

# Bezold–Jarisch reflex-mediated asystole during dobutamine stress testing: a case report

Nimrah Hossain <sup>1\*</sup>, Naseem Hossain <sup>2</sup>, Mohammed Al-Sadawi <sup>2</sup>, and Salman Haq<sup>3</sup>

<sup>1</sup>Department of Medicine, NewYork-Presbyterian Brooklyn Methodist Hospital, 506 6th St, Brooklyn, NY 11215, USA; <sup>2</sup>Department of Medicine, SUNY Downstate Medical Center, 450 Clarkson Ave, Brooklyn, NY 11203, USA; and <sup>3</sup>Division of Cardiology, NewYork-Presbyterian Brooklyn Methodist Hospital, 506 6th St, Brooklyn, NY 11215, USA

Received 14 April 2020; first decision 21 May 2020; accepted 3 September 2020; online publish-ahead-of-print 15 November 2020

## Background

The Bezold–Jarisch reflex (BJR) is a cardioinhibitory parasympathetic response to activation of ventricular mechanoreceptors, which can result in bradycardia, atrioventricular block, or asystole. This phenomenon has been triggered by acute myocardial ischaemia, intra-arterial nitroglycerine use, natriuretic peptides, and with exceptional rarity, in middle-aged women only, by dobutamine infusion during stress echocardiography.

## Case summary

We present the case of a 61-year-old woman who suffered a 5.1-s sinus pause during her 20 µg/kg/min infusion of dobutamine. Recovery was immediate following termination of dobutamine infusion. Concurrent echocardiography was normal, and subsequent cardiac catheterization and electrophysiologic study were normal.

## Discussion

This is the fifth documented case of a severe BJR causing asystole during dobutamine infusion, which adds to the accumulating evidence supporting the benign nature of the condition.

## Keywords

Bezold–Jarisch reflex • Asystole • Dobutamine stress testing • Case report

## Learning points

- The Bezold–Jarisch reflex (BJR) is a cardioinhibitory parasympathetic response to activation of ventricular mechanoreceptors, which can result in bradycardia, atrioventricular block, or asystole.
- It can be triggered by acute myocardial ischaemia, intra-arterial nitroglycerine use, natriuretic peptides, and rarely, by dobutamine infusion during stress echocardiography.
- Asystole caused by dobutamine-induced BJR is a benign condition; with return of normal cardiac rhythm seen on termination of the infusion.

## Introduction

The Bezold–Jarisch reflex (BJR) is a cardioinhibitory parasympathetic response to activation of ventricular mechanoreceptors, which can result in bradycardia, atrioventricular block, or asystole, associated with hypotension, decreased inotropy, and coronary vasodilation.<sup>1</sup> The clinical manifestations of BJR are infrequently recognized yet lead to devastating outcome.<sup>2</sup> This phenomenon has been triggered by acute myocardial ischaemia, intra-arterial nitroglycerine use, natriuretic peptides, and with exceptional rarity, in middle-aged women only, by dobutamine infusion during stress echocardiography.

\* Corresponding author. Tel: +1 443 799 2824, Email: [drhossaindo@gmail.com](mailto:drhossaindo@gmail.com)

Handling Editor: Christian Fielder Camm

Peer-reviewers: Bogdan Enach; Jonathan M. Behar

Compliance Editor: Max Sayers

Supplementary Material Editor: Vishal Shahil Mehta

© The Author(s) 2020. Published by Oxford University Press on behalf of the European Society of Cardiology.

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact [journals.permissions@oup.com](mailto:journals.permissions@oup.com)

## Timeline

Admission to inpatient service	Presented with atypical angina associated with palpitations, dizziness, decreased exercise tolerance, and dyspnoea on exertion; normal electrocardiogram (ECG)
Given intermediate pretest probability	Referred for dobutamine stress echocardiogram
Starting dobutamine stress echocardiogram at 10 µg/kg/min	No ECG changes
Dobutamine at 20 µg/kg/min	ECG demonstrated asystole with 5.1 s sinus arrest
Exam was terminated	Following resolution of the sinus arrest, the patient developed brief sinus bradycardia followed by resumption of normal sinus rhythm
Referred for coronary angiography	Normal coronary angiography
Referred for electrophysiology study	Normal study
Loop recorder implanted	To record any further arrhythmia events
No further events noted	4 months after the event
No follow-up for device interrogation	12 months after the event

## Case presentation

A 61-year-old South Asian female with past medical history of hypertension, hyperlipidaemia, diabetes mellitus complicated by neuropathy, and gastroesophageal reflux disease presented to the emergency department for atypical angina associated with palpitations, dizziness, decreased exercise tolerance, and dyspnoea on exertion. On examination she was overweight, breathing comfortably on room air at rest, cardiac exam was normal, and there was no jugular venous distension. Given her risk factors, the patient was considered to have intermediate pretest probability for coronary artery disease. She was admitted as an inpatient and an acute coronary syndrome was excluded by serial negative cardiac enzymes and normal electrocardiogram (ECG). She was therefore referred for dobutamine stress echocardiography.

Rest ECG demonstrated normal sinus rhythm (Figure 1A). Baseline heart rate (HR) 65 b.p.m., systolic blood pressure (SBP) 120 mmHg, diastolic blood pressure (DBP) 80 mmHg, asymptomatic (Table 1). Baseline echocardiogram demonstrated normal cardiac wall motion, normal left ventricular size and systolic function, and an estimated ejection fraction of 65%. Dobutamine infusion was begun at 10 µg/kg/min, with increase in HR to 93 b.p.m. accompanied by SBP 137, DBP 73 without electrocardiographic changes. Dobutamine infusion rate

**Table 1** Blood pressure and pulse rate recordings during exam compared with timing of infusions

Vital signs measurements			
Stage	BP (mmHg)	HR (b.p.m.)	Time (MM:SS)
Preinfusion	120/80	65	00:00
Dose 1		69	02:34
Dose 1	137/73	93	03:34
Dose 1		91	04:34
Dose 2		70	05:34
Dose 2	201/96	83	06:34
Dose 2	181/85	107	07:34
Dose 3	181/85	109	07:59
Dose 3		42	08:19
Post-infusion		0	08:49
Post-infusion		45	09:12
Post-infusion		62	09:26
Post-infusion		69	09:41
Post-infusion	154/69	48	11:45
Post-infusion	176/72	68	20:50

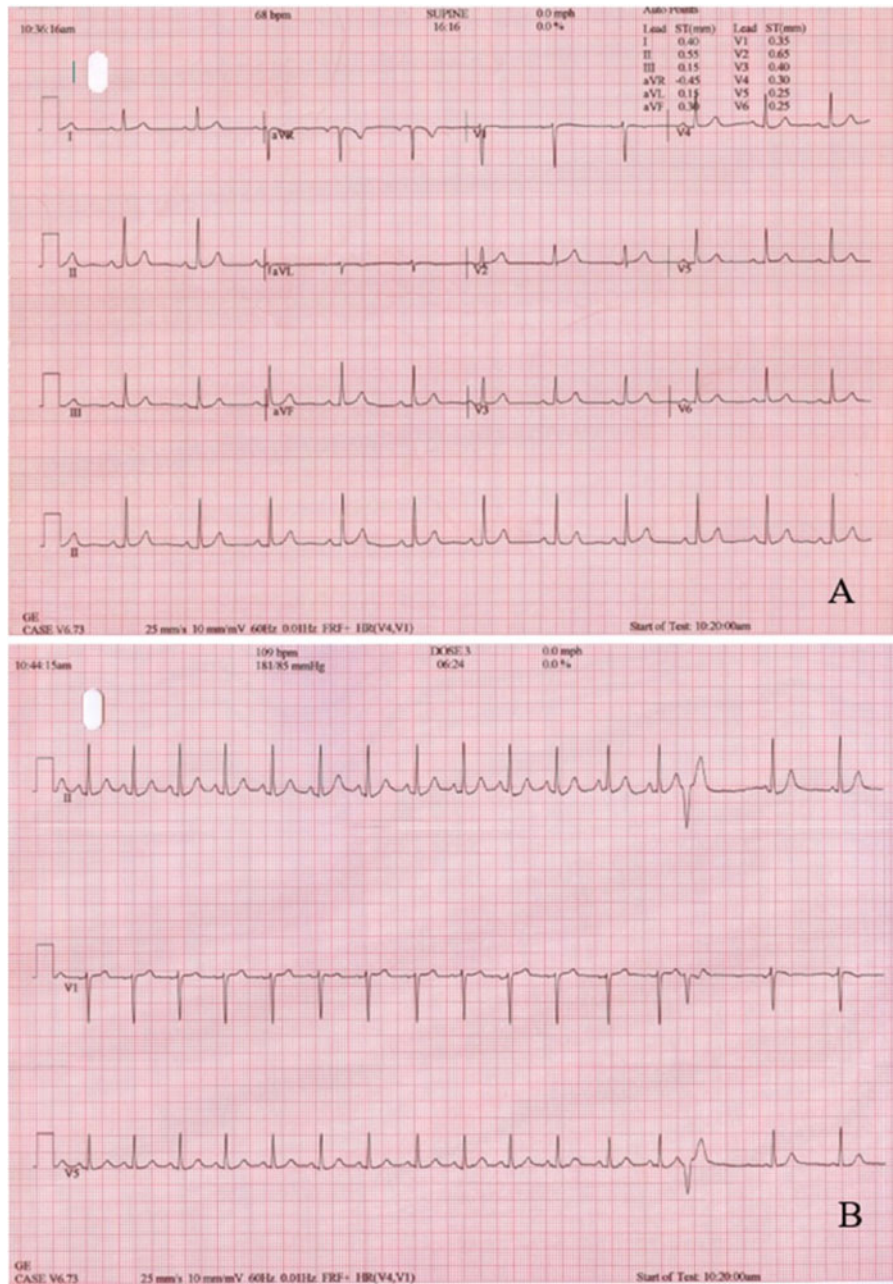
Dose 1: 5 µg/kg/min, Dose 2: 10 µg/kg/min, Dose 3: 20 µg/kg/min. HR, heart rate; BP, blood pressure.

was increased to 20 µg/kg/min with reproduction of chest pain. Shortly after the start of 20 µg/kg/min infusion, ECG demonstrated asystole with a 5.1-s sinus arrest (Figures 1B and 2A). Examination was terminated. Following resolution of the sinus arrest, the patient developed brief sinus bradycardia followed by resumption of normal sinus rhythm (Figure 2B). Throughout the exam, maximal heart rate achieved was 114 b.p.m. (72% of maximal predicted HR). At peak stress, there remained no regional wall motion abnormalities, and there was a reduction in left ventricular rate an augmentation in left ventricular function. The stress echocardiogram was non-diagnostic, though diagnostic sensitivity was limited by suboptimal stress.

Patient was subsequently referred for coronary angiography, which was normal (Figure 3). An electrophysiology study was performed during the patient's inpatient stay. The result was also normal, with mildly prolonged SnRT and normal atrioventricular nodal function. She then had a loop recorder implanted to record any further arrhythmia events 1 day after the asystole event. Patient was discharged without symptoms or sequelae. There was no follow-up as of 1 year after device placement, and remote monitoring did not reveal any events as of the last transmission 4 months after device placement.

## Discussion

The BJR is an inhibitory reflex that results in hypotension, vasodilation, and bradycardia.<sup>3,4</sup> It originates in cardiac sensory receptors which are responsive to both chemical and mechanical stimuli.<sup>1</sup> Stimulation of the reflex increases parasympathetic activity via vagal afferents and decreases sympathetic outflow, causing bradycardia, hypotension, and vasodilation. Several offending agents have elicited this reflex. In 1867, the BJR was discovered in animal models using



**Figure 1** (A) Resting electrocardiogram; (B) electrocardiogram during dobutamine infusion at 20  $\mu\text{g}/\text{kg}/\text{min}$ .

veratrum alkaloids.<sup>5</sup> Since then, several other eliciting factors have been described in the literature, including neuraxial and regional anaesthesia.<sup>6,7</sup>

In our literature search, there have been four previously documented cases of BJR-mediated cardiovascular collapse during dobutamine stress testing.

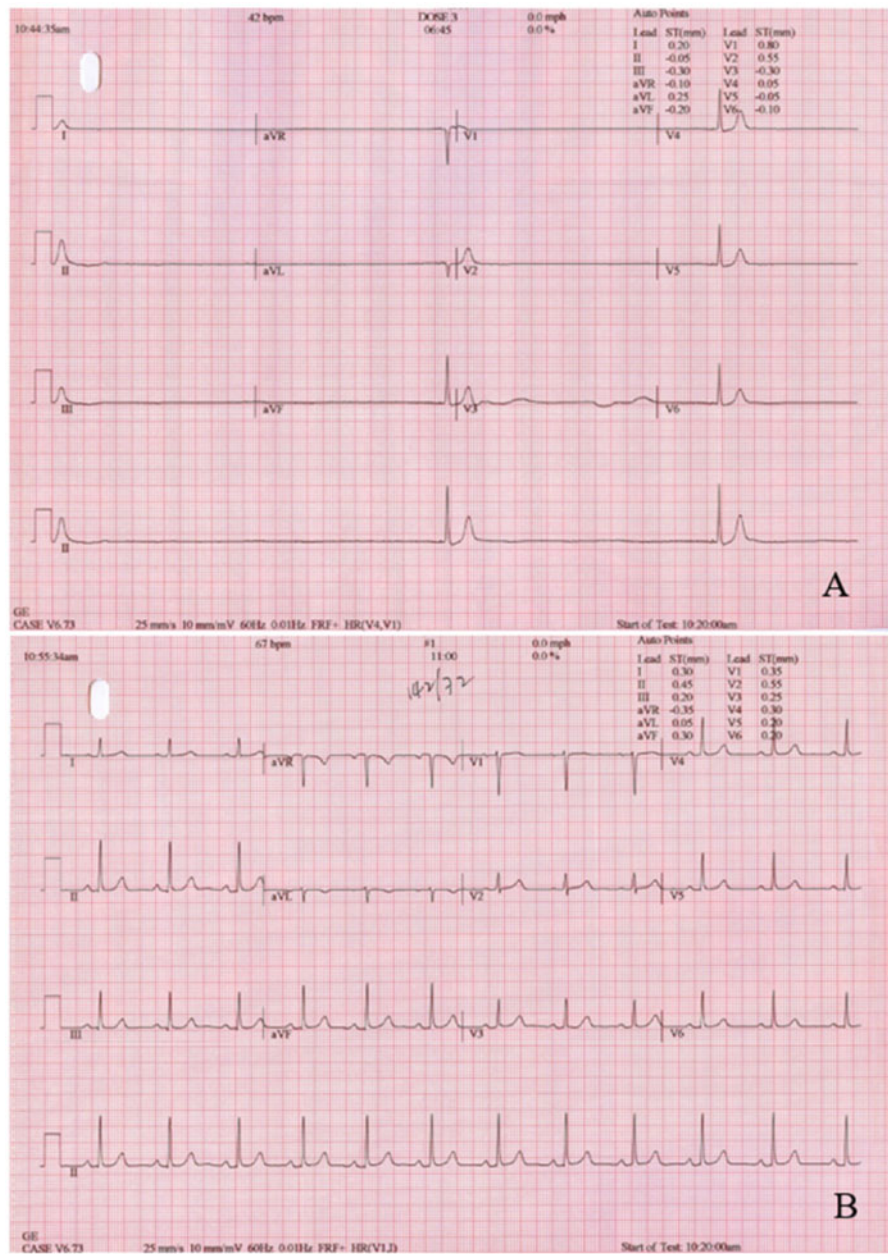
In the first case, a 60-year-old woman presented with chest pain and a non-diagnostic exercise test. A dobutamine stress echocardiographic test was performed. During the 30  $\mu\text{g}/\text{kg}/\text{h}$  infusion the patient was noted to have diffuse hypokinesia of the left ventricle. She was noted to have sinus arrest for 8 s, which responded to

intravenous atropine. The patient returned back to her previous state before the exam and subsequently refused coronary angiography and electrophysiological evaluation.<sup>8</sup>

In the second case, a 48-year-old woman was evaluated for chest pain after an equivocal exercise stress test. During the 40  $\mu\text{g}/\text{kg}/\text{h}$  infusion she developed an idioventricular rhythm followed by asystole. This resolved with cardiac massage. Further echocardiographic, coronary angiography, and electrophysiologic studies were normal.<sup>9</sup>

The third case of BJR-mediated asystole was in a 59-year-old woman with a positive treadmill test for ischaemia. She underwent a dobutamine stress echocardiography. During the 30  $\mu\text{g}/\text{kg}/\text{h}$  infusion





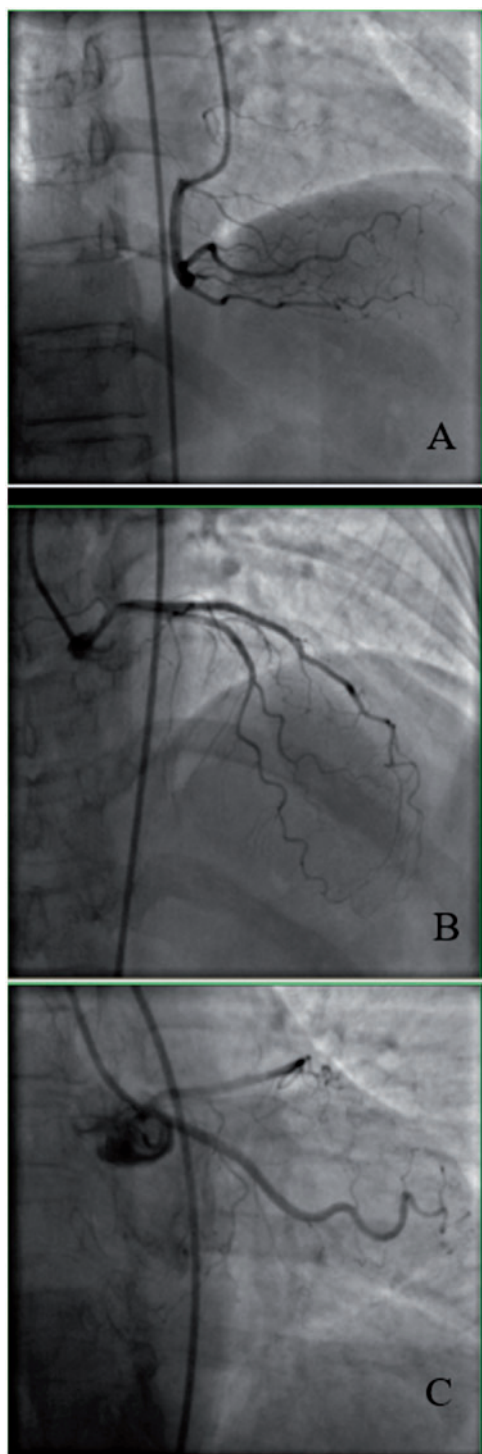
**Figure 2** (A) Electrocardiogram during dobutamine infusion at 20  $\mu\text{g}/\text{kg}/\text{min}$  (continued); (B) post-resuscitation electrocardiogram.

she was noted to have non-sustained ventricular tachycardia and bradycardia, ultimately progressing to asystole for 8.4 s. Intravenous atropine was given, and the patient's heart rate returned to baseline. Further coronary angiography and echocardiogram were normal, and the patient was discharged<sup>10</sup>

The last documented case, in 2015, describes a 60-year-old female who was referred for dobutamine stress echocardiography after complaints of exertional chest pain and an inconclusive exercise stress test done 1 month prior to presentation. During the stress echocardiography, shortly after the 20  $\mu\text{g}/\text{kg}/\text{h}$  infusion

she developed sinus arrhythmia, which progressed into asystole. Dobutamine infusion was stopped, chest compressions and intravenous atropine were given, resulting in return of sinus rhythm. An echocardiogram done immediately after resuscitation showed no apparent abnormalities, coronary angiography was normal.<sup>11</sup>

The management of dobutamine-induced asystole in the cases described in this article was managed with abrupt cessation of dobutamine infusion, followed by adherence to resuscitative protocols put forth by the American Heart Association.<sup>2,12</sup> In three of four cases,



**Figure 3** (A) Right coronary angiography; (B) left coronary angiography; and (C) left anterior descending angiography.

the patient received intravenous atropine, which is the recommended treatment for suspected asystole or bradycardia caused by cardioinhibitory reflexes.<sup>8,10,11</sup>

In cases of dobutamine-induced asystole, evaluation by coronary angiography is key to ruling out inferior wall ischaemia, which can

cause sinoatrial and atrioventricular nodal dysfunction.<sup>13</sup> In the patients described in this article, the asystole resolved with prompt management, and further workup was not indicative of other aetiologies. Paradoxical sinus deceleration occurring during dobutamine infusion occurs in 8% of patients. Most commonly, it can be seen in patients with pre-existing coronary artery disease. However, it can occur in patients in the absence of ischaemia and other significant cardiovascular pathology, which suggests the presence of a cardioinhibitory reflex.<sup>14</sup> In the cases described above, patients found to have asystole after dobutamine infusion usually had good baseline left ventricular function and an absence of myocardial ischaemia.<sup>8–11</sup>

## Conclusion

Dobutamine stress echocardiography is a commonly used and generally well-tolerated diagnostic modality for detection of cardiac ischaemia in suspected coronary artery disease. In a study of 3041 people, it was found that the BJR was elicited in only one patient.<sup>15</sup> In the five cases described in this article, it is notable that these events have occurred in women aged 40–60. It is unclear as to the relationship between age- and gender-specific sensitivities to the BJR during dobutamine stress testing. It is also notable that these events occur during high-dose dobutamine infusion and resolve with cessation of dobutamine and administration of atropine. Sinus arrest during dobutamine stress echocardiography remains a rare entity, which continues to be benign.<sup>12</sup>

## Lead author biography



Nimrah Hossain is a PGY-3 Resident in Internal Medicine at NewYork-Presbyterian Brooklyn Methodist Hospital in Brooklyn, New York. She is going on to chief residency at a university hospital with aspirations in cardiology and special interest in cardiac electrophysiology.

## Supplementary material

**Supplementary material** is available at *European Heart Journal - Case Reports* online.

**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.

## References

1. Mark AL. The Bezold-Jarisch reflex revisited: clinical implications of inhibitory reflexes originating in the heart. *J Am Coll Cardiol* 1983;**1**:90–102.
2. Geleijnse ML, Elhendy A, Fioretti PM, Roelandt JR. Dobutamine stress myocardial perfusion imaging. *J Am Coll Cardiol* 2000;**36**:2017–2027.
3. D'Alessio JG, Rosenblum M, Weller RS. The Bezold-Jarisch reflex. *Anesth Analg* 1996;**83**:201–202.
4. Chiladakis JA, Patsouras N, Manolis AS. The Bezold-Jarisch reflex in acute inferior myocardial infarction: clinical and sympathovagal spectral correlates. *Clin Cardiol* 2003;**26**:323–328.
5. Wartier David C, Campagna Jason A, Carter CMD. Clinical relevance of the Bezold-Jarisch reflex. *Anesthesiology* 2003;**98**:1250–1260.
6. Louro da Cruz J, Gomes C, Oliveira C, Fragoso P. Bezold-Jarisch reflex and cardiac arrest under spinal anaesthesia: 8AP6-6. *Eur J Anaesthesiol* 2013;**30**:133.
7. Caldas WJM, Barbosa MF, Dias CP. [Bezold-Jarisch reflex in a patient undergoing endoscopic sympathectomy for management of refractory angina pectoris: a case report]. *Rev Bras Anesthesiol* 2018;**68**:96–99.
8. Lanzarini L, Previtali M, Diotallevi P. Syncope caused by cardiac asystole during dobutamine stress echocardiography. *Heart* 1996;**75**:320–321.
9. Salustri A, Biferali F, Palamara A. Cardiac arrest during dobutamine stress echocardiography. *G Ital Cardiol* 1997;**27**:69–71.
10. Pinton R, F<sup>o</sup>h, Lemke W, França Neto OR. Assistolia Durante Ecocardiograma De Estresse Com Dobutamina. *Arq Bras Cardiol* 1998;**70**:435–436.
11. Parent M-E, Lepage S. A heart stopping case of the Bezold-Jarisch reflex. *Case Rep Cardiol* 2015;**2015**:1–3.
12. Geleijnse ML, Krenning BJ, Nemes A, van Dalen BM, Soliman OI, Ten Cate FJ et al. Incidence, pathophysiology, and treatment of complications during dobutamine-atropine stress echocardiography. *Circulation* 2010;**121**:1756–1767.
13. Cardoso R, Alfonso CE, Coffey JO. Reversibility of high-grade atrioventricular block with revascularization in coronary artery disease without infarction: a literature review. *Case Rep Cardiol* 2016;**2016**:1–6.
14. 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.
15. Pezzano A, Gentile F, Mantero A, Morabito A, Ravizza P. RITED (Registro Italiano Test Eco-Dobutamina): side effects and complications of echocardiographic stress test in 3041 examinations. *G Ital Cardiol* 1998;**28**:102–111.