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Research Article

Patients with hypertensive responses to exercise or dobutamine stress testing differ in resting hypertensive phenotype

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Abstract

Little is known of the importance of echocardiographic measures of resting systemic vascular resistance (SVR), cardiac output, and diastolic function in the development of a hypertensive response during dobutamine stress echocardiography. We performed a retrospective review of 325 subjects who underwent stress echocardiography and a resting echocardiogram on the same day. Logistical regressions were performed to determine associations between hypertensive response to each type of stress test and clinical and hemodynamic measurements obtained by transthoracic echocardiography. Patients with a hypertensive response to dobutamine or exercise stress modalities had Stage 1 hypertension. Those with a hypertensive response to dobutamine had a significantly elevated SVR and a lower cardiac output compared to those with a hypertensive response to exercise or a nonhypertensive response to dobutamine. An SVR $\geq$2000 dynes $\times$ sec/cm^5 showed excellent discrimination between patients who did and did not have a hypertensive response to dobutamine (c = 0.80). A hypertensive response to both stress modalities showed an association with measures of diastolic dysfunction. The hemodynamic and echocardiographic phenotypes of individuals with a hypertensive response to exercise differ from those with a hypertensive response to dobutamine. Further work is necessary to understand and guide antihypertensive therapy when a hypertensive response to stress testing is discovered and to inform choice of stress modality when resting hypertension is present. J Am Soc Hypertens 2017;■(■):1–9. © 2017 American Society of Hypertension. All rights reserved.

Keywords: Cardiac output; hypertension; stress echocardiography; systemic vascular resistance.

Introduction

In patients undergoing cardiac stress testing without known coronary artery disease or significant valvular disease, a hypertensive response to exercise (defined as a systolic blood pressure [SBP] $\geq$190 in women or $\geq$210 mm Hg in men or diastolic blood pressure [DBP] $\geq$110 mm Hg) independently predicts future hypertension and increased risk of adverse cardiovascular events and mortality.[1–5]

To date, little is known about a hypertensive response to dobutamine during stress echocardiography. Dobutamine has β1-cardiac adrenergic receptor agonist activity resulting in increased heart rate and contractility as well as β2-vascular adrenergic receptor activity resulting in vasodilation. Increased inotropy with dobutamine augments cardiac output (CO) by activating a reflexive withdrawal of vascular

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sympathetic tone leading to vasodilation. Prior work suggests that dobutamine infusion achieves similar heart rate and stroke volume augmentation to exercise, but at lower ventricular volumes and with lower blood pressure augmentation, supporting a greater vasodilatory response.[6]

The differences in cardiovascular physiological responses to exercise compared to dobutamine suggest hypertensive responses to these stimuli may relate to different physiological attributes. Prior work reports the hypertensive response to dobutamine is associated with male sex, age, baseline SBP, and atropine use.[7] However, there are no current data relating resting systemic vascular resistance (SVR), CO, or echocardiographic measures of diastolic function to the hypertensive response to dobutamine. The following study is designed to address whether resting systolic and diastolic functions are associated with hypertensive responses during exercise or dobutamine stress echocardiography (DSE). Additionally, we analyzed data from patients who underwent treadmill stress echocardiography (TSE) at our institution during the same study period to examine the contributions of systolic and diastolic function to a hypertensive response to exercise. We then compared the factors most commonly associated with a hypertensive response to each type of stress.

Methods

Subjects

In this retrospective cohort study, we reviewed 413 same-day resting and stress transthoracic echocardiograms (TTEs) completed between 2009 and 2011 at our institution. All stress echocardiograms were ordered to evaluate for cardiac ischemia for one of the following reasons: shortness of breath, palpitations, chest pain, or preoperative risk stratification. All exercise tests were performed following a standard Bruce protocol. Dobutamine stress echocardiograms were performed using a standard protocol that begins with a 10 mcg/kg/min dobutamine dose for 3 minutes, increasing the dose by 10 mcg/kg/min every 3 minutes until 85% of maximal predicted heart rate was achieved or the 50-mcg/kg/min dose was reached. If subjects were not making adequate progress on reaching their heart rate goal by the time the dobutamine dose was increased to 30 mcg/kg/min, 0.25 mg of atropine was administered every minute to a maximal dose of 1.5 mg.

Eighty-four subjects with coronary artery disease, resting left ventricle (LV) ejection fraction less than 50%, resting regional wall motion abnormalities, or inducible ischemia were excluded. An additional four subjects had technically inadequate images for measuring CO and SVR, leaving 181 subjects who underwent TSE and 144 subjects who underwent DSE for analysis. All subjects who were on chronic β-blockade had this medication held for at least 24 hours prior to stress testing.

Extracted Data

Following subject identification, data were extracted from both the stress test and resting TTE study for further analysis. These include subject age; sex; height; weight; body surface area (BSA); resting blood pressure prior to stress testing; peak blood pressure and heart rate responses to exercise; whether atropine was used (DSE only); whether the subject achieved 85% of the maximal predicted heart rate; and whether there was evidence of inducible ischemia. From the resting TTE, we obtained the septal e' peak velocity of the mitral annulus, mitral inflow E wave peak velocity, left atrial volume, indexed left ventricular mass, the left ventricular outflow tract (LVOT) diameter, and the velocity time integral for the LVOT in systole.

Resting arterial elastance (E_a) was calculated using 90% of the resting SBP (to estimate the end-systolic pressure) divided by the stroke volume from the resting TTE. Stroke volume was calculated using LVOT diameter measured in the parasternal long axis view during systole multiplied by the velocity time integral of the LVOT velocity during systole measured in the apical view. As an additional control for body habitus, we calculated the indexed resting E_a by dividing E_a by BSA.[8] Resting CO was calculated by multiplying the resting stroke volume by the resting heart rate. Resting SVR was calculated by dividing resting CO into the difference between the mean arterial pressure (calculated as two times the resting DBP plus resting SBP, all divided by three) and an assumed central venous pressure of 5 mmHg for all subjects. Left ventricular mass was calculated using the Deveraux formula and indexed to BSA. LV mass indices $\geq$95 g/m^2 in women and $\geq$115 g/m^2 in men were considered to be increased.

A hypertensive response to either exercise or dobutamine was a priori defined as a peak SBP was $\geq$190 mmHg in women or $\geq$210 mmHg in men during stress testing.[5] For dobutamine stress testing, note that recently published data categorize a hypertensive response as two or more standard deviations greater than the normative age-stratified means.[7]

Statistical Analyses

Subjects were stratified into two groups: those undergoing DSE and those undergoing TSE. Baseline subject characteristics were compared between groups using unpaired tests or chi-square testing as appropriate for a categorical variable. To determine associations between subject attributes and a hypertensive response to stress testing, we first constructed univariable logistical regression models stratified by stress testing modality. Variables tested included age, sex, resting SBP, resting DBP, resting hypertension, pulse pressure (PP), E_a, E_a/BSA, mitral annular septal e' velocity, mitral inflow peak E wave velocity, mitral E/e' ratio, mitral inflow E/A ratio, LV mass index, left atrial volume, and use of atropine.

Additionally, we created categorical variables to assess the predictive value of known clinical measurements of