# ROLE OF DOBUTAMINE STRESS ECHOCARDIOGRAPHY IN GUIDING THERAPEUTIC DECISION-MAKING IN CORONARY ARTERY DISEASE

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Keywords: coronary artery disease, dobutamine stress echocardiography, coronary artery spasm Abstract: Dobutamine stress echocardiography (DSE) is an established non-invasive diagnostic method used to assess the severity of coronary stenosis or to identify viable myocardium in patient with known or suspected coronary artery disease. During DSE wall motion abnormalities are frequently associated with ST segment depression in 12-lead electrocardiogram (ECG), while ST segment elevation during DSE is an uncommon finding. We report a case of a patient who developed wall motion abnormalities associated with ST segment elevation at DES and presented severe coronary spasm without significant coronary artery stenosis on angiography. The patient had no history of myocardial infarction or critical coronary artery stenosis to justify the ECG and echocardiographic abnormalities. These changes could be explained by a phenomenon of severe coronary spasm, an uncommon cause of false positive results of DSE. Hypercholesterolemia and smoking may have predisposed this abnormal coronary vasoconstricting response.

## INTRODUCTION

Dobutamine stress echocardiography (DSE) is an established non-invasive diagnostic method used to assess the severity of coronary stenosis or to identify viable myocardium in patient with known or suspected coronary artery disease.(1) It is a safe method with few complications, as the studies involving large numbers of patients have already shown.(2,3) The drug most widely used in pharmacological stress, dobutamine, is a well tolerated catecholamine with half-life of 2 to 3 minutes. Due to its sympathomimetic, positive inotropic and chronotropic effects, it increases myocardial consumption and may trigger ischaemia in patients with coronary artery stenosis. Both myocardial ischaemia an myocardial viability assessment is based on wall motion abnormalities and an accurate visualisation of left ventricle (LV) walls is required.(4)

In a significant proportion of patients with poor acoustic window, more frequently due to obesity and lung disease, echocardiography fails to produce diagnostically useful images.(5) 33% of patients referred for stress echocardiography have a suboptimal acoustic window, resulting in a subsequent referrals for other tests because uninterpretable images.(6) Ultrasound contrast agents significantly improves the detection of endocardial border delineation, and result in a better reproducibility in wall motion analysis.(7,8) Ultrasound contrast agent should be used during DSE in case of suboptimal images, defined as the inability to detect two or more contiguous segments in any three of the apical windows.(9)

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#### CASE REPORT

We report the case of a 55-year-old male referred in

our department for diagnostic investigation due to clinical suspicion of coronary artery disease. The patient reported several episodes of chest pain at rest and on exercise, a negative treadmill stress test was performed six months ago, and a medical treatment (acetylsalicylic acid, betablocker, angiotensin-converting enzyme inhibitors, statin) was administered. He had a history of hypertension, diabetes mellitus, dyslipidaemia, smoking (20 cigarettes / day) and chronic pulmonary disease. On admission he was asymptomatic, the baseline 12-lead ECG did not show any abnormality, transthoracic echocardiogram showed normal sized cardiac cavities, left ventricle with preserved systolic function, no abnormalities in segmental wall motion and mild diastolic dysfunction.

The patient underwent a standard protocol of DSE with progressive increased of intravenous dobutamine infusion from 5µg/kg/min to 10, 20, 30 and 40µg/kg/min every three minutes. If the patient did not achieve 85% of age-predicted maximal heart rate, angina or other endpoint, atropine is added to a maximal dose of 2 mg. Ultrasound contrast agent (Sonovue) was administrated due to poor acoustic window (obesity, lung disease). At 40µg/kg/min of dobutamine, the patient presented sudden intense chest pain, dyspnea and diaphoresis. Echocardiography showed akinesia of inferior wall, and the 12-lead ECG showed ST segment elevation in DII, DIII, aVF, depression in DI, aVL, V5-V6, and premature ventricular complexes and periods of bigeminism (figure no. 1). The dobutamine infusion was interrupted, sublingually nitrate was administrated, the chest pain disappeared within five minutes and the ST segment elevation after ten minutes. The test was considered positive and the patient was transferred to coronary care unit. There was a mild elevation of troponin I 0.5 ng/ml without an increase in CK-MB. Evolutionary electrocardiogram and echocardiography

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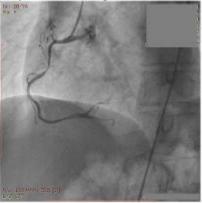
maintained the pre-test aspect.

Figure no. 1. 12-lead ECG showing ST segment elevation in DII, DIII, aVF, depression in DI, aVL, V5-V6, and premature ventricular complexes and periods of bigeminism



After 8 hours, the patient underwent coronary angiography. The right coronary artery was dominant and presented focal stenosis of 30% in the middle segment, the left main was normal and the left anterior descending and circumflex artery presented parietal irregularities. After injecting in the right coronary artery the patient developed a persistent spasm of the middle segment of right coronary artery requiring intracoronary nitrates (figures no. 2,3).

Figure no. 2. Coronary angiography. Persistent spasm of right coronary in the middle segment



A conservative medical treatment was chosen, betablocker theraphy was interrupted, calcium channel blocker and nitrates were introduced. The patient remained free from symptoms and three days later was discharged from hospital, with no other events at 1 respectively 3 and 6 months follow-up.

Figure no. 3. Coronary angiography. After administration of intracoronary nitrates the right coronary artery presented focal stenosis of 30% in the middle segment



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#### DISCUSSIONS

The significance of ST-segment elevation on the 12lead ECG during stress testing is controversial. ST-segment elevation during DSE is uncommon (3%) and mostly associated with LV wall asynergy of fibrotic area in patients with previous myocardial infaction or transmural ischaemia due to critical coronary stenosis. Temporary ST segment elevation without significant coronary artery disease is a very rare event.(10,11)

There are studies and case reports (12-17) showing that coronaryspasm may appear during dobutamine stress echocardiography. In the study by Arruda et al. from 4240 patients who had DSE, a number of 134 (3%) patients developed new stress-induced ST –segment elevation, the majority of patients had 3-vessel disease or high grade stenotic lesion and only 1 was diagnosed as spasm (0.02%).(18)

As a pharmacologic agent, dobutamine has not been associated with coronary spasm. The pharmacodynamic action in the coronary arteries is vasodilatation and increased coronary blood flow, which occurs because of  $\beta$ 2-adrenergic receptors stimulation in the presence of normofunctioning vascular endotheluim. This beta stimulation strongly predominantes over the alpha stimulation, which in turn may cause vasoconstriction. Gorgon et al. demonstrated that abnormal vasoconstricting response in small and medium arteries may occur in the presence of atherosclerotic parietal irregularities, indicating local endothelial dysfunction.

We described a case of a patient who developed ST segment elevation and wall motion abnormalities at DES and presented severe coronary spasm without significant coronary artery stenosis on angiography. The patient had no history of myocardial infarction or critical coronary artery stenosis to justify the ECG and echocardiographic abnormalities. It is also extremely important to point out the sudden onset of the chest pain associated with ST segment elevation and segmental LV dysfunction. These changes could be explained by a phenomenon of severe coronary spasm, an uncommon cause of false positive results of DSE. Hypercholesterolemia and smoking may have predisposed this abnormal coronary vasoconstricting response.(19)

#### CONCLUSIONS

Although DES is a safe method to evaluate patients with known or suspected coronary artery disease, in certain condition dobutamine may trigger coronary artery spasm with wall motion abnormalities and ST segment elevation. If these occur nitroglycerin rather than beta blockers is preferred as the first line of treatment after stopping the dobutamine infusion and if spasm is suspected in the presence of non- significant lesions on coronary angiography conservative medical treatment is recommended over PTCA.

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### REFERENCES

 Pellikka PA, Nagueh SF, Elhendy AA, Kuehl CA, Sawada S G, American Society of Echocardiography et al. Recommendations for performance, interpretation, and

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application of stress echocardiography. J Am Soc Echocardiogr. 2007;20(9):1021-41.

- Picano E, Mathias Jr W, Pingitore A, Bigi R, Previtali M. Safety and tolerability of dobutamine-atropine stress echocardiography: a prospective, multicentre study. Echo Dobutamine International Cooperative Study Group. Lancet. 1994;344:1190-2.
- Mathias Jr W, Arruda A, Santos FC, et al. Safety of dobutamine-atropine stress echocardiography: A prospective experience of 4,033 consecutive studies. J Am Soc Echocardiogr. 1999;12:785-91.
- Schinkel FL, Kaspar M, Staub D. Contrast-enhanced ultrasound: clinical applications in patients with atherosclerosis. Int J Cardiovasc Imaging. 2015;1-14.
- Senior R, Becher H, Monaghan M, Agati L, Zamorano J, Vanoverschelde JV, Nihoyannopoulos P. Contrast echocardiography: evidence-based recommendation by European Association of Echocardiography. European Journal of Echocardiography. 2009;10:194-212.
- Thanigaraj S, Nease RF, Schechtman KB, et al. Use of contrast for image enhancement during ecghocardiography is cost- effective and reduces sdditional diagnosting testing. Am J Cardiol. 2001 87:1430-2.
- Rainbird AJ, Mulvagh SL, Oh JK, McCully RB, Klarich KW, Shub C, Mahoney DW, Pellikka PA. Contrast dobutamine stress echocardiography: clinical practice assessment in 300 consecutive patients. J Am Soc Echocardiogr. 2001;14(5):378-385.
- Malhotra V, Nwogu J, Bondmass MD, Bean M, Bieniarz T, Tertell M, Conliss M, Devries S. Is the technically limited echocardiographic study an endangered species? Endocardial border definition with native tissue harmonic imaging and Optison contrast: a review of 200 cases. J Am Soc Echocardiogr. 2000;13(8):771-773.
- Porter TR, Abdelmoneim S, Belcik JT, McCulloch ML, Mulvagh SL, Olson JJ, Porcelli C, Tsutsui JM, Wei K. Guidelines for the cardiac sonographer in the performance of contrast echocardiography: a focused update from the American Society of Echocardiography. J Am Soc Echocardiogr. 2014;27(8):797-810. doi:10.1016/j.echo.2014.05.011.
- Arruda AL, Barretto RB, Shub C, Chandrasekaran K, Pellikka PA. Prognostic significance of ST-segment elevation during dobutamine stress echocardiography. Am Heart J. 2006;151(3):744.e1.
- Chacine RA, Rainzer AE, Ishimori T. The clinical significance of exercise induced ST segment elevation. Circulation. 1976;54:209-13.
- Yasue H, Omote S, Takizawa A, et al. Circadian variation of exercise capacity in patients with Prinzmetal's variant angina: role of exercise induced coronary arterial spasm Circulation. 1979;59:938-48.
- 13. Deligonul U, Armbruster R, Hailu A. Provocation of coronary spasm by dobutamine stress echocardiography in a patient with angiographically minimal coronary artery disease. Clin Cardiol. 1996;19:755 -8.
- Roffi M, Meier B, Allemann Y. Angiographic documented coronary arterial spasm in absence of critical coronary artery stenoses in a patients with variant angina episodes during exercise and dobutamine stress echocardiography. Heart. 2000;83:E4.
- Kardaras F, Bonou M, Kardara D, et al. Dobutamineinduced transmural myocardial ischemia in a patient with mild coronary lesions. Clin Cardiol. 1996;19:149-51.
- 16. Kawano H, Fujii H, Motoyama T, et al. Myocardial ischemia due to coronary artery spasm during dobutamine

stress echocardiography. Am J Cardiol. 2000;85:26-30.

- 17. Yamagishi H, Watanabe H, Toda I, et al. A case of dobutamine induced coronary arterial spasm with ST-segment elevation. Jpn Circ J. 1998;62:150-1.
- Gordon JB, Ganz P, Nabel EG, et al. Atherosclerosis influences the vasomotor response of epicardial coronary arteries to exercise. J Clin Invest. 1989;83:1946-52.
- 19. Nobuyoski M, Abe M, Nosaka H, et al. Statistical analysis of clinical risk factors for coronary artery spasm: identification of the most important determinant. Am Heart. J. 1992;124:32-8.