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EDITORIAL

Paroxysmal sinus deceleration: an under-recognized show stopper

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This editorial refers to 'Paradoxical sinus deceleration during dobutamine stress echocardiography: case series and review of the literature', by E. Sulo *et al*. https://doi.org/10.1093/ehjcre/ytac180.

Dobutamine stress echocardiography is a routine workhorse in the assessment of myocardial ischaemia. Dobutamine is preferred over vasodilators for stress echocardiography, due to its higher sensitivity for the detection of myocardial ischaemia.[1] Dobutamine stress echocardiography is safe and well tolerated, with a reported rate of significant complications of just 0.2%.[2,3] Side effects of dobutamine administration include arrythmias, chest pain, nausea, hypertension, and hypotension. Paroxysmal sinus deceleration is a significant but often under-reported side effect of dobutamine administration, occurring in up to 8% of all dobutamine stress echocardiograms.[4] This phenomenon is often symptomatic and frequently results in premature termination of dobutamine stress echocardiography prior to the achievement of target heart rate, thereby reducing the sensitivity of the test for the detection of myocardial ischaemia.

Dobutamine acts predominantly at beta-1 adrenergic receptors resulting in positive chronotropic and ionotropic responses in cardiac myocytes. Additional marginal activity at beta-2 adrenergic receptors results in some concomitant peripheral vasodilation. This combination results in increased heart rate and augmented cardiac output, typically with only minimal changes in blood pressure. Dobutamine may also reduce cardiac sympathetic activity, with one study showing decreased cardiac sympathetic activity among congestive heart failure patients.[5]

Although cardiac conduction system ischaemia has previously been postulated as a mechanism for paroxysmal sinus decelerations, there is no clear association between the presence of coronary artery disease and development of paroxysmal sinus decelerations during dobutamine stress echocardiography. In fact, Sulo and colleagues report coronary artery disease in just 1 of 6 (17%) patients with paroxysmal sinus deceleration, while Attenhofer and colleagues report this phenomenon in 8 of 14 (57%) of their patients.[4,6] The broad definition of coronary artery disease used by Attenhofer and colleagues may account for these differences, whereby inclusion of coronary arterial stenoses of ≥50% may have encompassed some patients with non-haemodynamically significant coronary arterial stenosis.[4] Regardless, there has been no demonstrated increase in the incidence of right coronary arterial disease as a mechanism for this phenomenon.[4] Hence, based on available evidence, paroxysmal sinus decelerations should not be used as an indicator of myocardial ischaemia, but rather conventional assessment of regional wall motion abnormalities should be utilized for the identification of myocardial ischaemia.

The mechanism for paroxysmal sinus decelerations during dobutamine stress echocardiography is likely to be vagally mediated via the Bezold–Jarisch reflex. Here vigorous myocardial contractility stimulates cardiac mechanoreceptors resulting in parasympathetic stimulation.[3] This causes abrupt heart rate deceleration with reflex hypotension, which in some cases may be severe enough to induce an asystolic pause lasting a number of seconds. Further, beta-1 adrenergic stimulation when combined with intravascular volume depletion has been shown provoke a paradoxical bradycardia through stimulation of cardiac vagal afferents.[7] Thus, prolonged pre-procedural fasting may predispose to the development of paradoxical sinus deceleration during dobutamine stress echocardiography.

Atropine, an anticholinergic, blocks parasympathetic activity and is frequently utilized during stress echocardiography. Parasympathetic blockade during dobutamine stress echocardiography may be useful in preventing paroxysmal sinus deceleration. The concomitant use of atropine with dobutamine to achieve target heart rate has been shown to improve sensitivity for the identification of myocardial ischaemia without sacrificing specificity, among those patients who fail to achieve target heart rate utilizing dobutamine alone.[8] Current American Society of Echocardiography guidelines recommend the concomitant use of atropine with dobutamine during pharmacologic stress echocardiography, in the absence of contraindications.[1] Atropine may be administered in 0.25–0.5 mg doses increments at 1 min intervals up to a total dose of 1–2 mg.[1] Early administration of atropine commencing at 20 μg/kg/min of dobutamine, particularly among those patients who fail to increment heart rate as expected, has been shown to reduce test duration without an increase in side effects.[9,10] Given that paroxysmal sinus deceleration typically develop at a dobutamine dose of at least 20 μg/kg/min, early administration of atropine commencing at 20 μg/kg/min may attenuate this effect.[4,6,11]

In our experience, dobutamine should be administered for stress echocardiography using a gradually escalating protocol typically commencing at 5 μg/kg/min and then escalating to 10, 20, 30, and 40 μg/kg/min, at 3 min intervals until target heart rate is achieved. Where detailed myocardial viability assessment is required, incrementing doses at 5 min intervals should be considered. Gradual uptitration of dobutamine dosing may prevent sudden changes in cardiac contractility and hence avoid inadvertent stimulation of cardiac parasympathetic receptors. Careful assessment of heart rate response to initial dobutamine dosing may highlight those

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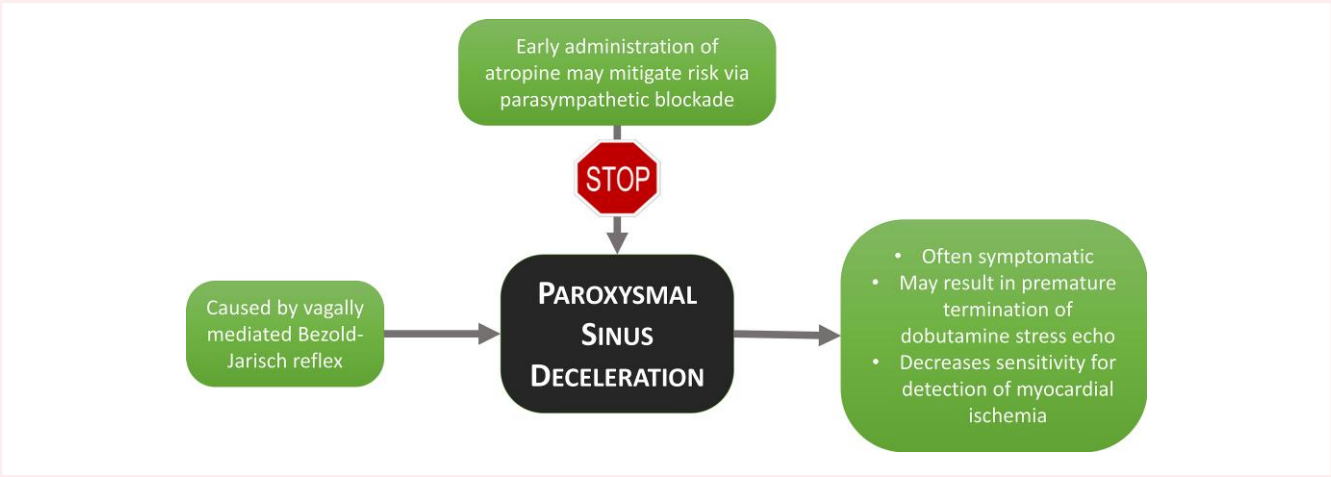

Figure 1 Central illustration: paroxysmal sinus deceleration - cause, effect and mitigating factors.

patients with suboptimal heart rate responses to dobutamine, who we speculate may be at a higher risk of paroxysmal sinus deceleration. Early implementation of atropine, commencing at a dobutamine dose of 20 μg/kg/min, may help to mitigate the risk of paroxysmal sinus deceleration by blocking parasympathetic vagal stimulation. Dobutamine dose escalation can be performed together with atropine administration to achieve target heart rate. It is imperative that target heart rate is achieved, wherever possible, to optimize test sensitivity for the detection of myocardial ischaemia.

In summary, paroxysmal sinus deceleration is an under-reported adverse effect of dobutamine stress echocardiography (*Figure 1*). This phenomenon frequently leads to early discontinuation of dobutamine stress echocardiography, reducing its sensitivity for the detection of myocardial ischaemia due to failure to achieve target heart rate. It should be noted that paroxysmal sinus decelerations are not associated with myocardial ischaemia, but rather represent a vagally mediated phenomenon. Multiple strategies may be employed to mitigate the risk of paroxysmal sinus decelerations including avoidance of intravascular volume depletion and gradual uptitration of dobutamine dosing. More importantly, close observation of heart rate response to low doses of dobutamine together with early atropine administration are useful strategies to avoid provoking paroxysmal sinus decelerations. In order to achieve the goal of reaching target heart rate and optimize the sensitivity of dobutamine stress echocardiography for the assessment of myocardial ischaemia, meticulous care is required on the part of the supervising physician to address and mitigate the potential risk of paroxysmal sinus decelerations.

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References

1. Pellikka PA, Arruda-Olson A, Chaudhry FA, Chen MH, Marshall JE, Porter TR, Sawada SG. Guidelines for performance, interpretation, and application of stress echocardiography in ischemic heart disease: from the American Society of Echocardiography. *J Am Soc Echocardiogr* 2020;**33**:1–41.e48.
2. Varga A, Garcia MA, Picano E. International Stress Echo Complication Registry. Safety of stress echocardiography (from the International Stress Echo Complication Registry). *Am J Cardiol* 2006;**98**:541–543.
3. Geleijnse ML, Krenning BJ, Nemes A, van Dalen BM, Soliman O II, ten Cate FJ, Schinkel AFL, Boersma E, Simoons ML. Incidence, pathophysiology, and treatment of complications during dobutamine-atropine stress echocardiography. *Circulation* 2010;**121**:1756–1767.
4. Attenhofer CH, Pellikka PA, McCully RB, Roger VL, Seward JB. Paradoxical sinus deceleration during dobutamine stress echocardiography: description and angiographic correlation. *J Am Coll Cardiol* 1997;**29**:994–999.
5. Al-Hesayen A, Azevedo ER, Newton GE, Parker JD. The effects of dobutamine on cardiac sympathetic activity in patients with congestive heart failure. *J Am Coll Cardiol* 2002;**39**:1269–1274.
6. Sulo E, Davidsen ES, Lønnebakken MT, Bleie Ø, Saeed S. Paradoxical sinus deceleration during dobutamine stress echocardiography: case series and review of the literature. *Eur Heart J Case Rep* 2022;**6**. doi:10.1093/ehjcr/ytac180.
7. Waxman MB, Asta JA, Cameron DA. Vasodepressor reaction induced by inferior vena cava occlusion and isoproterenol in the rat. Role of beta 1- and beta 2-adrenergic receptors. *Circulation* 1994;**89**:2401–2411.
8. McNeill AJ, Fioretti PM, El-Said SM, Salustri A, Forster T, Roelandt JRTC. Enhanced sensitivity for detection of coronary artery disease by addition of atropine to dobutamine stress echocardiography. *Am J Cardiol* 1992;**70**:41–46.
9. Lewandowski TJ, Armstrong WF, Bach DS. Reduced test time by early identification of patients requiring atropine during dobutamine stress echocardiography. *J Am Soc Echocardiogr* 1998;**11**:236–242.
10. Burger AJ, Notarianni MP, Aronson D. Safety and efficacy of an accelerated dobutamine stress echocardiography protocol in the evaluation of coronary artery disease. *Am J Cardiol* 2000;**86**:825–829.
11. Hossain N, Hossain N, Al-Sadawi M, Haq S. Bezold-Jarisch reflex-mediated asystole during dobutamine stress testing: a case report. *Eur Heart J Case Rep* 2020;**4**:1–6.