsalva maneuver. The results are summarized in Table 2.

The deviations of myocardial strain were more obvious when measured during stress test. The increased prognostic significance of these parameters measured after the Valsalva maneuver makes it possible to include this examination in the early diagnosis and prognosis of HFpEF.

Statistically significant decrease in the following strain indicators was observed in patients with HFpEF after the test compared to the resting state: total global longitudinal strain (GLS average), global longitudinal strain in the 2D view, global longitudinal strain in the LAX view, in segments BP, MP, MI, BAS, MAS, for the MA and BA segments. The involved segments are located in the blood supply zones of the left anterior descending and circumflex arteries. Such indicators as left ventricular end-diastolic volume (LVEDV) and left ventricular end-systolic volume (LVESV) increased during the Valsalva maneuver in the study group. At the same time, there was a statistically significant increase in HR during phase III of the test.

The diagnostic significance of the test is confirmed by the statistically significant differences in patients with HFpEF and the control subjects. Differences in global longitudinal strain in the LAX view, the AS and BA segments, as well as BAS, MS and MA, and for the MAS segment, were

Table 1. Comparative characteristics of baseline data of subjects with HFpEF and the control group

Parameter	HFpEF group, n = 43	Control group, n = 39	p
Age, years	65.3 ± 8.36	50.3 ± 13.24	< 0.001
Female, n (%)	21 (48)	21 (54)	< 0.001
Body mass index, kg/m²	27.6 ± 4.46	25.8 ± 4.76	< 0.084
Arterial hypertension, n (%)	9 (20)	7 (18)	< 0.001
Edema, n (%)	15 (35)	6 (15)	< 0.001
CAD, n (%)	8 (19)	3 (8)	< 0.001
Absence of CHF, n (%)	0	39 (100)	< 0.001
CHF NYHA FC I, n (%)	13 (30)	0	< 0.001
CHF NYHA FC II, n (%)	2 (5)	0	< 0.001
HR, bpm	63.29 ± 1.76	68.17 ± 1.4	< 0.001
NT-proBNP, pg/mL	147.92 ± 35.3	0.244 ± 0.1	< 0.022
Echocardiographic parameters			
LVEF, %	56.23 ± 5.49	56.79 ± 5.16	< 0.565
LVEDV, mL	93.07 ± 28.42	89.49 ± 26.86	< 0.474
LVESV, mL	43.8 ± 19.23	40.97 ± 14.70	< 0.467
LA volume index, mL/m²	17.15 ± 5.18	15.94 ± 3.86	< 0.243
LA /BSA	18 ± 2.3	16.73 ± 1.8	< 0.009
LVM index, g/m²	101.91 ± 27.75	80.74 ± 17.35	< 0.001
E, m/s	0.69 ± 0.18	0.74 ± 0.16	< 0.237
A, m/s	0.73 ± 0.19	0.65 ± 0.15	< 0.156
E/A, %	1.04 ± 0.44	1.2 ± 0.35	< 0.069
DT, s	204.7 ± 82.03	185.97 ± 43.6	< 0.248
e'sept, m/s	0.07 ± 0.02	0.1 ± 0.02	< 0.001
e'lat, m/s	0.08 ± 0.03	0.13 ± 0.03	< 0.001
E/e', %	9.3 ± 2.66	6.67 ± 1.66	< 0.001
GLS, %	19.1 ± 2.84	20.2 ± 2.79	< 0.121

The data are presented as the means and standard deviations or the absolute numbers and percentages. NT-proBNP, N-terminal pro-brain natriuretic peptide; LVEF, left ventricular ejection fraction; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; LA, left atrium; BSA, body surface area; LVM, left ventricular mass; E, peak transmitral flow velocity in rapid filling phase; A, peak transmitral flow velocity in the atrial systole phase; e'sept and e'lat, early septal and lateral velocities at the mitral valve base.

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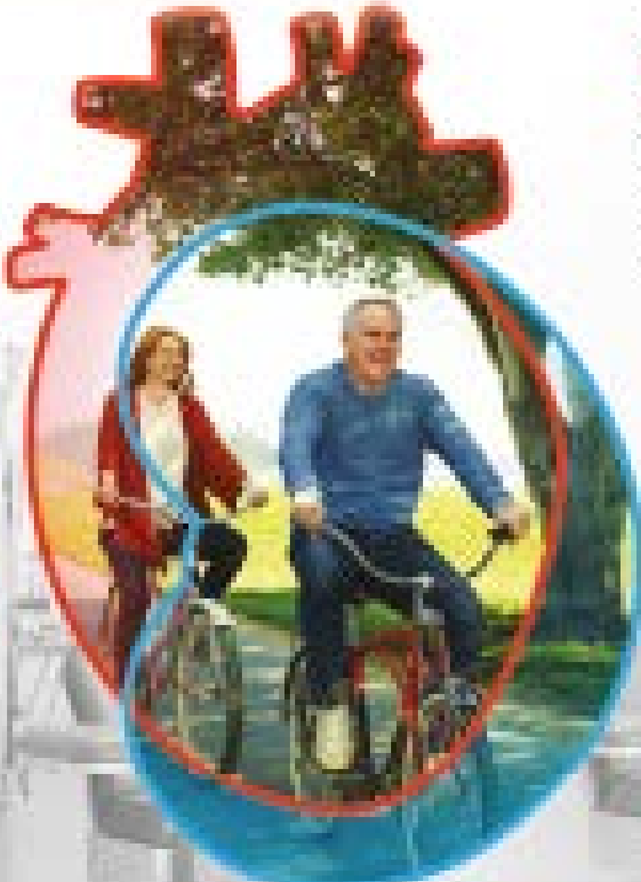

У пациентов с ХБП*

ФОРСИГА – ЕДИНСТВЕННЫЙ* ПРЕПАРАТ, ДОКАЗАВШИЙ ЗАМЕДЛЕНИЕ** ПРОГРЕССИРОВАНИЯ ХБП НА 39%[1,4]

39%

Table 2. Parameters of longitudinal strain by segments at rest and during the Valsalva maneuver in patients with HFpEF and the control subjects

Parameter	At rest		p	During the test		p
	HFpEF group	Control group		HFpEF group	Control group	
GLS average	19.18 ± 0.42	20.16 ± 0.45	0.122	17.96 ± 0.42	18.87 ± 0.56	0.061
GLS 2 CH	17.96 ± 0.56	19.3 ± 0.57	0.102	16.32 ± 0.53	17.7 ± 0.61	0.022
GLS 4 CH	19.62 ± 0.56	20.93 ± 0.51	0.090	21.35 ± 2.17	19.45 ± 0.68	0.621
GLS lax	19.58 ± 0.54	20.35 ± 0.59	0.339	18.28 ± 0.68	19.8 ± 0.67	0.180
BS	15.91 ± 0.56	16.33 ± 0.66	0.623	14.69 ± 0.63	15.97 ± 0.58	0.591
MS	19.27 ± 0.65	20.59 ± 0.54	0.132	18.29 ± 0.63	19.38 ± 0.61	0.812
AS	26.82 ± 2.79	25.49 ± 0.76	0.666	22.51 ± 0.85	24.2 ± 0.89	0.493
BL	16.73 ± 0.8	17.33 ± 0.63	0.571	15.93 ± 0.9	16.15 ± 0.67	0.292
ML	23.22 ± 3.89	20.3 ± 0.58	0.492	19.4 ± 0.68	19 ± 0.86	0.112
AL	22.98 ± 0.91	24.72 ± 0.73	0.149	23.18 ± 0.77	23.87 ± 0.99	0.111
BI	18.58 ± 0.48	17.77 ± 0.87	0.412	15.49 ± 0.9	15.87 ± 0.89	0.332
MI	19.53 ± 0.59	19.46 ± 0.77	0.940	16.8 ± 0.86	17.64 ± 0.78	0.011
AI	21.78 ± 0.99	23.54 ± 0.77	0.175	19.56 ± 0.86	20.69 ± 0.95	0.022
BA	12.07 ± 0.73	14.54 ± 0.94	0.037	11.09 ± 0.88	13.49 ± 0.97	0.410
MA	15.96 ± 0.93	18.92 ± 0.8	0.019	13.9 ± 0.97	17.18 ± 0.78	0.051
AA	21.38 ± 1.16	24.39 ± 0.8	0.037	18.6 ± 1.1	21.67 ± 1.03	0.038
BP	17.53 ± 0.69	17.12 ± 0.92	0.721	16.76 ± 0.99	15.4 ± 0.92	0.021
MP	18.71 ± 0.64	19.51 ± 0.67	0.394	17.78 ± 0.9	17.79 ± 0.77	0.011
AP	22.16 ± 0.89	25.23 ± 0.8	0.013	21.27 ± 0.86	23.77 ± 0.83	0.010
BAS	16.93 ± 0.58	17.02 ± 0.79	0.921	15.04 ± 0.73	16.64 ± 0.77	0.771
MAS	20.8 ± 0.66	21.15 ± 0.82	0.736	18.56 ± 0.71	20.64 ± 0.78	0.262
AAS	24.44 ± 1.64	25.18 ± 0.86	0.731	21.78 ± 0.88	24.2 ± 0.98	0.051
HR, bpm	63.29 ± 1.76	68.17 ± 1.4	0.036	77.42 ± 1.6	83.53 ± 1.7	0.011
LVEF, %	56.11 ± 0.83	56.79 ± 0.83	0.563	52.13 ± 1.06	55.51 ± 1.18	0.771

The data are presented as the means ± standard errors. GLS average, total global longitudinal strain, GLS 2 CH, longitudinal strain measured in two-chamber view; GLS 4 CH, longitudinal strain measured in four-chamber view, GLS lax, longitudinal strain measured in three-chamber view. Segments: BS, basal septal; MS, median septal; AS, apical septal; BL, basal lateral; ML, median lateral; AL, apical lateral; BI, basal inferior; MI, median inferior; AI, apical inferior; BA, basal anterior; MA; median anterior; AA, apical anterior; BP, basal posterior; MP, median posterior; AP, apical posterior; BAS, basal anterior septal; MAS, median anterior septal; AAS, apical anterior septal.

statistically significant in patients with HFpEF. It should also be noted that patients with HFpEF had a statistically significant increase in such indicators as LVEDV and LVESV compared to the control group. Our data on changes in LVEDV and LVESV are consistent with the findings of Zema et al. [9].

In our study, there was a statistically significant decrease in HR during the Valsalva maneuver in patients with HFpEF compared to the control subjects.

Conclusion

The benefits of assessing left ventricular global longitudinal strain with spectral tracking echocardiography include good reproducibility, accuracy, angular independence, non-invasiveness, and availability in the outpatient setting, which is important for the early diagnosis of heart failure with preserved ejection fraction. It is appropriate to carry out a test that would allow a more accurate assessment of myocardial systolic and diastolic function for the early diagnosis of this pathology. Our study demonstrated the efficacy of the Valsalva maneuver in detecting heart failure with preserved ejection fraction. Patients with heart failure with preserved ejection fraction have heterogeneous changes in the left ventricular global longitudinal strain during this test, and the absolute change of the left ventricular global longitudinal strain is greater in such patients than in the control subjects. In addition to measuring left ventricular global longitudinal strain, special attention should be paid to segmental analysis of strain parameters, which, unlike total left ventricular global longitudinal strain, allows identifying more differences between patients with heart failure with preserved ejection fraction and the control subjects and assuming impaired perfusion in a particular zone of coronary circulation.

No conflict of interest is reported.

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