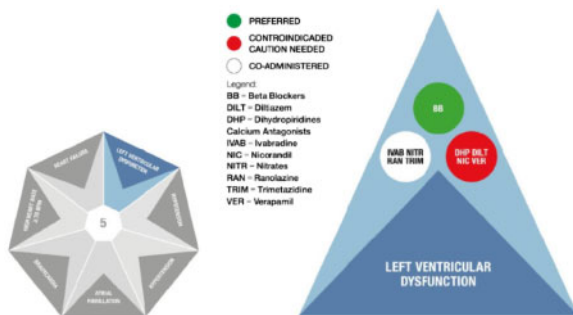


# Angina due to coronary artery disease with left ventricular systolic dysfunction

Yury Lopatin\*

Volgograd State Medical University, Volgograd Regional Cardiology Centre, 106, Universitesky prospekt, Volgograd, 400008, Russian Federation



A 56-year-old Caucasian smoking man with a history of anterior non-ST-segment elevation myocardial infarction, hypertension, hypercholesterolaemia, and obesity consulted the cardiology department for effort-induced angina triggered by different levels of exertion, reaching Canadian Cardiovascular Society (CCS) Class III with strenuous effort. The patient had undergone a percutaneous coronary intervention and drug-eluting stent implantation in the mid left anterior descending coronary artery 5 years before. In addition to angina, which gradually progressed from CCS Class II to CCS Class III over the preceding 3 months, the patient reported fatigue and a decrease in exercise tolerance. He was treated with aspirin 100 mg o.d., atorvastatin 20 mg o.d., perindopril 5 mg o.d., bisoprolol 2.5 mg o.d., and isosorbide dinitrate 20 mg b.i.d. Attempts to increase the daily dose of antianginal medications were unsuccessful due to the development of arterial hypotension.

On physical examination, he showed a regular cardiac rhythm with normal S1 and S2, a mild systolic murmur, and clear lungs. His blood pressure of 110/72 mmHg and his heart rate was 80 b.p.m. Laboratory examinations revealed normal haemoglobin, blood glucose, and creatinine levels. His low-density lipoprotein (LDL) was 82 mg/dL and

N-terminal pro-B type natriuretic peptide was 120 pg/mL. The resting electrocardiography showed a sinus rhythm without significant ST-T wave changes. The 2D echocardiogram detected a mild dilatation of the left ventricle with hypokinesia in the anterior and apical segments and mild mitral regurgitation. Left ventricular ejection fraction was 44%, abnormal left ventricular diastolic indices were also noted (Figure 1). Coronary angiography showed a patent stent in the left anterior descending artery with no obstructive lesions in the coronary arteries (Figure 2).

Based on the results of the evaluation, a decision was taken to manage the patient conservatively.

## What changes should be made in the treatment of this patient?

First, recommendations on lifestyle modification had to be and indeed were given.<sup>1</sup> Smoking cessation, diet, physical activity, and weight management were discussed in detail with the patient. Counselling by professionals about cardiac rehabilitation was also planned. Second, as the LDL target was not reached, it was recommended to increase the dose of atorvastatin to 40 mg o.d. Third, antianginal treatment also had to be optimized. To this end, the long-acting nitrates were stopped and substituted for the selective  $I_f$  current inhibitor ivabradine 5 mg b.i.d. and the anti-ischaemic metabolic modulator trimetazidine 35 mg b.i.d. Five days later, the heart rate was 68 b.p.m., and the dose of ivabradine was increased to 7.5 mg b.i.d. This uptitration was done quickly as the patient was hospitalized at the time and under constant monitoring.

## Why was bisoprolol combined with ivabradine?

The choice of a beta-blocker for this patient is based on the ability of these agents to effectively reduce both angina and cardiovascular morbidity and mortality in patients with stable angina and left ventricular systolic dysfunction.<sup>2</sup>

\*Corresponding author. Tel: +7 (8442) 415623,  
Email: yu.lopatin@gmail.com

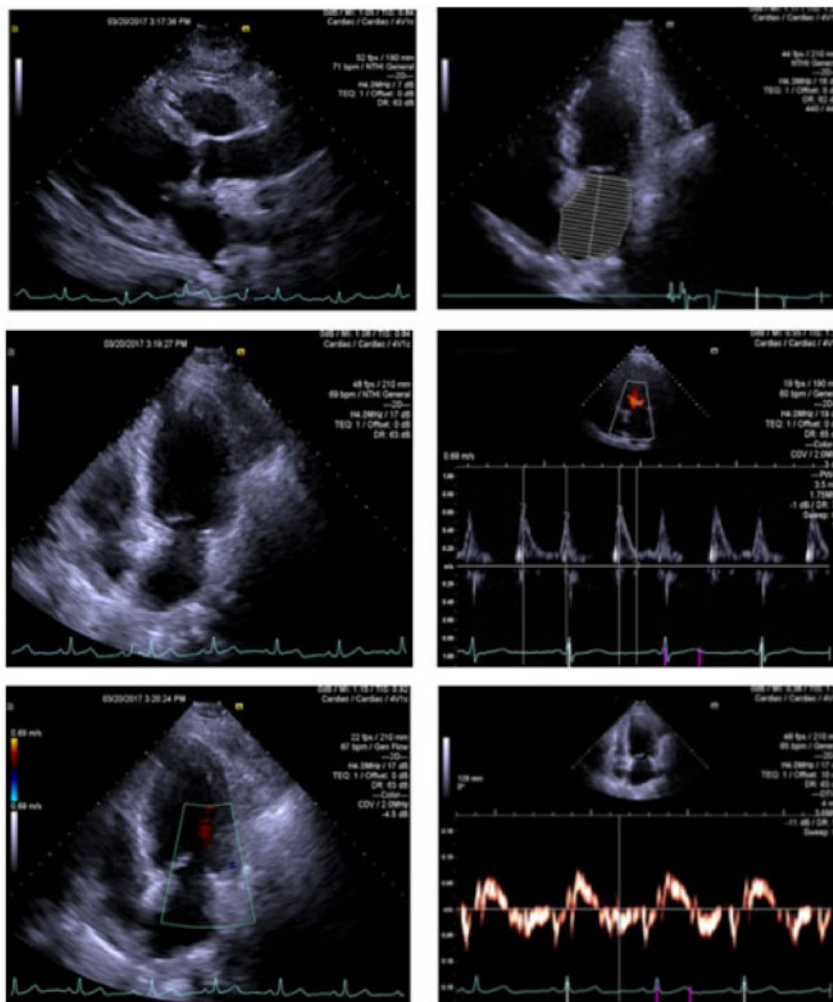


Figure 1 Two-dimensional echocardiogram showing left ventricular remodelling and mild mitral regurgitation.

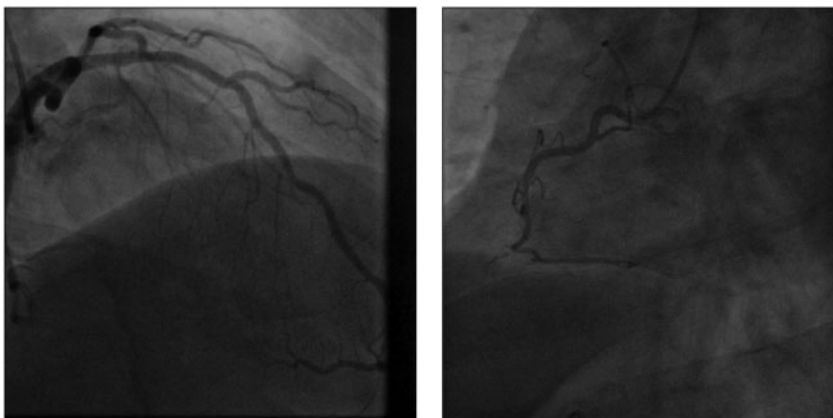


Figure 2 Coronary angiography showing a patent stent in the left anterior descending artery and no obstructive lesions.

Since these beneficial effects are directly correlated with the heart rate-lowering effect of beta-blockers, the daily bisoprolol dose of 2.5mg in a patient with a heart rate of 80b.p.m. should be uptitrated. However, episodes of arterial hypotension occurred in this patient, limiting

beta-blocker uptitration. Taking all this into account, a combination of bisoprolol and ivabradine was the most rational choice. The combination of two heart rate-lowering antianginal agents in this clinical setting is characterized by a greater antianginal efficacy, good tolerability, as well

as the ability to slow down the progression of left ventricular remodelling.<sup>3</sup>

### What additional benefits can be expected by the addition of trimetazidine?

Trimetazidine is considered an effective and safe antianginal treatment for patients with angina and heart failure. There is evidence showing that, in heart failure patients, treatment with trimetazidine is associated with a reduction in hospitalizations and mortality, an improvement in left ventricular ejection fraction, and a positive effect on left ventricular remodelling.<sup>4</sup>

One month later, the patient's angina CCS class decreased to I. The patient demonstrated a good adherence to recommendations on lifestyle modifications: he no longer smokes, he follows the dietary recommendations and he has increased his physical activity. His blood pressure was 120/78 mmHg, heart rate 62 b.p.m., and LDL 70 mg/dL. Six months later, the beneficial effects of the prescribed treatment continued, and an improvement in systolic and diastolic functions was also noted.

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