

Orthostatic intolerance and coronary reserve: a matter of a certain gravity

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A 74-year-old woman came to our attention complaining of the recent onset of shortness of breath during light physical activity. She reported orthostatic light-headedness, occasional dizziness, and pre-syncope symptoms for a duration of the prior year.

The past history included mitral valve prolapse with mild regurgitation, dyslipidemia, and paroxysmal atrial fibrillation. At presentation, the current medications included propafenone, aminosalicilic acid, and simvastatin. A 24-h-ECG demonstrated the presence of polymorphic ventricular premature beats and asymptomatic ST-segment depression. The treadmill exercise test showed limited exercise tolerance, and a significant downward sloping ST-segment depression in leads V₄–V₆ at the beginning of step 2 of the Bruce protocol. An exercise myocardial perfusion scan was consistent with a reduced coronary reserve of the anterior wall.

Upon admission, lying and up-right arterial pressures were 130/80 and 90/50 mmHg, respectively, while a physical examination documented a systolic click and a

late systolic murmur. After medications were suspended, a new treadmill exercise test (Fig. 1, left panel) demonstrated orthostatic hypotension [1] with tachycardia upon standing, and a further decline of arterial pressure and heart rate increase during the Bruce stage 1. Exercise was interrupted due to pre-syncope symptoms after 2'46" when 88% of the predicted maximal heart rate had been reached, and ST depression (–1.0 mm, V₅–V₆) observed.

Considering the patient's characteristics, the estimated pre-test probability of a significant coronary stenosis was 20–50% [2, 3]. The positive likelihood ratio of exercise stress test and myocardial perfusion scan for a significant coronary artery disease was about 10 [4]. Thus, the patient's post-test probability of a significant coronary stenosis was in the 70–90% range. A coronary angiography was thus performed, but ruled out a stenosis of the major coronary vessels.

In the absence of stenosis, a reduction of coronary reserve may be secondary to functional mechanisms [5], including the originally misdiagnosed orthostatic hypotension. We thus hypothesized a critical decline in coronary blood flow during upright physical activity due to an exercise-induced significant decrease in arterial pressure on a pre-existing orthostatic hypotension background.

To test our hypothesis, an exercise bicycle test was performed in the lying posture, a position unlikely to affect arterial pressure. Exercise was interrupted at 7'35" because of physical exhaustion (Fig. 1, right panel). Neither a significant reduction in arterial pressure nor ST-segment changes was observed along the exercise-induced heart rate increase. The maximum heart rate systolic pressure product [6], a broad index of cardiovascular function, increased more when exercise was performed in a lying position than during up-right posture, compared to baseline, although the increase in heart rate was lower in the supine than in the standing position (Fig. 1).

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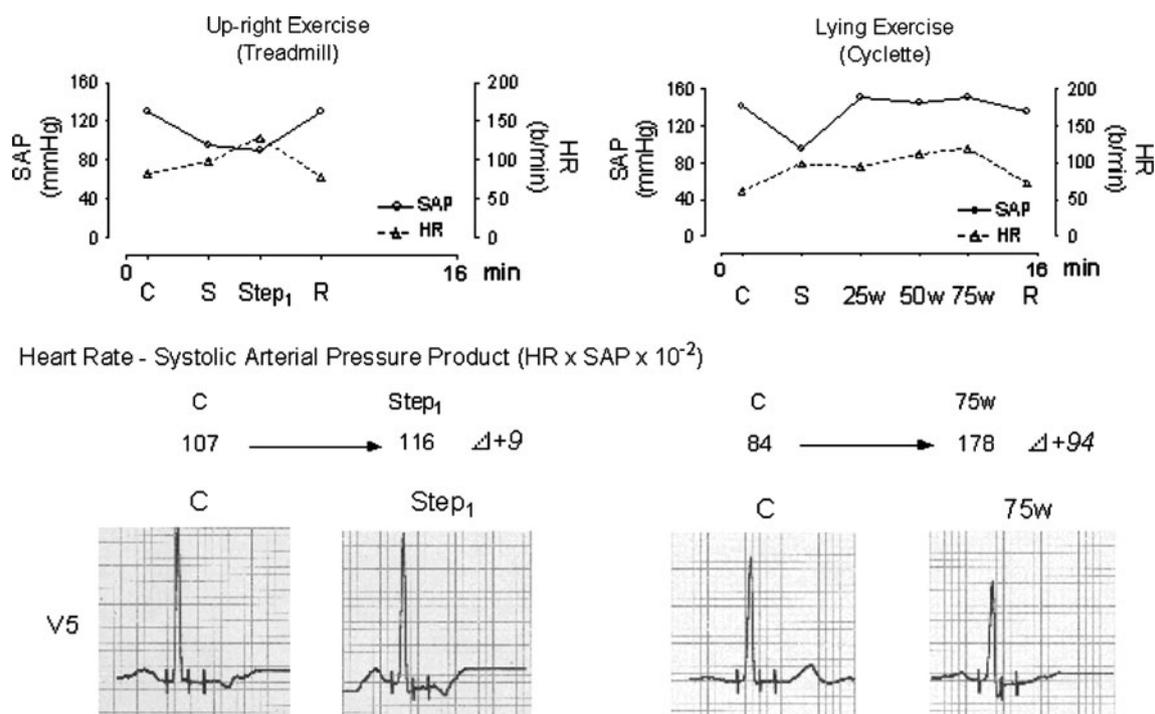


Fig. 1 Time course of the haemodynamics, heart rate: systolic pressure product and ECG S-T segment changes, observed during treadmill up-right exercise (*Step₁*) and cyclette lying exercise (25, 50

and 75 Watts) when compared with lying control condition (C). S indicates standing, R recovery

The diagnosis of functional coronary insufficiency during up-right exercise because of orthostatic hypotension induced by a multiple system atrophy (MSA), and possibly favored by the rise in heart rate with increased oxygen consumption, was ultimately made. This was supported by abnormal sinus arrhythmia and Valsalva maneuver, absence of amyloid substance in umbilical fat, and low resting plasma norepinephrine (81 pg/ml) that increased upon standing (411 pg/ml).

Symptoms and signs of ischemic heart disease may be present in dynamic conditions characterized by a functional reduction of coronary reserve as that observed in our case of MSA, and possibly in other syndromes with orthostatic hypotension including diabetes, alcoholism and Parkinson's disease.

In patients with orthostatic hypotension determining a functional reduction of coronary reserve a lying exercise test could be utilized to stratify the risk before coronary angiography. This could also exclude the influence of heart rate on coronary reserve.

From a therapeutic standpoint, these patients should not have commenced a vasodilator/beta-blocker regimen that might further reduce coronary perfusion by decreasing systemic pressure. Conversely, arterial vasoconstrictors (midodrine) and educational measures (dietary salt and water intake, leg muscles strengthening) aimed at increasing

blood pressure might prove beneficial as it was in our patient who had a longer exercise tolerance after 12 months.

Conflict of interest None.

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