

# Metabolic approach to ischemic heart disease in the elderly

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## Abstract

A 79-year-old hypertensive, diabetic woman with known ischemic heart disease, previously revascularized, was referred to our Cardiology Department because of effort-induced dyspnoea associated with bilateral calf stiffness during a walk at high altitude. A thallium scan with intravenous (i.v.) dipyridamole stress showed a fixed inferior perfusion defect and a reversible perfusion defect in the posterior and lateral wall. Medical therapy was optimized before undergoing further interventional procedures. Anti-hypertensive medications were optimized and anti-anginal therapy implemented with trimetazidine. The patient also began a cardiac rehabilitation program. After 2 weeks, dyspnoea with effort disappeared, and after 3 months her exercise capacity improved by 50%.

**Keywords:** elderly; ischemic heart disease; arterial peripheral disease; trimetazidine

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## Case report

A 79-year-old woman was referred to our Cardiology Department because of dyspnoea with effort associated with bilateral calf stiffness during a walk at high altitude (1800 m) while on holiday. The woman was a writer with a negative family history for ischemic heart disease (IHD), but one brother 18 year her younger brother with diabetes and hypertension. She had an early surgical menopause at the age of 41 years and had never received hormone replacement therapy. She was a heavy smoker (30 cigarettes/day since the age of 45) and overweight (body mass index 27 kg/m<sup>2</sup>). She had a 23-year history of arterial hypertension, treated in recent years with enalapril (5 mg/day) and manidipine (5 mg/day), and a 18-year history of type-2 diabetes treated with gliclazide (30 mg od).

At the age of 68, the patient suffered from an acute inferior myocardial infarction (MI), treated with intravenous thrombolysis, and subsequently underwent coronary artery bypass grafts (left internal mammary artery on left anterior descending artery, right mammary artery on distal right coronary and saphenous graft on I and II obtuse marginal). She was also prescribed aspirin, simvastatin and diltiazem. A low dose of beta-blockers was discontinued after 10 days because of the occurrence of fatigue and bradycardia (45 bpm).

She remained asymptomatic on conventional medical therapy, reporting general satisfactory health condition and took her medication conscientiously. Being a writer, she spent the major part of her time at home and rarely exercised.

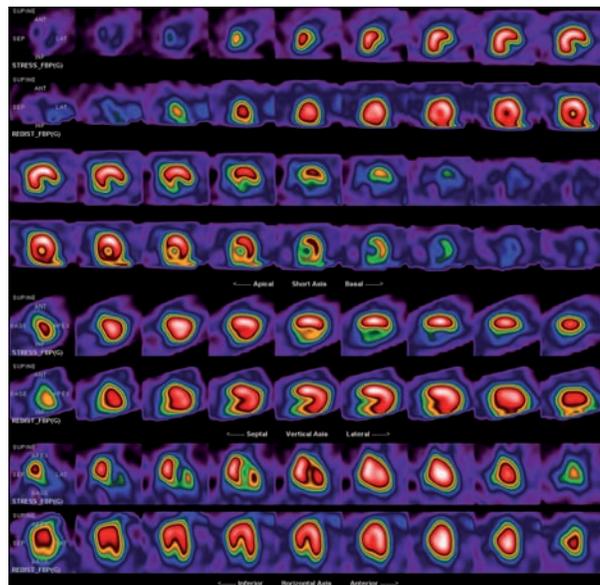
During a trip in a mountain resort she began to feel weak and complained about vertigo and during a walk uphill she stopped because of worsening dyspnoea associated with bilateral calf claudication. Symptoms were repetitively induced by exercise at a fixed level of effort and were both partially relieved by rest.

Because she was limited in her daily activities she decided to return home and was referred to our Cardiology Department. Clinical evaluation revealed slightly elevated blood pressure values (BP 150/90 mmHg) and a non-optimal glycaemic control (fasting plasma glucose 142 mg/dl, HbA1c 7.8%). The other routine blood chemistry was normal.

An electrocardiogram showed sinus bradycardia (56 bpm), and the signs of a previous inferior MI. An echocardiogram showed left ventricular hypertrophy (septum 13 mm, posterior wall 10 mm), a dilated left ventricle (left ventricular end-diastolic diameter [LVEDD] 62 mm, left ventricular end-systolic diameter [LVESD] 48mm, left ventricular ejection fraction [LVEF] of 45%) with infero-posterior and lateral hypokinesia.

A vascular ultrasound assessment showed both the presence of a left carotid stenosis of 70% and peripheral arterial disease (ankle-brachial index 0.8 on both sides).

Due to the presence of bilateral claudicatio, we decided not to prescribe an exercise test but a thallium scan with intravenous (i.v.) dipyridamole stress. The test showed a stress-induced reversible perfusion defect of the infero-posterior and lateral wall (Fig. 1). It was, therefore, decided to prioritize the optimization of medical therapy before undergoing further interventional procedures. Her medical therapy was implemented as follows: aspirin 100 mg od; atorvastatin 20 mg od, perindopril 10 mg od, amlodipine 10 mg od, metformin 500 mg bd, and trimetazidine 35 mg bd (that she bought at the Vatican pharmacy in Rome). She was also started on a cardiac rehabilitation program. After 2 weeks she reported a significant improvement in dyspnoea on effort. At the end of the rehabilitation program her exercise capacity had improved by 270 to 540 meters and she was limited only by fatigue; she obtained a good control of blood pressure (BP 120/75 mmHg) and glucose metabolism (HbA1c 6.5%). A pre-discharge exercise test was stopped in stage 4 of the modified Bruce protocol because of fatigue at 2 minutes without symptoms or electrocardiogram (ECG) changes. The patient was



**Fig. 1** Thallium scan shows a stress-induced reversible perfusion defect of the infero-posterior and lateral wall. Ejection fraction was 45%

seen in our outpatient clinic after 3 months and reported being well and asymptomatic. She was still smoking but she had reduced at 15 cigarettes/day. After 1 year the patient was still in good clinical condition, and she walked every day for 1 hour without dyspnea or claudication.

## Discussion

This case depicts an elderly woman with type-2 diabetes and arterial hypertension affected by cardiac and peripheral atherosclerotic disease. Although she suffered a previous revascularized MI, she remained in good clinical condition for quite a long time. The absence of symptoms, however, may be related, at least in part, to her sedentary lifestyle. The low level of exercise she was used to was below her ischemic threshold for both myocardial and peripheral ischemia, and, for this reason, she remained asymptomatic despite the progression of multivessel disease. However, when she exercised, she developed both coronary and peripheral symptoms probably because the associated increase in blood pressure, due to the exposure to altitudes, lowered her ischemic threshold.

According to her clinical status and age, conservative management was adopted. Indeed, several studies have shown that the optimization of medical therapy reduces events and allows good event-free survival in the treatment of chronic patients with IHD.

The medical management included both the optimization of medical therapy and a program of cardiac and vascular rehabilitation.

It is known that diabetic elderly patients developing a multivessel and accelerated atherogenesis, involving peripheral segments of major coronary arteries and distal peripheral branches, experience changes in myocardial glucose utilization [1, 2], and may have several comorbidities that do not make them the ideal candidates for revascularization procedures (whether surgical or transcatheter) [3]. Transcatheter revascularisation should therefore be reserved for those elderly patients with refractory angina despite optimal medical therapy, and those in whom angina compromises quality of life or the activities of daily living or those with a large area of ischemic myocardium at risk. Therefore, in this elderly woman the main aim of therapy was the reduction of frequency and severity of symptoms (dyspnoea and claudicatio) and the improvement of myocardial ischemia in order to achieve an ischemic threshold greater than that reached during her daily activities, thus leading beneficial effects on quality of life.

As, in this patient, symptoms were precipitated by an instability of the clinical condition, it is clear that any optimal medical treatment cannot be unnoticed without achieving normal blood pressure and glycaemic control.

In addition to hemodynamic optimal medical therapy, a cycle of rehabilitation and trimetazidine were prescribed with the aim of increasing functional performance, to better control cardiovascular risk factors and to improve quality of life. Belardinelli et al showed that the combination of trimetazidine with exercise training is associated with a more marked improvement in functional capacity than trimetazidine or exercise training given alone [4]. More recently, our group showed that the addition of trimetazidine improves functional performance in patients with multivessel

atherosclerosis and claudication undergoing regular exercise training [5], suggesting that the metabolic effect of trimetazidine may be effective not only in the heart but also in the peripheral skeletal muscle. It is, therefore, plausible that therapeutic strategies focusing on metabolic regulation of energy production may exert cardiac and systemic effects. In addition to improving cardiac symptoms, the overall cardiac effects of trimetazidine lead to an improvement of functional capacity allowing a more active lifestyle, and to an improvement in quality of life.

### Conclusion

This case shows that the association of optimal medical therapy and exercise represents a valid alternative to revascularization, not only in those patients for whom surgery is contraindicated, but for most patients with IHD. The adjunct of a metabolic drug, such as trimetazidine, in a patient with multivessel atherosclerotic disease improves myocardial metabolism and may have additional positive effect on skeletal muscles that altogether translate into a beneficial effect on symptoms, functional performance, and quality of life. •

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