Angina due to obstructive coronary artery disease and microvascular dysfunction

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A 69-year-old Caucasian man with diabetes, hypertension, and dyslipidaemia presented with asthenia and recent-onset angina during moderate-intensity effort [Canadian Cardiovascular Society (CCS) Class II]. Sixteen years before, he had undergone a percutaneous coronary intervention (PCI) with stenting of the right coronary artery due to stable angina. He remained clinically stable and asymptomatic for 14 years, when a recurrence of angina with positive exercise electrocardiographic (ECG) testing led to a new PCI procedure with a drug-eluting balloon for a critical right coronary artery in-stent restenosis, as well as to another stent implantation on the proximal left anterior descending artery due to a newly developed critical stenosis. This revascularization procedure was followed by 2 years of clinical stability, then angina recurred, and the patient came to our attention. He admitted that his main concern was no longer angina, which did not have a significant impact on his quality of life, but rather the prognosis of his disease because of the recurrent hospital admissions.

On physical examination, he was in sinus rhythm, bradycardic (heart rate 45 b.p.m.), with a blood pressure of 135/80 mmHg and an oxygen saturation of 98% while breathing ambient air. His blood cholesterol was 184 mg/dL, low-density lipoprotein (LDL) 105 mg/dL, high-density lipoprotein 45 mg/dL, fasting blood glucose 78 mg/dL, and serum creatinine 1.53 mg/dL. High-sensitivity troponin and N-terminal pro-B-type natriuretic peptide were normal. An echocardiogram showed preserved ejection fraction (left ventricular ejection fraction 56%), no regional wall motion abnormalities, mild diastolic dysfunction, and trivial mitral and aortic valve regurgitations.

In your normal clinical practice, which tests would you do at this stage?

Exercise ECG, stress echocardiography, or myocardial perfusion imaging (e.g. nuclear perfusion scan or cardiovascular magnetic resonance imaging) may be considered in this patient.1 We performed an exercise ECG, which was the functional test most frequently performed by the patient during follow-up, and with which he felt more confident. Exercise ECG was positive for ischaemia, and the patient was scheduled for elective coronary angiography. He was on aspirin 100 mg o.d., bisoprolol 2.5 mg b.i.d., ramipril 5 mg o.d., and atorvastatin 20 mg o.d.

Coronary angiography showed a good result of the previous PCIs without significant in-stent restenosis on the right coronary artery and left anterior descending artery, while two angiographically intermediate coronary stenoses (i.e. 50–60% angiographic diameter stenosis) were observed on the proximal segment of the left circumflex and on the ostial left anterior descending arteries (proximal to the previously implanted stent) (Figure 1).

How would you proceed at this point?

Considering the combination of the patient’s symptoms with a positive non-invasive ischaemia testing, as well as the ‘prognostic relevance’ of the diseased coronary segments (i.e. proximal segments of both the left circumflex and left anterior descending arteries, representing a
potential left main equivalent), we decided to proceed with invasive functional testing by measuring fractional flow reserve (FFR) during maximal hyperaemia induced by intravenous adenosine infusion.\textsuperscript{2} Measured FFR values were 0.83 on the left anterior descending artery and 0.87 on the left circumflex; therefore, the two lesions were considered to be haemodynamically non-significant. Recurrent effort angina after successful PCI is probably caused by coronary microvascular dysfunction.\textsuperscript{3}

**Treatment**

Based on the clinical findings and on the results of the coronary angiography and FFR evaluation, the overall consensus was to continue managing the patient by medically optimizing his therapy. The importance of lifestyle, in particular of regular physical exercise and diet, was explained to the patient. The patient was also reminded of the recommendation to continue aspirin indefinitely. Due to the suboptimal lipid profile (LDL 105 mg/dL), atorvastatin was increased to 40 mg o.d. Blood pressure control was appropriate; therefore, the dosage of the angiotensin-converting enzyme inhibitor was confirmed. Based on the observation of persistent bradycardia (which had never been very pronounced in the past with the same dose of beta-blockers) associated with the recent worsening of asthenia disclosed by the patient, we decided to discontinue bisoprolol. Ranolazine 375 mg b.i.d. was also introduced as an adjuvant therapy for this patient, as it improves ischaemia by limiting sodium influx, without affecting heart rate; the dosage was increased to 500 mg b.i.d. after 3 weeks of well-tolerated therapy.

Six months later, the patient admitted an improvement in his symptoms, without asthenia and only mild angina on intense effort (CCS Class I), heart rate was 57 b.p.m., and blood pressure 120/75 mmHg.

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