CASE REPORT

Intraparenchymal haemorrhage and uncal herniation resulting from dobutamine stress echocardiography

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SUMMARY

Intracranial haemorrhage (ICH) resulting from dobutamine stress echocardiography (DSE) is a rare complication in an otherwise relatively safe procedure. There has been one previously reported case of ICH associated with DSE in a patient who was fully anticoagulated. The authors report a second case of ICH associated with DSE leading to a poor outcome. Unlike the previous report, this patient was not fully anticoagulated and bleeding resulted from uncontrolled hypertension. Clinicians should be attentive to the risk of ICH associated with DSE in the setting of uncontrolled hypertension.

BACKGROUND

The incidence of a cerebrovascular accident (CVA) associated with dobutamine stress echocardiography (DSE) is very low (<0.01%).¹ The authors located only one previous case of intracranial haemorrhage (ICH) following DSE in a PubMed search. That patient had a mechanical mitral valve implant and was receiving anticoagulation therapy with warfarin that increased the bleeding risk. Currently, there is no consensus regarding the prevention of this rare but fatal complication. However, both cases of ICH were associated with a significant hypertensive response to dobutamine infusion while marked sinus tachycardia also occurred in the present case. While the European Association of Cardiovascular Imaging (EACVI) consensus document lists endpoints for submaximal non-diagnostic testing,² the American College of Cardiology, American Heart Association, American Society of Echocardiography (ACC/AHA/ASE) guidelines do not specifically address the management of hypertensive patients presenting for DSE or those who experience an exaggerated hypertensive response.^{3–5} The significance of this case and discussion lie in advising caution for elderly patients (age >70 years) undergoing DSE with a systolic blood pressure (SBP) >180 mm Hg during the procedure, a heart rate (HR) that exceeds 85% of the maximal predicted for a participant's age, and in those with increased bleeding risk (especially in patients who are on anticoagulation).

CASE PRESENTATION

A 75-year-old African-American man with uncontrolled essential hypertension, hyperlipidaemia and coronary artery disease (CAD) treated with implantation of a drug eluting stent to the right coronary artery (RCA) 10 years previously presented to the University of Florida Health

cardiology clinic with Canadian Cardiovascular Society class II angina symptoms. A DSE suggested ischaemia in the RCA territory. Coronary angiography revealed in-stent restenosis that was treated by balloon angioplasty. He was discharged on aspirin 81 mg daily. Dual antiplatelet therapy was not started because of a history of non-compliance with medications. He presented 1 month later with atypical chest discomfort and was scheduled for a repeat DSE. Prior to the study he was in sinus rhythm with an HR of 57 bpm, and his resting blood pressure (BP) was 166/85 mm Hg. As per protocol, dobutamine infusion was initiated at 10 µg/kg/min increasing by 10 µg/kg/min at 3-min intervals until either a maximum dose of 40 µg/kg/min or HR of ≥85% of his maximum predicted HR (145 bpm) was achieved. During the study, his BP rose to 199/115 mm Hg at the peak dose of 30 µg/kg/min and the infusion was terminated despite an HR of 132 bpm. However, he developed a severe headache 2-min postinfusion, and was rapidly transferred to the emergency department where he underwent an emergency neurological evaluation. A non-contrast CT of his head revealed a large left intraparenchymal haemorrhage with mass effect, left-to-right midline shift and uncal herniation. He was admitted to the neurointensive care for ICH management.

INVESTIGATIONS

- Non-contrast head CT revealed a large left intraparenchymal temporal lobe haemorrhage with extra-axial extension. Significant mass-effect with left-to-right midline shift and left uncal herniation were noted (figure 1).
- CT angiography with and without contrast 2 days later revealed cortical and deep left hemisphere haemorrhage with left frontal subdural haematoma and left hippocampal herniation.
- Normal coagulation studies with an international normalised ratio (INR) of 1.2.

OUTCOME AND FOLLOW-UP

The patient rapidly lost consciousness which he never regained. His subsequent hospital course was complicated, and he died 10 days after undergoing DSE testing.

DISCUSSION

DSE, along with other diagnostic and prognostic tests, is routinely used in the clinical assessment of patients with known or suspected CAD.^{3 4} Dobutamine, an inotropic agent with a short

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Figure 1 CT of the head without contrast demonstrating large left intraparenchymal temporal lobe haemorrhage with extra-axial extension. Significant mass-effect with left-to-right midline shift and left uncal herniation are also seen.

half-life, increases HR and myocardial contractility resulting in increased myocardial oxygen demand. CAD is most frequently diagnosed by induction of left ventricular (LV) wall motion abnormalities that develop in response to myocardial oxygen supply–demand mismatch. Analogous to exercise stress echocardiography and myocardial perfusion imaging (MPI), the sensitivity of DSE rises with increasing extent and severity of CAD, but DSE is reported to be more specific when compared to either of those modalities.^{5 6} DSE does not expose the patient to radiation, and requires a shorter data acquisition time compared to MPI. The major disadvantages of DSE are operator and patient factor dependence of image acquisition, especially at peak infusion rates, and interobserver variability of image interpretation. Rapid recovery of ischaemic wall abnormalities may lead to false-negative results. LV opacification by intravenous injection of echo-contrast agent (Definity, Lantheus Medical Imaging or Optison GE Healthcare) to enhance endocardial border demarcation can improve the sensitivity and specificity of the technique. The use of these agents is now routine in most laboratories.

Adverse events associated with DSE include, but are not limited to, myocardial ischaemia or infarction, ventricular arrhythmias, hypertension, hypotension, rarely myocardial rupture and CVAs.^{1 7 8} These complications are not more frequent with accelerated dobutamine infusions.^{9 10} Unpredictable variability of the pharmacological response to dobutamine is a potential problem. Dobutamine, a synthetic catecholamine, is a racemic mixture that has both β -1 and β -2 agonist activity by the (+) isomer and α -1 agonist activity by the less potent (–) isomer. A hypertensive response during DSE occurs in 1% of patients as a consequence of both β -1 and α -1 receptor agonism.^{11–13} It is well known that hypertension increases the risk of ICH irrespective of any other underlying aetiologies and this typically involves small penetrator arteries.^{14–16} ICH accounts for 15% of all CVA and results in death in over a third of patients, and the typical risk factors for ICH include but not limited to hypertension, cerebral amyloid angiopathy, neoplasms and vascular malformations.¹⁷ Intraparenchymal haemorrhage can result from an episode of acute severe hypertension, a condition that can occur or be exacerbated by dobutamine infusion, especially in patients with poorly controlled BP prior to testing. Furthermore, the risk of ICH increases with age, doubling every 10 years after age 35.¹⁸

Shah and Chaudhry¹⁹ reported the first documented case of ICH complicating a DSE in a 72-year-old man with a prosthetic mitral valve on warfarin therapy. His INR was 3.8 at the time of the test. ICH is reported to occur in 12% of patients on oral anticoagulants.²⁰ In the current case ICH occurred immediately following DSE and we believe it to be the first case in which the patient

suffered massive ICH associated with uncal herniation resulting in death in the absence of full anticoagulation. The patient was only on aspirin 81 mg daily. In addition, he did not achieve a maximum SBP that would have required termination of the stress test protocol. Current ACC/AHA/ASE guidelines do not discuss the management of patients with hypertension presenting for DSE or who experience hypertensive response during infusion.^{3–5} The EACVI consensus document recommends terminating the stress test in the presence of symptoms that limit further testing: extremes in BP (hypertension; SBP >220 mm Hg, diastolic BP (DBP) >120 mm Hg or hypotension; >40 mm Hg drop in BP) and/or the presence of either supraventricular arrhythmias and or complex ventricular arrhythmias.² In comparison, the recently published ACC/AHA guideline entitled: Exercise Standards for Testing and Training, recommends terminating a treadmill test for an SBP >250 mm Hg or DBP >115 mm Hg during the test and postponing the test if the resting SBP is >200 mm Hg or the DBP >115 mm Hg.²¹ In contrast, no clear parameters exist to guide levels of BP deemed to be acceptable to start or terminate a DSE protocol. This is left to the discretion of the clinical operators.

Learning points

- ▶ Intracranial haemorrhage is a rare and potentially fatal adverse outcome of dobutamine stress echocardiography (DSE).
- ▶ Based on reported cases, caution should be exercised in patients with a bleeding tendency (eg, anticoagulation or antiplatelet therapy) with poorly controlled hypertension undergoing DSE.
- ▶ There are no clear cut evidence-based guidelines by the American College of Cardiology, American Heart Association, American Society of Echocardiography (ACC/AHA/ASE) as to submaximal non-diagnostic endpoints for DSE; however the European Association of Cardiovascular Imaging (EACVI) suggests that terminating the study in the presence of symptoms, symptomatic hypertension or hypotension or the presence of cardiac arrhythmias.
- ▶ Although there have been no studies to support recommending a terminal endpoint/limit for blood pressure (BP; in the absence of symptoms), the authors suggest that patients undergoing DSE should have optimally controlled blood pressure preprocedure with a goal of a systolic BP <140 mm Hg and advise that the procedure should be terminated in elderly patients (>70 years) attaining a systolic BP >180 mm Hg during testing.

Although DSE is a relatively safe test, we recommend increased vigilance for development of severe hypertension that could increase the risk for ICH. Special care should be taken with patients with uncontrolled hypertension presenting for DSE, especially if the patient is >70 years of age, is taking anticoagulation or antiplatelet therapy, and has other risk factors for ICH. Although there is little clinical evidence, the authors will adopt the recommendations from the published AHA scientific statement on exercise standards for testing and training and recommend that the dobutamine infusion be terminated for patients undergoing DSE who reach a maximum predicted HR $\geq 85\%$, develop an SBP >250 mm Hg or DBP >115 mm Hg. It is worth noting that in both cases described ICH resulted with SBP >180 mm Hg during DSE suggesting that, especially in the elderly (>70 years), this may be a more appropriate conservative terminal endpoint.

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Competing interests None.

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REFERENCES

- Geleijnse ML, Krenning BJ, Nemes A, *et al.* Incidence, pathophysiology, and treatment of complications during dobutamine-atropine stress echocardiography. *Circulation* 2010;121:1756–67.
- Sicari R, Nihoyannopoulos P, Evangelista A, *et al.*; European Association of Echocardiography. Stress echocardiography expert consensus statement: European Association of Echocardiography (EAE) (a registered branch of the ESC). *Eur J Echocardiogr* 2008;9:415–37.
- Pellikka PA, Nagueh SF, Elhendy AA, *et al.* American Society of Echocardiography recommendations for performance, interpretation, and application of stress echocardiography. *J Am Soc Echocardiogr* 2007;20:1021–41.
- Fihn SD, Gardin JM, Abrams J, *et al.* 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *J Am Coll Cardiol* 2012;60:e44–164.
- Cheitlin MD, Armstrong WF, Aurigemma GP, *et al.* ACC/AHA/ASE 2003 guideline update for the clinical application of echocardiography-summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/ASE Committee to Update the 1997 Guidelines for the Clinical Application of Echocardiography). *J Am Coll Cardiol* 2003;42:954–70.
- Marwick TH. Stress echocardiography. *Heart* 2003;89:113–18.
- Picano E, Mathias W Jr, Pingitore A, *et al.* Safety and tolerability of dobutamine-atropine stress echocardiography: a prospective, multicentre study. Echo Dobutamine International Cooperative Group. *Lancet* 1994;344:1190–2.
- Mertes H, Sawada SG, Ryan T, *et al.* Symptoms, adverse effects, and complications associated with dobutamine stress echocardiography. Experience in 1118 patients. *Circulation* 1993;88:15–19.
- Lu D, Greenberg MD, Little R, *et al.* Accelerated dobutamine stress testing: safety and feasibility in patients with known or suspected coronary artery disease. *Clin Cardiol* 2001;24:141–5.
- Minardi G, Manzara C, Pulignano G, *et al.* Feasibility, safety and tolerability of accelerated dobutamine stress echocardiography. *Cardiovasc Ultrasound* 2007;5:40.
- Parker K, Brunton L, Goodman LS, *et al.* *Goodman & Gilman's manual of pharmacology and therapeutics*. McGraw-Hill Medical, 2008:159.
- Leier CV, Unverferth DV. Dobutamine. *Ann Intern Med* 1983;99:490–6.
- Arima H, Tzourio C, Anderson C, *et al.*; PROGRESS Collaborative Group. Effects of perindopril-based lowering of blood pressure on intracerebral hemorrhage related to amyloid angiopathy: the PROGRESS trial. *Stroke* 2010;41:394–6.
- Thrift AG, McNeil JJ, Forbes A, *et al.* Three important subgroups of hypertensive persons at greater risk of intracerebral hemorrhage. Melbourne Risk Factor Study Group. *Hypertension* 1998;31:1223–9.
- Ritter MA, Droste DW, Hegedüs K, *et al.* Role of cerebral amyloid angiopathy in intracerebral hemorrhage in hypertensive patients. *Neurology* 2005;64:1233–7.
- Lee CY, Pellikka PA, Shub C, *et al.* Hypertensive response during dobutamine stress echocardiography. *Am J Cardiol* 1997;80:970–1.
- Sahni R, Weinberger J. Management of intracerebral hemorrhage. *Vasc Health Risk Manag* 2007;3:701–9.
- Stein M, Misselwitz B, Hamann GF, *et al.* Intracerebral hemorrhage in the very old: future demographic trends of an aging population. *Stroke* 2012;43:1126–8.
- Shah SP, Chaudhry GM. Intracranial hemorrhage as a complication of dobutamine stress echocardiography: case report and review of the literature. *Echocardiography* 2012;29:E119–21.
- Morgenstern LB, Hemphill JC, Anderson C, *et al.*; AHA/ASA Guideline. Guidelines for the management of spontaneous intracerebral hemorrhage. *Stroke* 2010;41:2108–29.
- Fletcher GF, Ades PA, Kligfield P, *et al.* Exercise standards for testing and training: a scientific statement from the American Heart Association. *Circulation* 2013;128:873–934.

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