Standing and Exercise Doppler Echocardiography in Obstructive Hypertrophic Cardiomyopathy: The Range of Gradients with Upright Activity

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Background: The ideal provocative maneuver in patients with hypertrophic cardiomyopathy (HCM) is a subject of ongoing investigation. Standing is a fundamental activity of daily life. This study examined acquisition of standing, Valsalva, and post-exercise left ventricular outflow tract gradients in HCM.

Methods: Rest supine, standing, and post-Valsalva gradients were measured in 98 consecutive patients with HCM who were referred for outpatient echocardiography. In 53 (54%) of the 98 patients, symptom-limited treadmill exercise was also performed, with gradients measured immediately after in the supine position.

Results: Fifty-six (57%) of the 98 patients had resting gradient < 30 mm Hg and would thus be characterized as nonobstructive at rest. In the 98 patients, median gradients were 25 mm Hg at rest (range 0–205 mm Hg), increasing to 44 mm Hg after standing (range 0–309 mm Hg), an increase of 76%, and were again higher after Valsalva, 64 mm Hg (range 0–256 mm Hg) ($P < .001$). In the 53 patients who had gradient assessed after exercise, they were higher still, 100 mm Hg (range 0–256 mm Hg) ($P < .001$). In 29 patients (30%), standing provoked a higher gradient than Valsalva.

Conclusion: Although standing increased gradients by 76%, it is not as potent a provocative maneuver as Valsalva or treadmill exercise. Nevertheless, standing is recommended as a physiologic provocative maneuver. In some patients standing may guide therapy; in others, the standing and exercise gradient provide a correct appreciation of the range of physiologically experienced gradients during daily upright activity. (J Am Soc Echocardiogr 2011;24:75-82.)

Keywords: Exercise, Hypertrophic cardiomyopathy, Hypertrophic obstructive cardiomyopathy, Left ventricular outflow gradient, Standing, Valsalva

Hypertrophic cardiomyopathy (HCM) is a complex genetic disorder characterized by thickening of the myocardium, most commonly of the septum and anterior wall, that occurs in the absence of any clinical condition that might explain such hypertrophy.[1-4] Resting left ventricular outflow tract (LVOT) obstruction occurs in 25% to 30% of patients, most commonly caused by systolic anterior motion (SAM) of the mitral valve and mitral septal contact.[2,5-12] Obstruction worsens symptoms and increases mortality.[2,12-14] LVOT gradients are dynamic in nature and change with activities of daily life.[2] This study investigated Doppler echocardiographic LVOT gradients after standing, Valsalva, and exercise provocation. Assuming the standing position may increase LVOT gradients because decreased venous return and decreased left ventricular (LV) volume enhance the propensity for SAM of the mitral valve, and earlier mitral-septal contact.

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0894-7317/$36.00

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doi:10.1016/j.echo.2010.10.006

MATERIALS AND METHODS

Study Subjects

The diagnosis of HCM was confirmed in all patients by demonstrating a hypertrophied (≥15 mm wall thickness) non-dilated left ventricle in the absence of a secondary cause of hypertrophy. Patients were excluded if they had severe mitral regurgitation deemed not due to HCM, aortic stenosis, or more than mild aortic regurgitation.

All patients were assigned a New York Heart Association (NYHA) classification and completed the Minnesota Living with Heart Failure questionnaire (quality of life). All patients signed consent approved by the institutional review board of St. Luke's-Roosevelt Hospital Center, New York, New York, for use of their clinical data for research purposes.

Echocardiography

The patients were referred outpatients studied while clinically stable in the course of treatment evaluation at the St. Luke's-Roosevelt HCM Program. Echocardiograms with standard imaging planes were performed on commercially available echocardiographs, Acuson Sequoia C256 (Mountainview, CA) or Philips 5500 (Andover, MA). An experienced sonographer performed the two-dimensional echocardiograms using conventional broadband transducers with

Abbreviations

HCM = Hypertrophic cardiomyopathy

LV = Left ventricular

LVOT = Left ventricular outflow tract

NYHA = New York Heart Association

SAM = Systolic anterior motion

harmonic imaging. Continuous-wave Doppler was used to measure LVOT gradient from the apical four-chamber and apical three-chamber views to record maximum velocity parallel to the systolic flow of the LVOT. Care was taken to separate LVOT signal from that of mitral regurgitation by angling the beam medially so that it excluded the left atrium. Jets that began during isovolumetric systole, and were early peaking, and not concave-to-left, were assumed to be mitral regurgitation. The simplified Bernoulli equation was used to calculate LVOT gradient, ignoring the velocity proximal to the LVOT narrowing, as described previously,[15] and the highest instantaneous gradient was reported. In all patients, LVOT gradient was measured in the supine position and during three separate Valsalva maneuvers. The patient was then asked to stand, and after 2 minutes of equilibration Doppler gradient was acquired over the next minute. To facilitate imaging while standing, the sonographer positioned the patient's left arm on the patient's head. This opened rib spaces and improved imaging.

Patients capable of exercising underwent treadmill testing with the Bruce protocol and had gradients acquired after exercise.[16-26] Patients were excluded from exercise if they had orthopedic disabilities or such severe heart failure symptoms that they were deemed incapable of performing even a modified, reduced treadmill protocol, or for rest gradients ≥ 80 mm Hg. Beta-blockers were held the morning of stress test, whereas other medications were continued. After stress exercise, continuous-wave Doppler gradients from apical views were acquired in supine left lateral decubitus position as soon as possible after completion of exercise within 30 to 60 seconds and then again 3 minutes later.

Measurements

Maximum LV wall thickness and LV end-diastolic dimensions were measured from parasternal long- and short-axis views from the two-dimensional echocardiogram as previously described.[27] Two experienced readers selected and measured the highest gradient for each provocation. The mean of the two observers' data was the reported gradient. When there was no mitral-septal contact and LVOT velocities were ≤ 1.8 m/sec, a zero gradient was assigned. Interobserver variability was assessed by comparing the standing gradients measured by the 2 readers in 36 patients. Intraobserver variability also was assessed. Mitral regurgitation was scored from 0 to 3 by the jet area/left atrial area method.

Statistics

SPSS 10.0.5 (SPSS Inc., Chicago, IL) was used for statistical analysis. Data are presented as mean value ± standard deviation. Skewed distributions are presented as median (range). To compare the Doppler gradients and the increase in gradients with rest, after standing, Valsalva, and post-exercise, analysis of variance with the Kruskal–Wallis test was used. Pairwise comparisons were performed using the Wilcoxon rank-sum test with Bonferroni corrections for multiple analyses. Correlations were performed using Pearson's correlation coefficient. A P value < .05 was considered significant. For interobserver and intraobserver variability, Cronbach's alpha analysis was used.

Table 1 Demographics and echocardiographic measurements in 98 patients with hypertrophic cardiomyopathy

Age (y)	56.4 ± 16
Female (n, %)	42 (43%)
NYHA class (I–IV)	2.1 ± 0.8
QOL (MLHF)	28.3 ± 22
Maximal LV wall thickness (mm)	22.6 ± 5
Resting LVOT gradient (mm Hg)	35.7 ± 39
Mitral regurgitation (0–3)	1.4 ± 1.0
Treadmill time (min), N = 53	8.8 ± 3
Mets achieved, N = 53	11.8 ± 6
Beta blocker therapy n (%)*	76 (78)
Calcium channel blocker n (%)	26 (27)
Disopyramide n (%)	24 (24)
Amiodarone, n (%)	2 (2)
Prior myectomy, n (%)	4 (4)
Prior alcohol ablation, n (%)	2 (2)

NYHA, New York Heart Association; *QOL*, quality of life; *MLHF*, Minnesota Living with Heart Failure; *LV*, left ventricle; *LVOT*, left ventricular outflow tract.

*Beta-blocker was held the morning of stress echocardiography, but other medications were continued.

RESULTS

Patient characteristics are noted in Table 1. Rest, standing, and Valsalva gradients were obtained in 98 patients. Standing gradients were not difficult to acquire; acceptable traces were obtained in 98% of patients attempted by an experienced sonographer. Acquisition of standing Doppler gradient adds approximately 4 minutes to the examination. Post-exercise gradients were acquired in 53 of 98 patients (54%).

Change in Gradient after Standing

Resting gradients were 36 ± 39 mm Hg, median 25 mm Hg (range 0–205 mm Hg), skew 2.1 ± 0.24. Fifty-six (57%) of the 98 patients had resting gradients < 30 mm Hg and would thus be characterized as nonobstructive at rest.

Compared with the supine position, standing provoked an increase in LVOT gradient ≥ 10 mm in 51 of 98 patients (52%). Median gradient increased from 25 to 44 mm Hg (range 0–309), an increase of 76% (P < .001). The distribution of the absolute increase in gradient with standing is shown in Figure 1. In 47 of 98 patients (48%), gradient was essentially unchanged after standing, increasing < 10 mm Hg; in 18 of 98 patients (18%) gradients increased by 10 to 30 mm Hg, and in 33 of 98 patients (34%), standing provoked a gradient increase of > 30 mm Hg. Of the 56 patients who had supine resting gradients < 30 mm Hg, 23 of 56 (41%) had an increase to ≥ 30 mm Hg with standing, thus placing them in the domain of obstructive HCM. Of the 75 patients who had supine resting gradients < 50 mm Hg, 34 of 74 (46%) had an increase to ≥ 50 mm Hg.

Valsalva and Exercise Gradients

Valsalva gradients were a median of 64 mm Hg (range 0–256 mm Hg), again higher than supine (P < .001) and standing (P = .004).

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