

Squat-to-stand provocation of dynamic left ventricular outflow tract obstruction in hypertrophic cardiomyopathy: a case report

Lillian T. Peng ¹, D. Brian Newman ², and Jeffrey B. Geske ^{2*}

¹Mayo Clinic Alix School of Medicine, 200 1st St SW, Rochester, MN 55905, USA; and ²Department of Cardiovascular Medicine, Mayo Clinic, 200 1st St SW, Rochester, MN 55905, USA

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Background

Left ventricular outflow tract (LVOT) obstruction is an important determinant of the management of hypertrophic cardiomyopathy (HCM). With a nationwide shortage of amyl nitrite in 2019, we implemented a 'repetitive squat-to-stand' manoeuvre to provoke LVOT obstruction during echocardiography.

Case summary

A 64-year-old female was referred with symptomatic HCM refractory to pharmacologic therapy. Transthoracic echocardiography showed minor LVOT obstruction with conventional imaging at rest and during Valsalva manoeuvre, but severe obstruction was confirmed with the repetitive squat-to-stand manoeuvre. Alcohol septal ablation via the first septal perforator was performed with subsequent resolution of symptoms.

Discussion

Due to the dynamic nature of LVOT obstruction, a series of provocative manoeuvres including Valsalva manoeuvre, inhalation of amyl nitrite, and exercise are often necessary to maximally augment ventricular obstruction. The recent unavailability of amyl nitrite during a nationwide shortage prompted the implementation of a protocol of repetitive squat-to-stand manoeuvre in our echocardiography laboratory. Rising from the squatting position decreases preload and afterload, both of which augment dynamic LVOT obstruction. Repetition of squatting and standing appears to enhance the sensitivity of the manoeuvre, particularly when exertional symptoms are reproduced. In this case, repetitive squat-to-stand manoeuvre led to the identification of severe LVOT obstruction which may not have been diagnosed otherwise, alteration of treatment to septal reduction therapy, and subsequent resolution of symptoms.

Keywords

Hypertrophic cardiomyopathy • Squat-to-stand • Echocardiography • Left ventricular outflow tract • Obstruction • Gradient • Case report

Learning points

- Squat-to-stand is a pragmatic, cost-effective provocative manoeuvre for augmenting dynamic left ventricular obstruction in hypertrophic cardiomyopathy (HCM).
- Squat-to-stand manoeuvre should be considered when other manoeuvres are unavailable or fail to induce obstruction, as results can alter treatment decision-making.
- In HCM, severe dynamic left ventricular outflow tract obstruction resulting in medically refractory symptoms is an indication for septal reduction therapy.

* Corresponding author. Tel: (507) 284-4442, Email: Geske.Jeffrey@mayo.edu

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Introduction

Dynamic left ventricular outflow tract (LVOT) obstruction in hypertrophic cardiomyopathy (HCM) patients is associated with increased cardiac morbidity and mortality,¹ including the development of atrial fibrillation, embolic complications, and sudden cardiac death, with LVOT obstruction comprising a component of the HCM risk-SCD (sudden cardiac death) calculator.² The presence of dynamic LVOT obstruction is also important in determining the therapeutic management of HCM. Medically refractory symptoms attributable to LVOT obstruction are optimally treated with septal reduction therapy.³

Severe obstruction, defined as a maximal instantaneous gradient (MIG) ≥ 50 mmHg at rest or with physiologic provocation, should be confirmed when considering septal reduction therapy. Because LVOT obstruction is dynamic in nature, a series of provocative manoeuvres, such as Valsalva, amyl nitrite inhalation, and stress echocardiography, is often necessary to identify maximal obstruction.¹

With the recent nationwide shortage of amyl nitrite throughout 2019, our echocardiography laboratory implemented a new protocol of 'repetitive squat-to-stand' during transthoracic echocardiography (TTE) for patients with known or suspected HCM and a left ventricular MIG < 50 mmHg at rest and with Valsalva manoeuvre.

We report the case of severe dynamic LVOT obstruction detected by this provocative manoeuvre which subsequently altered treatment.

Timeline

Index date	Diagnosis of gene-positive hypertrophic cardiomyopathy
Index date to 6 months	Two syncopal episodes, lightheadedness, and dyspnoea on exertion
6 months	Transthoracic echocardiography showed severe left ventricular outflow tract (LVOT) obstruction with squat-to-stand that was absent at rest and with Valsalva manoeuvre
7 months	Confirmation of LVOT gradient with cardiac catheterization
8 months	Alcohol septal ablation of 1st septal perforator
8 months	Outpatient clinic visit: no adverse clinical events reported; the patient denied chest discomfort, dyspnoea on exertion, palpitations, lightheadedness, and syncope

Case presentation

A 64-year-old female with TNNI3 gene-positive HCM presented to cardiovascular medicine clinic with occasional lightheadedness, two prior episodes of exertional syncope, and New York Heart Association Class III exertional dyspnoea despite beta-blockade at maximally tolerated doses. Titration of her medical management was

significantly limited due to side effects and allergies; she was intolerant to angiotensin receptor blockers, angiotensin-converting enzyme inhibitors, metoprolol, hydrochlorothiazide, amlodipine, and diltiazem. Her current medication regimen was carvedilol 12.5 mg orally twice a day. The first syncopal episode occurred when climbing a flight of stairs at home and the second occurred the following day at work, with fall-associated head trauma. Her past medical history was pertinent for systemic hypertension, pulmonary hypertension, Stage 3 chronic kidney disease, and chronic heart failure with preserved ejection fraction.

Physical exam at outpatient clinic revealed severe systolic hypertension (174/92 mmHg) with a normal heart rate (64 b.p.m.). There were no signs of peripheral or pulmonary oedema. Cardiac examination revealed a high-pitched, crescendo-decrescendo, systolic ejection murmur best heard at the left lower sternal border. Laboratory studies showed elevated high-sensitivity cardiac troponin T of 32 ng/L (normal range: < 14 ng/L for women, < 22 ng/L for men) and significantly elevated N-terminal pro-B-type natriuretic peptide of 4420 pg/mL (normal range: < 125 pg/mL). A resting electrocardiogram demonstrated normal sinus rhythm with non-specific ST and T-wave abnormalities. Holter monitor showed a mean heart rate of 66 b.p.m. and no evidence of ventricular tachyarrhythmias.

Transthoracic echocardiography showed sigmoid septal hypertrophy (maximum wall thickness 16 mm) with a calculated left ventricular ejection fraction of 75%. The right ventricular systolic pressure was estimated to be 86 mmHg, consistent with severe pulmonary hypertension. The LVOT MIG was 12 mmHg at rest, with no further augmentation during the Valsalva manoeuvre (*Figure 1A*). Amyl nitrite was not available at the time of evaluation given a nationwide shortage. The patient then performed a repetitive squat-to-stand manoeuvre (5–10 repetitions) which resulted in systolic anterior motion of the mitral valve (*Video 1*) and 2D colour Doppler evidence of LVOT obstruction (*Video 2*). Continuous-wave Doppler performed after repetitive squat-to-stand revealed severe LVOT obstruction (MIG 85 mmHg, *Figure 1A*). Because severe dynamic LVOT obstruction had been identified during the initial TTE inclusive of repetitive squat-to-stand, exercise echocardiography was not needed for the purposes of determining if the severe latent obstruction was present.

Given medically refractory symptoms and severe dynamic obstruction, septal reduction therapy was recommended. After consideration of medical comorbidities (including severe pulmonary hypertension) and informed discussion, alcohol septal ablation was pursued. Invasive haemodynamics at the time of septal ablation confirmed severe dynamic LVOT obstruction (*Figure 1B*) with post-premature ventricular contraction (PVC) augmentation accompanied by 'spike and dome configuration' (asterisk, *Figure 1B*, Brockenbrough–Braunwald–Morrow sign). The Brockenbrough–Braunwald–Morrow sign, observed in obstructive HCM, describes a paradoxical decrease in arterial pulse pressure in the beat after a PVC due to dynamic outflow obstruction. Following a PVC, there is a compensatory pause in the cardiac cycle. During this longer RR interval, more calcium is accumulated in the sarcoplasmic reticulum. The increased calcium release results in augmented contractility on the beat after the PVC. The increased contractility results in increased obstruction.⁴ The aortic pressure tracing demonstrates the 'spike'

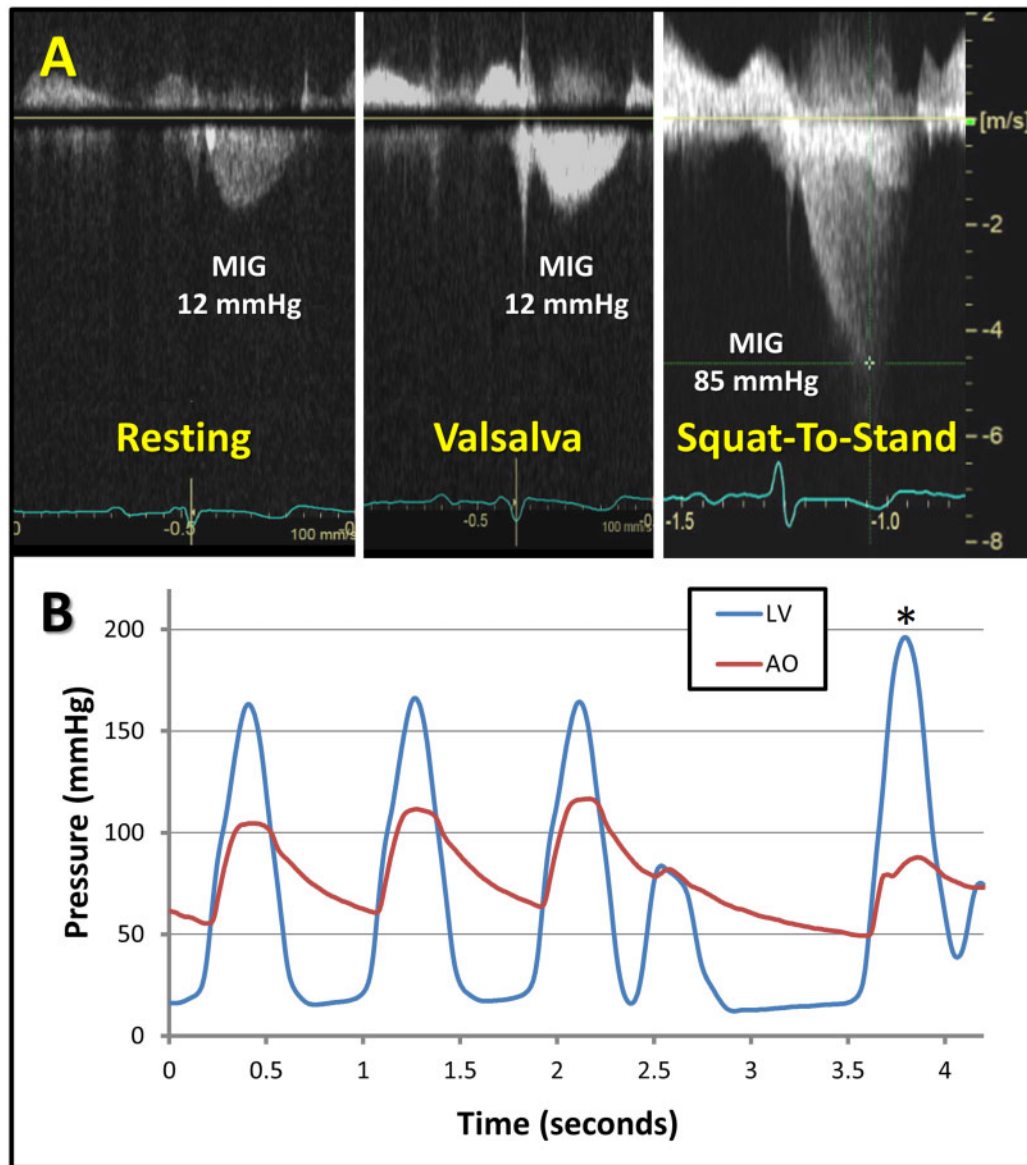


Figure 1 (A) Echocardiography with continuous wave Doppler of left ventricular outflow tract gradient at rest (left), with Valsalva manoeuvre (middle), and with squat-to-stand manoeuvre (right). (B) Pressure tracings of left ventricle (LV) and aorta (AO) from invasive haemodynamic monitoring at time of ablation. MIG, maximal instantaneous gradient.

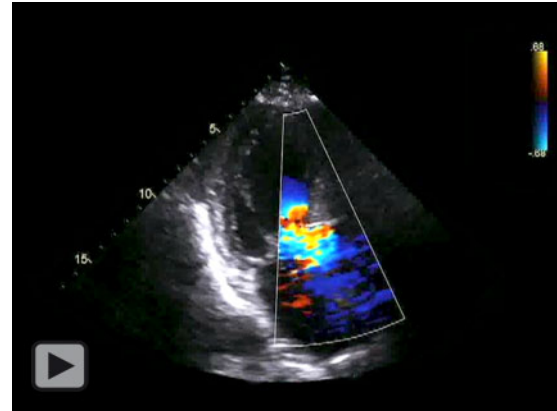
(initial ejection), mid-systolic drop in amplitude due to reduced forward flow from LVOT obstruction and systolic anterior motion of the mitral valve, and 'dome' in the aortic pulse pressure tracing as obstruction and systolic anterior motion resolves. The first septal perforator was ablated with 1 cc of alcohol, with resolution of dynamic obstruction. The patient developed transient high-grade atrioventricular block during the procedure which necessitated a temporary pacemaker. After 3 days of close cardiac monitoring, the pacemaker was removed and the patient was discharged. At 1-month follow-up, her medication regimen included carvedilol 12.5 mg orally twice a day. She denied chest discomfort, dyspnoea on exertion, palpitations, syncope, or near syncope and had not experienced further events.

Discussion

Left ventricular outflow tract obstruction is an important determinant of clinical management in HCM, particularly as one of the criteria for septal reduction therapy. Obstruction is dynamic, dependent on factors such as volume status, physical activity, general anaesthesia, intra-thoracic pressure, posture, and pharmacotherapy, and often may need to be induced by various provocative manoeuvres. Prior studies have suggested that different provocative manoeuvres may be effective in different patients and some patients may progress step-wise through all manoeuvres (Valsalva manoeuvre, amyl nitrite inhalation, exercise echocardiography, observing the aortic pressure



Video 1 Transthoracic echocardiography performed following repetitive squat-to-stand manoeuvre: apical long-axis 2D echocardiography demonstrates systolic anterior motion of the mitral valve.



Video 2 Transthoracic echocardiography performed following repetitive squat-to-stand manoeuvre: apical long-axis 2D colour Doppler echocardiography demonstrates turbulent flow within the left ventricular outflow tract (provoked obstruction) and mitral regurgitation associated with systolic anterior motion of the mitral valve.

contour and pulse pressure response following a PVC, as well as isoproterenol infusion during hemodynamic catheterization) to confirm severe dynamic obstruction.⁵ Recommendations on the selection of provocative manoeuvres vary by societal guidelines. The 2014 European Society of Cardiology (ESC) guidelines place an emphasis on physiological augmentation of LVOT obstruction with a systematic progression from the assessment at rest to Valsalva in sitting and semi-supine position, Valsalva on standing, and exercise stress echocardiography. Pharmacological augmentation of the gradient with dobutamine is no longer recommended and nitrates are reserved for patients who cannot perform physiologically stressful procedures.⁶ The 2011 American College of Cardiology Foundation and the American Heart Association (ACCF/AHA) guidelines similarly give preference to physiologic augmentation of the gradient and no longer recommend dobutamine infusion, but acknowledge the role of amyl nitrite and cardiac catheterization with isoproterenol infusion in select cases.³

With the recent nationwide shortage of amyl nitrite,⁷ our echocardiography laboratory implemented a novel protocol employing 'repetitive squat-to-stand' manoeuvre to provoke LVOT obstruction starting in February 2019. Squatting increases preload by augmentation of venous return from the legs,^{8–10} and increases afterload by enhancement of aortic wave reflection.¹¹ Rising from the squatting position decreases venous return and simultaneously reduces left ventricular afterload. Reduced preload and afterload both augment dynamic LVOT obstruction along with a closer approximation of the mitral valve to the hypertrophied septal wall.¹² We have observed that repetitive squatting (often 10 or more repetitions) appears to increase the sensitivity of the manoeuvre compared to a single squat-to-stand, particularly when exertional symptoms are reproduced.

This clinical case highlights the utility of the 'repetitive squat-to-stand' manoeuvre and the potential of a new addition to the toolbox of provocative manoeuvres both at the bedside and during TTE. The repetitive squat-to-stand manoeuvre does not require any special equipment and can be performed during a regular 'resting' TTE examination, which can streamline management by avoiding the need to schedule additional testing with exercise echocardiogram or hemodynamic catheterization on another day. This reduces cost,

imposes less time burden on the patient, and frees up resources for other patients. Although the repetitive squat-to-stand manoeuvre is dependent on the experience of the sonographer, as well as patient factors such as imbalance and/or orthopaedic concerns, these same limitations impact the utilization of exercise echocardiography, the 'gold standard' of noninvasive quantitation. While the squat-to-stand manoeuvre by no means replaces exercise echocardiography, the latter is more cost-, time-, and labour-intensive than resting TTE, and it is not logistically feasible for the majority of cardiology clinics to perform all resting echocardiograms in a stress echocardiography workroom. Use of the 'repetitive squat-to-stand' manoeuvre as a complement to the resting echocardiography warrants further study, particularly with regards to cost savings and diagnostic performance, in comparison to traditional manoeuvres such as the Valsalva manoeuvre and inhalation of amyl nitrite.

Lead author biography



Lillian Peng is a third-year medical student at Mayo Clinic Alix School of Medicine in Rochester, Minnesota. She received her undergraduate degree from the University of California, Los Angeles in 2017. She has clinical and research interests in cardiology and critical care.

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The authors would like to thank the patient for allowing us to share her case.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as [Supplementary data](#).

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: None declared.

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