Differential Effects of Dobutamine Versus Treadmill Exercise on Left Ventricular Volume and Wall Stress

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Background: Dobutamine and exercise echocardiography are well-validated modalities used for the evaluation of patients with suspected myocardial ischemia. Patients undergoing dobutamine stress echocardiography (DSE), however, experience less angina, ST-segment depressions, and wall motion abnormalities. Other than the effect on heart rate, the physiologic and volumetric differences between pharmacologic and exercise-induced stress that affect myocardial oxygen demand are not well defined. The aim of this study was to test the hypothesis that in the absence of ischemia, dobutamine reduces left ventricular (LV) volume, wall tension (WTN), and peak systolic stress (PSS) compared with exercise.

Methods: Seventy patients without ischemia were prospectively enrolled (35 underwent exercise echocardiography and 35 DSE), and various hemodynamic parameters were measured and LV volumes calculated (using the Simpson and Teichholz formulas). Systolic WTN and PSS were determined at rest and stress.

Results: LV end-diastolic volume index fell significantly more with dobutamine than with exercise (−34% vs −9%, $P < .0001$), as did mean end-systolic volume index (−55% vs −37%, $P = .07$). Systolic blood pressure increased more with exercise (41 ± 22 vs 1 ± 33 mm Hg, $P < .0001$), as did cardiac index (2.5 ± 0.7 vs 1.0 ± 0.8 L/min/m^2, $P < .0001$). Systolic WTN increased with exercise by 24% ($P < .0001$) but decreased with dobutamine by 18% ($P < .0001$). PSS increased with exercise by 21% ($P < .0001$) but decreased with dobutamine by 23% ($P < .0001$).

Conclusions: The degree of stress achieved with DSE appears to be considerably different than with exercise. DSE produces greater reductions in LV end-diastolic and end-systolic volumes than exercise and decreases rather than increases in WTN and PSS. The lower WTN and PSS were related to both a decrease in LV volume and lower systolic blood pressure with dobutamine. These observations support recommendations favoring exercise stress testing in patients able to exercise and reinforce the notion that high-risk echocardiographic features of ischemia such as stress-induced LV dilatation may be less striking or absent with DSE. (J Am Soc Echocardiogr 2012;25:911-8.)

Keywords: Stress echocardiography, Dobutamine, Exercise, Volume, Wall stress

Dobutamine and treadmill echocardiography are two well-validated and widely used stress modalities for the evaluation of myocardial ischemia. These tests are frequently viewed as equivalent at comparable heart rates and are therefore used interchangeably by some. Several prior observations, however, have suggested fundamental differences. Exercise stress has been shown to induce a greater magnitude of ischemia as calculated by the wall motion score compared with dobutamine stress in the same patients with coronary artery disease.[1,2] Moreover, compared with dobutamine stress echocardiography (DSE), patients with coronary artery disease are known to exhibit a higher frequency of angina with more ST-segment deviation during exercise stress.[1-4] The mechanism that causes these commonly observed differences has not been defined. Higher risk echocardiographic features of ischemia such as stress-induced left ventricular (LV) dilatation may also be less striking or absent with DSE. In a study of patients with angiographically defined left main stenosis, the majority of patients who underwent exercise echocardiography (80%) had increases in end-diastolic volume index (EDVI), compared with only 12% undergoing DSE ($P = .0001$).[2]

The purpose of this study was to compare the hemodynamic changes during treadmill and dobutamine stress that may underlie the clinical differences between these two modalities. Specifically, we hypothesized that patients with normal stress echocardiographic results receiving dobutamine would have significantly lower EDVIs and end-systolic volume indexes (ESVIs) at peak stress, resulting in lower peak LV wall tension (WTN) and peak systolic stress (PSS) compared with subjects who exercised on a treadmill.

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Abbreviations

DSE = Dobutamine stress echocardiography

EDVI = End-diastolic volume index

ESVI = End-systolic volume index

LV = Left ventricular

PSS = Peak systolic stress

SVI = Stroke volume index

WTN = Wall tension

METHODS

Patients

Seventy patients referred for stress echocardiography were prospectively enrolled in the study. The choice of stress modality was not randomized and was decided by the ordering clinician. Thirty-five patients underwent stress testing with dobutamine, while the remaining 35 patients exercised on a treadmill. Enrollment occurred at the time of image acquisition during preliminary review of images. Only patients without resting regional or global systolic dysfunction or any stress-induced wall motion abnormalities were included in the study. Those with clinical diagnoses of angina, history of myocardial infarction, or any prior cardiac surgery were also excluded. Participants with histories of percutaneous coronary intervention, however, were not excluded if they remained free from angina or other evidence of ischemia. Patients with more than mild LV hypertrophy (posterior wall thickness $>$ 12 mm), mild valvular heart disease, or systolic anterior motion of the mitral valve were also not enrolled. Patients with advanced liver failure undergoing preoperative evaluation were excluded because of the compensatory physiologic factors related to their underlying illness that may influence the hemodynamic and volumetric parameters bring studied. Baseline clinical characteristics including a comprehensive medical history were recorded for each patient. Only those with technically good quality echocardiographic images and achieving $\geq$85% of their age-predicted maximum heart rates were included in the study. Tests that were prematurely discontinued because of patient request, severe hypertension or hypotension, or arrhythmia were also excluded. This study was approved by our institutional review board.

DSE

Dobutamine was infused intravenously at an initial dose of 10 μg/kg/min. Every 3 min thereafter, the dose was increased to a maximum dose of 50 μg/kg/min. Atropine was administered to those patients who had a blunted chronotropic response to dobutamine or who did not achieve 85% of their maximum predicted heart rates. Atropine was administered concurrently with dobutamine, typically starting at a dobutamine dose of 30 μg/kg/min and repeated up to a maximum dose of 1.5 mg. Echocardiographic images were acquired using a Philips Sonos 5500 (Philips Medical Systems, Andover, MA). Standard two-dimensional images were recorded in the parasternal long-axis, parasternal short-axis, apical four-chamber, apical two-chamber, and apical three-chamber views. When peak heart rate was achieved with dobutamine, images were again recorded in the same standard views. Blood pressure (automated) and heart rate measurements were recorded at baseline and then at 3-min intervals through recovery. Electrocardiographic monitoring and symptom notation were also performed throughout the entire study. Dobutamine infusion was discontinued when the heart rate achieved equaled or exceeded 85% of the age-predicted maximum heart rate or if the maximum doses of dobutamine and atropine had been administered. Withdrawal of medications, including β-blockers, before stress testing was left to the discretion of the referring physician.

Treadmill Echocardiography

Symptom-limited treadmill exercise testing with echocardiography was performed according to the standard Bruce protocol. Echocardiographic images were obtained in the parasternal long-axis, parasternal short-axis, apical four-chamber, apical two-chamber, and apical three-chamber views before exercise. Blood pressure (manual) and heart rate measurements were recorded at baseline and then at 3-min intervals into recovery. Immediately after exercise, echocardiographic images were again recorded in the same standard views. Electrocardiographic recording and symptom notation were also performed throughout the study. Exercise was terminated either at the request of the patient or if the end of the protocol was reached.

Analysis of Echocardiograms

Analysis of echocardiograms was performed by experienced echocardiographers. All measurements and calculations were made at baseline, after peak exercise, or during peak dobutamine infusion offline after patient enrollment. The primary end points of this study were changes in EDVI, ESVI, WTN, and PSS from rest to peak stress. LV end-diastolic and end-systolic dimensions were measured using two-dimensional imaging in the parasternal long-axis view at the level of the mitral valve leaflet tips. LV end-diastolic and end-systolic volumes were calculated according the biplane Simpson's method in the apical four-chamber and apical two-chamber views. LV volumes were also calculated according to the Teichholz formula, which is less affected by apical foreshortening. Stroke volume, cardiac output, ejection fraction, and systemic vascular resistance were calculated using Simpson-derived volumes with appropriate parameters indexed for body surface area. Systemic vascular resistance was calculated assuming a central venous pressure of 5 mm Hg using the following formula:

$$\text{systemic vascular resistance} = \frac{(\text{mean arterial pressure} - \text{central venous pressure}) \times 80}{\text{cardiac output}}.$$

Because peak LV systolic pressure, WTN, and wall stress occur early after QRS onset and not at end-diastole or end-systole,[5] we calculated peak systolic WTN and PSS using one-third dimensions. This distance is the LV internal dimension one third through fractional shortening and is calculated as detailed by previous authors as follows[6,7]:

$$D_{1/3} = {}^{2}/_{3} \times \text{end-diastolic dimension} + {}^{1}/_{3} \times \text{end-systolic dimension}.$$

Peak LV WTN was calculated using this method with the following formula[8]:

$$\text{WTN (dynes/cm)} = 1{,}333 \times P \times (D_{1/3}/2),$$

where P is systolic blood pressure, and $D_{1/3}$ is defined above. PSS was also calculated with one-third dimensions using a cylindrical model as circumferential midwall stress with the following formula[9,10]:

$$\text{PSS (dynes/cm}^2) = P \times a^2 \times \frac{[1 + (b^2/c^2)]}{a^2},$$

where a is the LV endocardial radius, b is the LV epicardial radius, and c is the LV midwall radius.