Association of Exercise Tolerance with Effective Arterial Elastance Obtained Noninvasively in Patients with Exertional Dyspnea

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Background: Ventricular-arterial stiffening is a part of the aging process that is amplified by various comorbidities. It affects normal cardiovascular reserve and limits exercise capacity. The aim of this study was to explore the association of physiologic determinants of ventricular-arterial interaction with exercise capacity in patients referred for exercise echocardiography with exertional dyspnea.

Methods: A total of 93 patients with exertional dyspnea without chest pain were evaluated using the Bruce protocol. Patients with left ventricular ejection fractions < 50% and those with exercise-induced myocardial ischemia were excluded. Poor exercise tolerance was defined as inability to achieve 8 metabolic equivalents.

Results: Thirty-seven patients (40%) had poor exercise tolerance. These patients were older (mean age, 60 vs 54 years, $P = .01$), more likely to carry the diagnosis of hypertension (84% vs 41%, $P < .01$), and more likely to be treated with antihypertensive medications. In multivariate logistic regression analysis, left atrial volume index ($P = .04$) and arterial elastance ($P < .01$) were significant predictor of poor exercise capacity, while left ventricular ejection fraction, tissue Doppler indices, and global longitudinal strain were not significant.

Conclusions: Effective arterial elastance determined noninvasively before stress echocardiography appears to be an independent predictor of exercise tolerance in patients with exertional dyspnea. (J Am Soc Echocardiogr 2014;■:■-■.)

Keywords: Stress testing, Stress echocardiography, Arterial elastance

Prior studies in patients with dyspnea referred for stress testing have consistently demonstrated higher all-cause mortality compared with patients with chest pain, although the rates of ischemia do not appear to be different.[1] Exertional dyspnea is a ubiquitous complaint that can be caused by a variety of clinical conditions, including pulmonary disease, obesity, deconditioning, anemia, and structural heart disease.[2] In patients with preserved left ventricular ejection fractions, the compliance of the left ventricle and the arterial tree plays a major role in maintaining normal cardiovascular reserve.[3] In addition to the markers of diastolic dysfunction and two-dimensional strain, echocardiography allows the noninvasive assessment of the left ventricular pressure-volume relationship, which can potentially provide incremental diagnostic information in this high-risk patient group. The aim of the present study was to investigate the association of physiologic determinants of ventricular-arterial interaction derived noninvasively before exercise echocardiography with exercise capacity in patients referred for exertional dyspnea.

METHODS

Patient Population

This retrospective study involved patients referred for exercise echocardiography with exertional dyspnea without chest pain from August 2008 to March 2012, as previously described.[2] We excluded patients with left ventricular ejection fractions < 50%, severe valvular abnormalities, and exercise-induced myocardial ischemia on echocardiographic imaging. Of 114 patients who underwent exercise echocardiography for exertional dyspnea, 93 qualified for the study and had interpretable image quality. The study was approved by the hospital institutional review board.

Echocardiographic Image Acquisition and Measurements

Transthoracic echocardiographic images were obtained with the patient in the left lateral decubitus position using commercially available ultrasound equipment (Acuson Sequoia, Siemens Medical Solutions USA, Inc, Mountain View, CA; Vivid 7 and 9, GE Healthcare, Wauwatosa, WI). Seven standard echocardiographic views were obtained with each acquisition: parasternal long-axis, parasternal short-axis (at the papillary muscle level), apical four-chamber, apical two-chamber, apical three-chamber, subcostal four-chamber, and

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Abbreviations

Ea = Effective arterial elastance

Ees = Left ventricular end-systolic elastance

ICC = Intraclass correlation coefficient

MET = Metabolic equivalent

subcostal short-axis (at the papillary muscle level) views. Echocardiographic images were acquired at baseline (rest images) and immediately after exercise (postexercise images). Resting echocardiograms were read by an experienced echocardiographer, and left atrial quantification was performed per American Society of Echocardiography guidelines.[4] Left ventricular hypertrophy was defined as left ventricular mass index > 95 g/m^2 for women and >115 g/m^2 for men.[4] End-systolic pressure was estimated as 0.9 × arm-cuff systolic blood pressure.[5] Stroke volume was estimated from the left ventricular outflow tract diameter and the pulsed-wave Doppler signal using the continuity equation.[5,6] Left ventricular ejection fraction was determined using Simpson's biplane planimetry.[4] Effective arterial elastance (Ea) was defined as the ratio of the end-systolic pressure and stroke volume.[7,8] Left ventricular end-systolic elastance (Ees) was determined using a modified single-beat algorithm using arm-cuff blood pressure, Doppler-derived stroke volume, left ventricular ejection fraction, and systolic time intervals.[5] Tricuspid regurgitant jet velocity was obtained from multiple views, and the highest velocity is reported.[9] Valvular disease was defined as moderate stenosis or regurgitation affecting the aortic and mitral valves.[10,11] Left ventricular global longitudinal strain was evaluated at rest using two-dimensional speckle-tracking in standard two-chamber, three-chamber, and four-chamber views (syngo Velocity Vector Imaging software; Siemens Medical Solutions USA, Inc).[12,13]

Exercise Echocardiography

Symptom-limited exercise treadmill testing was performed using the Bruce protocol. Beta-blockers and calcium channel blockers were held the day before the test. The target heart rate was defined as 85% of the patient's age-predicted maximal heart rate. Ischemic electrocardiographic changes were defined as ≥1 mm of horizontal or down-sloping ST-segment depression occurring 80 msec after the J point. The reason for termination in this patient group was limiting symptoms, including fatigue and dyspnea. Postexercise echocardiographic images were acquired within 30 to 60 sec after the termination of treadmill exercise.[2] For the purpose of the study, poor exercise capacity was defined as an inability to achieve 8 metabolic equivalents (METs).[14]

Statistical Analysis

Analysis was performed using a standard statistical package (SPSS for Windows version 16.0; SPSS, Inc, Chicago, IL). Patient groups were compared using Student's *t* test for continuous variables and χ^2 or Fisher's exact tests for categorical variables. The initial multivariate logistic regression model included important potential predictors of exercise capacity as determined by univariate analysis. The final parsimonious multivariate logistic regression model was created by a stepwise backward elimination strategy using goodness-of-fit assessment. Intraobserver and interobserver agreement was determined using intraclass correlation coefficients (ICCs) for left ventricular ejection fraction (by Simpson's biplane planimetry), Ea, and Ees. In a sample of 10 randomly selected patients, intraobserver agreement was excellent for all measures (left ventricular ejection fraction ICC = 0.84, Ea ICC = 0.97, Ees ICC = 0.95), and interobserver agreement was substantial for all measures (left ventricular ejection fraction ICC = 0.79, Ea ICC = 0.76, Ees ICC = 0.79).[15] *P* values < .05 were considered significant.

RESULTS

Patient Characteristics

The study population consisted of 93 patients with exertional dyspnea without chest pain evaluated by exercise echocardiography. Ethnic minorities such as African Americans and Hispanics were prevalent, with Caucasians constituting 10% of the cohort (Table 1). The prevalence of known coronary artery disease with prior acute coronary syndrome or revascularization was low (2%). Thirty-seven patients (40%) had poor exercise tolerance (<8 METs). These patients were older (mean age, 60 vs 54 years; $P = .01$), more likely to carry the diagnosis of hypertension (84% vs 41%, $P < .01$), and more likely to be treated with antihypertensive medications such as diuretics and calcium channel blockers compared with patients with good exercise capacity (Table 1). Although there was a high burden of obesity in the whole cohort, there was no difference in mean body mass index between the groups (31 vs 31 kg/m^2, $P = .98$).

Echocardiographic Characteristics

Left atrial dilation was more common (51% vs 30%, $P = .04$) and the mean tricuspid regurgitant velocity was higher (2.5 vs 2.3 m/sec, $P = .03$) in patients with poor exercise tolerance. Also, both the mean left ventricular ejection fraction (61% vs 66%, $P = .02$) and mean global longitudinal strain (16.5 vs 17.8, $P = .04$) were lower in these patients. There were no statistically significant differences in the left ventricular end-diastolic volume indices and the tissue velocity measures of diastolic dysfunction between the groups (Table 2). Patients with poor exercise tolerance had higher resting systolic blood pressures (135 vs 125 mm Hg, $P < .01$) and higher estimated Ea (2.0 vs 1.6 mm Hg/mL, $P < .01$) compared with patients with exercise capacity ≥ 8 METs. Also, they had higher Ees (2.3 vs 1.8 mm Hg/mL, $P < .01$), whereas the Ea/Ees ratio was similar between the groups (0.96 vs 0.97, $P = .84$).

Ea

In multivariate logistic regression analysis adjusted for age among other covariates (hypertension, left atrial volume index, tricuspid regurgitant velocity, left ventricular ejection fraction, global longitudinal strain, and Ees) using a sequential backward elimination strategy, Ea remained a highly significant predictor of poor exercise capacity ($P < .01$). In the final parsimonious model, left atrial volume index also remained a significant predictor ($P < .04$), whereas left ventricular ejection fraction ($P = .68$), global longitudinal strain ($P = .26$), and Ees ($P = .07$) were not significant. Ea showed a linear correlation with exercise capacity in METs ($r = -0.46$, $P < .01$) as shown in Figure 1.

DISCUSSION

Ventricular-arterial stiffening is a part of the aging process that is amplified by various comorbidities, such as hypertension, renal