Left ventricular outflow tract and mid-cavity obstruction may cause false-positive dobutamine stress echocardiograms

Manish B. Jhawar1,2, Sudarshan Balla1,2, Martin A. Alpert1,2, and Anand Chockalingam1,2*

1Department of Internal Medicine, Division of Cardiovascular Medicine, University of Missouri School of Medicine, Columbia, MO 65212, USA; and 2Harry S Truman VA Medical Center, Columbia, MO 65212, USA

Received 31 August 2010; accepted after revision 28 September 2010; online publish-ahead-of-print 25 October 2010

Left ventricular (LV) outflow tract obstruction (LVOTO) occurs in up to 20% of patients undergoing dobutamine stress echocardiography (DSE). Mid-cavity LV obstruction occurs less commonly during DSE. LV regional wall motion abnormalities during DSE may occur despite normal coronaries due to hypertensive blood pressure response and takotsubo stress cardiomyopathy. We describe herein two cases of LVOTO and one case of mid-cavity LV obstruction during DSE associated with transient apical hypokinesis.

Keywords
Left ventricular outflow tract obstruction • Mid-cavity left ventricular obstruction • Apical hypokinesis • Dobutamine stress echocardiography

Introduction

Dobutamine stress echocardiography (DSE) is commonly used to detect myocardial ischaemia due to coronary artery disease.1,2 Diagnosis of myocardial ischaemia using this technique is based primarily on the induction of regional left ventricular (LV) wall motion abnormalities during intravenous dobutamine infusion.1,2 Reported sensitivity and specificity values for DSE range from 70 to 90% and 60 to 90%, respectively, using coronary angiography as a diagnostic standard.1,2 LV outflow tract obstruction (LVOTO) occurs in ~20% of patients undergoing DSE.3–5 Dynamic mid-cavity obstruction may also occur, particularly in patients with papillary muscle hypertrophy. Regional wall motion abnormalities (RWMA) during DSE in the absence of severe coronary artery disease are not typically attributed to LVOTO. We report herein two cases of LVOTO and one case of mid-cavity LV obstruction during DSE associated with apical hypokinesis in the absence of apical ballooning or significant epicardial coronary artery obstruction.

Dobutamine stress echocardiography protocol

LV diastolic and systolic volumes were measured in the apical four-chamber view using Simpson’s rule. LV ejection fraction (%) was measured by subtracting LV end-systolic volume from LV end-diastolic volume, then dividing the remainder by LV end-diastolic volume and then multiplying the dividend by 100. Sixteen segments representing blood supply from the three major coronary arteries were analysed.1,2 Regional LV wall motion was classified as normal, hypokinetic, akinetic, or dyskinetic.1,2 After the collection of baseline haemodynamic, electrocardiographic, and echocardiographic data, dobutamine was infused intravenously during 3 min stages at baseline and at doses of 10, 20, 30, 40, and 50 μg/kg/min. The electrocardiogram and the heart rate were monitored continuously. Blood pressure (BP) was measured at baseline, at the end of each stage and in recovery. If the target heart rate (220 – age) was not achieved with dobutamine infusion alone, atropine was administered intravenously in doses of 0.4 mg each at divided intervals up to a total dose of 1.2 mg. Dobutamine infusion was terminated with the achievement of the target heart rate, the onset of typical angina pectoris, the development of hypotension (systolic BP <90 mmHg), or the development of ventricular tachycardia.1,2 Echocardiographic images were obtained at baseline, after 3 min of infusion of dobutamine 20 μg/kg/min, following infusion of the peak dose of dobutamine (with or without atropine) and during recovery.

* Corresponding author. Tel: +1 573 814 6000, Fax: +1 573 884 7743, Email: chockalingama@health.missouri.edu

Published on behalf of the European Society of Cardiology. All rights reserved. © The Author 2010. For permissions please email: journals.permissions@oup.com

doi:10.1093/ejechocard/jeq158
Case reports

Case 1
A 51-year-old woman presented to a cardiology clinic with a several month history of intermittent chest pain. Chest pain episodes typically lasted few minutes and occurred sporadically. The patient had a history of hypertension, hypercholesterolaemia, and ~120 pack year history of cigarette smoking. Cardiovascular medications prior to DSE were Aspirin 81 mg daily, Simvastatin 40 mg daily, and Lisinopril 40 mg daily. Her baseline BP and pulse were 124/64 mmHg and 60 bpm, respectively. Her cardiovascular and pulmonary examinations were normal. LV chamber size, wall thickness, regional LV wall motion, and systolic function were normal at baseline. Following infusion of dobutamine 50 μg/kg/min, she developed severe apical hypokinesis despite having a normal BP response. She was asymptomatic and ECG monitoring revealed no ST segment depression. Systolic anterior motion of the anterior mitral leaflet was observed at peak stress as was a dynamic LVOT gradient (peak velocity: 8.4 m/s and peak gradient of 282 mmHg, Figure 1 LVOTO with mitral regurgitation contamination). As the highest systolic BP recorded was 161 mmHg and assuming left atrial pressure of 10 mmHg, we can indirectly estimate the LVOT gradient to be at least 130 mmHg (peak LV systolic pressure = transmitral pressure gradient + LA pressure = systolic BP + LVOT peak gradient). LVOTO with systolic anterior motion resolved and apical wall motion returned to normal during recovery. Subsequent left heart catheterization showed a normal left ventriculogram, normal LV end-diastolic pressure, and no intracavitary or LVOT pressure gradient. Coronary angiography was normal. The patient was treated with β-blockers and has experienced a marked reduction in the frequency of chest pain episodes.

Case 2
A 53-year-old woman presented with dyspnoea, palpitations, and exertional chest pain of 3 months duration. Cardiovascular risk factors were diabetes mellitus type-2, hypertension, and dyslipidaemia. Her baseline BP and pulse were 124/74 mmHg and 62 bpm, respectively, her cardiovascular and pulmonary examinations were normal, and her resting electrocardiogram was normal. Dobutamine infusion at 50 μg/kg/min produced chest pain without ST segment changes, moderate apical hypokinesis despite having a normal BP response. She was asymptomatic and ECG monitoring revealed no ST segment depression. Systolic anterior motion was not identified. Mid-cavity obstruction was absent and apical wall motion returned to normal during recovery. Subsequent left heart catheterization showed a normal left ventriculogram, normal LV end-diastolic pressure, and no intracavitary or LVOT pressure gradient. Coronary angiography was normal. The patient was treated with β-blockers and has experienced a marked reduction in the frequency of chest pain episodes.

Case 3
A 40-year-old woman was referred to a cardiology clinic for evaluation of precordial pressure-like pain, which occurred sporadically and inconsistently with similar amounts of exertion. There were no other cardiovascular symptoms. Cardiovascular risk factors included hypertension and tobacco abuse. Her only cardiovascular medication was lisinopril. Her resting electrocardiogram was normal. Her baseline BP and pulse were 121/71 mmHg and 65 bpm, respectively. Her cardiovascular and pulmonary examinations were normal. Her baseline echocardiogram showed...
normal LV chamber size, wall thickness, and systolic function with no regional LV wall motion abnormalities or LVOTO at rest (5.19 mmHg and peak velocity of 1.14 m/s). Infusion of 50 μg/kg/min of dobutamine produced severe apical hypokinesis without ballooning, systolic anterior motion of the anterior mitral leaflet, and a late peaking LVOTO gradient that was not quantified with Doppler. Dobutamine infusion did not produce chest pain or ST segment depression. LVOTO and systolic anterior motion resolved and apical wall motion returned to normal during recovery. Subsequently, an adenosine sestamibi myocardial perfusion scan was performed and was normal. No therapeutic intervention was initiated. Patient continued to experience symptoms of non-exertional chest discomfort periodically. Coronary angiogram was done which showed normal coronaries, good LV function with no significant gradient on pull back. Patient was started on β-blocker therapy.

Discussion

Prevalence of LVOTO during DSE studies is ≈20%.3,4 However, in older hypertensive women, up to 80% may develop significant LVOTO during DSE and this may be the basis for their reduced exercise tolerance.5 The presence of LVOTO during DSE does not predict the presence of coronary artery disease, nor is it associated with an increased risk of ischaemic events.3–5 Mid-cavity obstruction occurs less commonly, often in patients with papillary muscle hypertrophy.5

LVOTO during DSE is thought to relate to the physiological effects of dobutamine and LV chamber size during infusion.3–5 The inotropic effects of dobutamine combined with reduced venous return due to vasodilation and lack of exercise decreases the LV chamber size. Increased blood flow velocity and relative narrowing of the LVOT create a Venturi effect resulting in systolic anterior motion of the anterior mitral leaflet and subsequent dynamic LVOTO.3–5,7,8 LVOTO with systolic anterior motion of the anterior mitral leaflet has been described during exercise stress echocardiography, but is rare.3 Use of β-adrenergic blocking agents and calcium channel blockers may mask LVOTO during DSE.3–5 Conversely, withholding these drugs just prior to their testing may theoretically exaggerate the frequency and severity of LVOTO due to up-regulation of adrenergic receptors.3–5 Other factors that may affect the ability to detect stress-induced LVOTO include sonographer expertise, image quality, and time constraints for acquisition of data.3–5 Simultaneous development of eccentric mitral regurgitation due to systolic anterior motion may contaminate the LVOT Doppler signal (Figure 1) limiting the ability to accurately quantify the severity and the haemodynamic significance of LVOTO.3–5,9

Acute hypertension during DSE has been cited in the echocardiographic literature as a cause of transient LV RWMA leading to a false-positive diagnosis.10 In our cases as in previously cited cases of LVOTO during DSE, pressure gradients were exceedingly high, possibly simulating an acute hypertensive response during stress testing. Although the precise mechanism remains uncertain, our cases suggest that LV apical wall motion abnormalities associated with LVOTO or mid-cavity LV obstruction may be induced by dobutamine infusion in patients without severe coronary stenosis leading to a false-positive diagnosis of myocardial ischaemia. Non-coronary distribution and symmetrical extent of anterior, lateral, and inferior of hypokinesia from the apex may increase the likelihood of LVOTO instead of CAD as aetiology of RWMA during DSE. Our first case had intermediate grade CAD which along with the LVOTO-related wall stress might have resulted in the predominantly septal location of the RWMA. In most cases, however, myocardial perfusion imaging, computed tomographic coronary angiography, or invasive coronary angiography will be necessary to exclude high-grade stenosis of one or more of the coronary arteries or its branches.

All three of the patients in this report were women. This may be more than coincidence. Smaller LV cavity size, the presence of
hypertension with LV hypertrophy, and an exaggerated responsiveness to sympathetic stimulation may predispose to LVOT and mid-cavity LV obstruction in women.\textsuperscript{2,11}\n
Two studies\textsuperscript{12,13} and multiple case reports\textsuperscript{14–18} have described various transient regional LV wall motion abnormalities in patients undergoing DSE, exercise stress echocardiography, or receiving dobutamine for other purposes in patients without obstructive coronary artery disease. Mid-ventricular and apical wall motion abnormalities (including apical ballooning) occurred more commonly than basal wall motion abnormalities. Normalization of LV regional wall motion, when documented, occurred 1–3 weeks after stress testing. Hypertension was frequently present prior to or during stress in these patients. LVOTO was described in only one of these cases, a patient who developed apical ballooning and myocardial infarction and died shortly after DSE.\textsuperscript{18} Recent literature suggests the forme frusta of takotsubo stress cardiomyopathy with related apical or global hypokinesia may account for regional wall motion abnormalities in patients. LVOTO or mid-cavity obstruction was present in all our cases. Also, regional LV wall motion returned to normal within minutes during the recovery phase of DSE and not over days as would be expected with typical takotsubo cardiomyopathy.\textsuperscript{19}

**Conclusion**

The cases presented in this report suggest that LVOTO and mid-cavity obstruction of the LV during DSE may be associated with transient apical LV wall motion abnormalities in the absence of severe obstructive coronary artery disease.

**Supplementary data**

Supplementary data are available at EJECO online.

**Conflict of interest:** none declared.

**Funding**

MU Research Council Grant Award to A.C. VISN 15 Veterans Administration Research award to A.C.

**References**


