Usefulness of the Evaluation of Left Ventricular Diastolic Function Changes During Stress Echocardiography in Predicting Exercise Capacity in Patients with Ischemic Heart Failure

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Background: Diastolic dysfunction and elevated left ventricular (LV) filling pressure at rest are key factors of exercise intolerance in patients with heart failure (HF). There are few studies, however, that have addressed the issue of changes of LV diastolic function and filling pressure during exercise in patients with HF with severe systolic dysfunction. The ratio of early diastolic velocity of mitral inflow (E) and early myocardial diastolic velocity (E′) strongly correlates with invasively obtained LV filling pressure.

Objective: We sought to assess dynamic changes of diastolic function, including LV filling pressure using Doppler tissue imaging, during stress echocardiography and its impact on exercise capacity in patients with ischemic HF.

Methods: We studied 50 adult patients (44 male and 6 female) with a mean age of 62.9 $\pm$ 8.8 (46-79) years, mean New York Heart Association class of 1.97 $\pm$ 0.86, and mean ejection fraction of 28.4 $\pm$ 9.5 (10%-45%). The following conventional and tissue Doppler parameters were measured at baseline and peak exercise during semisupine stress echocardiography (20 W, 2-minute increments): peak early (E) and late (A) diastolic velocity of the mitral inflow, E/A ratio, peak early myocardial diastolic velocity (E′), and E/E′ ratio. Diastolic Doppler tissue imaging indices were derived from septal, lateral, anterior, and inferior border of the mitral annulus in the apical 4- and 2-chamber views. Simultaneously during stress echocardiography peak oxygen uptake was measured. Patients were divided into two groups according to peak oxygen uptake value: group 1 with 23 patients (<14 mL/kg/min) and group 2 with 27 patients (≥14 mL/kg/min).

Results: There were significant differences in terms of E′ and E/E′ ratios both at rest and peak exercise between the two groups. The best correlation with exercise capacity was E/E′ at peak stress ($r = -0.75$, $P < .0001$). The most useful parameter for identifying severe exercise intolerance, as indicated by peak oxygen uptake less than 14 mL/kg/min, was E/E′ at peak stress with an area under receiver operating characteristic curve of 0.92. The cut-off of 18.2 for E/E′ at peak stress showed a sensitivity of 85.2% with a specificity of 95.6%.

Conclusions: The evaluation of hemodynamic response of diastolic function, including LV filling pressure, during exercise is feasible during stress echocardiography and provides valuable information in predicting exercise capacity in patients with ischemic HF.

Keywords: Heart failure, Stress echocardiography, Filling pressure, Exercise capacity

The hallmark of heart failure (HF) is impaired exercise tolerance. The pathophysiology of functional impairment is complex and includes dysfunction of the heart itself (central mechanism) but associated changes in peripheral factors, such as abnormalities in skeletal muscle morphology and metabolism, ergoreflex activation, abnormalities in blood flow, and endothelial dysfunction also play a significant role.[1-3] Both systolic and diastolic dysfunction contribute to low exercise capacity in HF. Virtually all patients with depressed left ventricle (LV) systolic function have diastolic dysfunction.[1] Reduced ventricular compliance and inappropriately elevated filling pressure are important causes of dyspnea on exertion and early termination of exercise.[4] The combination of conventional Doppler early diastolic velocity of the mitral inflow (E) and early myocardial diastolic velocity (E′) from the mitral annulus by Doppler tissue imaging (DTI) technique has previously shown the best relationship with invasively obtained LV filling pressure.[5,6] This study was designed to evaluate diastolic function, including noninvasive estimation of LV filling pressure using E/E′ ratio, both at rest and peak stress and to assess its impact on exercise tolerance in patients with HF and severely depressed LV systolic function.

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Table 1 Baseline clinical characteristics

Parameters	All patients (n = 50)	VO_2peak < 14 mL/kg/min (n = 23)	VO_2peak ≥ 14 mL/kg/min (n = 27)	*P* value
Age (y)	62.9 ± 8.9	63.1 ± 9.8	62.5 ± 8.1	NS
Women/men	6/44	4/19	2/25	
Height (cm)	170 ± 7.2	169.8 ± 8.2	171.6 ± 6.5	NS
Weight (kg)	78.7 ± 15.5	79.6 ± 14.9	76.6 ± 14.9	NS
BMI (kg/m^2)	28.7 ± 3.4	28.9 ± 3.9	27.9 ± 4.3	NS
NYHA class	1.98 ± 0.86	2.5 ± 0.8	1.52 ± 0.65	.0001
Hypertension	36 (72%)	17	19	NS
Diabetes mellitus	13 (26%)	7	6	NS
Dyslipidemia	45 (90%)	21	24	NS
Myocardial infarction	43 (86%)	20	23	NS
PCI	24 (48%)	9	15	.05
CABG	12 (24%)	5	7	NS
Hemoglobin (g/dL)	14.3 ± 1.2	14.08 ± 1.36	14.5 ± 1.02	NS
Creatinine (μmol/L)	97.8 ± 33.2	106.1 ± 38.9	89.9 ± 26.8	NS
CRP (mg/L)	4.12 ± 4.14	4.83 ± 4.65	3.01 ± 3.14	NS
NT-proBNP (pg/mL)	421.5 ± 320.8	525.2 ± 336.9	367.4 ± 246.8	NS
Aspirin	48 (96%)	22	26	NS
Beta-blocker	45 (90%)	20	25	NS
ACE inhibitor	46 (92%)	21	25	NS
ARB	3 (6%)	1	2	NS
Furosemide	31 (62%)	15	16	NS
Spironolactone	39 (78%)	17	22	NS
Statin	41 (82%)	18	23	NS

ACE, Angiotensin-converting enzyme inhibitor; *ARB*, angiotensin receptor blocker; *BMI*, body mass index; *CABG*, coronary artery bypass graft; *CRP*, C-reactive protein; *NS*, not significant; *NT-proBNP*, plasma N-terminal probrain natriuretic peptide; *NYHA*, New York Heart Association; *PCI*, percutaneous coronary intervention; *VO_2peak*, peak oxygen uptake.

Table 2 Hemodynamic, cardiopulmonary, and conventional Doppler parameters at rest and peak exercise

Parameters	All patients (n = 50)	VO_2peak < 14 mL/kg/min (n = 23)	VO_2peak ≥ 14 mL/kg/min (n = 27)	*P* value
Load (W)	65.2 ± 23.3	50 ± 14.5	78.1 ± 21.7	.00001
Heart rate rest (beats/min)	73 ± 14	75 ± 17	71 ± 11	NS
Heart rate stress (beats/min)	111 ± 19	107 ± 21	114 ± 17	NS
Systolic BP rest (mm Hg)	112 ± 11	108 ± 16	116 ± 19	NS
Systolic BP stress (mm Hg)	142 ± 32	139 ± 36	147 ± 27	NS
VO_2peak (mL/kg/min)	14.66 ± 4.6	10.64 ± 2.01	18.08 ± 3.3	.00001
VO_2peak (%N)	55.7 ± 11.9	40.6 ± 11.3	70.4 ± 14.1	.00001
AT (mL/kg/min)	10.6 ± 3.6	9.3 ± 2.8	12.6 ± 3.3	.004
VE/CO_2	34.9 ± 4.3	39.7 ± 8.4	32.1 ± 5.9	.002
RER	1.15 ± 0.33	1.18 ± 0.35	1.14 ± 0.27	NS
LVEF rest (%)	28.4 ± 9.5	26.2 ± 8.6	30.6 ± 10.1	.09
LVEF stress (%)	31 ± 13.3	27.3 ± 11.9	33.7 ± 13.8	.08
E velocity rest (m/s)	0.71 ± 0.28	0.75 ± 0.21	0.68 ± 0.33	NS
E velocity stress (m/s)	0.94 ± 0.22	0.97 ± 0.21	0.92 ± 0.24	NS
DT rest (ms)	166 ± 58	156 ± 51	170 ± 62	NS
DT stress (ms)	101 ± 45	100 ± 32	104 ± 54	NS
A velocity rest (m/s)	0.54 ± 0.23	0.55 ± 0.27	0.53 ± 0.21	NS
A velocity stress (m/s)	0.62 ± 0.28	0.54 ± 0.24	0.67 ± 0.31	NS
E/A ratio rest	1.77 ± 1.5	1.99 ± 1.3	1.64 ± 1.3	NS
E/A ratio stress	1.86 ± 1.04	2.14 ± 1.27	1.68 ± 0.78	NS

A, Late diastolic mitral velocity; *AT*, anaerobic threshold; *BP*, blood pressure; *DT*, deceleration time; *E*, early diastolic mitral velocity; *LVEF*, left ventricle ejection fraction; *NS*, not significant; *RER*, respiratory exchange ratio; *VE/CO_2*, ventilatory equivalent for carbon dioxide; *VO_2peak*, peak oxygen uptake; *VO_2peak (%N)*, percentage of predicted maximal exercise oxygen consumption related to age and sex.

MATERIALS AND METHODS

Study Population

Our institutional review board approved the protocol and all patients gave written informed consent to participate in the study. The study group consisted of 50 consecutive patients with chronic, stable HF with the capability to perform the exercise test, referred to our echocardiography laboratory for a period of 9 months. HF was diagnosed according to the criteria proposed recently by the European Society of Cardiology.[1] Clinical stability meant that there were no hospitalizations required as a result of worsening of HF and there were no changes in medication