The combination of coronary artery disease and type 2 diabetes: a therapeutic challenge

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Case description

The patient is a Caucasian, single 45-year-old man who runs a computer business and spends long workdays before the screen. He smokes 5–10 cigarettes per day, attends after-works and parties with considerable alcohol consumption and does not regularly do physical activity. His father had episodes of chest pain at 75 years of age, no family history of type 2 diabetes.

During a ski vacation in February 2016, he suddenly experienced episodes of chest discomfort, shortness of breath, and ‘tiredness’ in the arms and the shoulders. Seeking medical assistance, he was referred to a regional hospital where he was investigated with suspected acute coronary syndrome. Physical examination (detailed in Table 1) disclosed overweight and increased blood pressure. Laboratory analysis further revealed high cholesterol, as well as fasting plasma glucose and HbA1c, confirming type 2 diabetes, but no release of cardiac troponins. Electrocardiogram (ECG) at admission was normal.

The asymptomatic patient was admitted to the cardiology unit for further evaluation and shortly after experienced reoccurrence of chest pain with T-wave inversion on the ECG. Coronary angiography revealed a number of wall-irregularities and diffuse atherosclerosis but no significant stenosis in the left coronary artery (circumflex and left anterior descending), whereas in the right coronary artery a tight stenosis just after crux, before the bifurcation was found. Early intervention with percutaneous coronary intervention and stent implantation was performed with optimal angiographical results. A pharmacological treatment in accordance with guidelines for secondary prevention of coronary artery disease (CAD) with antihypertensive, antianginal, antiplatelet, and glucose-lowering treatment was initiated.1,2 Detailed recommendations for life style changes were also given.

At 1-year follow-up in the outpatient clinic of the same hospital, the patient was asymptomatic and reported good compliance to the pharmacological treatment. A reduction of 4 kg in body weight was observed (Table 1).

Discussion

Here we have an adult obese, smoking male with type 2 diabetes, dyslipidaemia, hypertension, and CAD. The concomitant presence of all these conditions makes him a ‘very high risk’ patient with a markedly increased 10-year risk for cardiovascular fatal/non-fatal events.3 The patient came to our attention almost 2 years after the revascularization procedure and implementation of secondary preventive pharmacological strategies. Despite smoking cessation, reduction in alcohol consumption, moderate weight loss, and pharmacological treatment with statins, antihypertensive, antianginal, antiplatelet, and glucose-lowering agents, several modifiable risk factors remained not at target (Table 1).

The patient had improved his risk factor profile at 1-year follow-up. Using the UKPDS Risk Engine v2.01 (validated in populations with diabetes), the 10-year risk of cardiovascular disease went from 36.9% (17.4% fatal coronary heart disease (CHD); 5.4% risk of stroke; 1.2% fatal stroke) to 18.0% (7.5% fatal CHD; 2.6% risk of stroke; 0.5% fatal stroke).4 However, there is still room for considerable improvement. The achievement of treatment targets for the relevant risk factors, as set by the ESC Guidelines on diabetes and cardiovascular disease (Table 1),5 would reduce his 10-year risk to below 10%.4

Evidence of the impact of optimal multifactorial treatment for the reduction of future cardiovascular risk is well established.5,6 However, this clinical case clearly shows how in the real world the picture is very disappointing. Real world data from Europe (EUROASPIRE IV),7 and from the US,8 suggest that there is a significant number of patients who do not meet the clinical practice guideline targets (e.g. 49% for HbA1c-, 53% for low-density lipoprotein...
cholesterol, and 31% for blood pressure). Thus, our current challenge is to reduce cardiovascular risk by broadening the implementation of optimal secondary preventive strategies.

It was indeed crucial to intensify the treatment of our patient as follows:

- **Antihypertensive drugs.** Initiate a combination treatment by adding to ramipril 10 mg o.d. either a calcium channel blocker or a thiazide-like diuretic with a blood pressure target of 130/80 mmHg.

- **Lipid-lowering drugs.** Increase atorvastatin dose or if it is not tolerated, add ezetimibe aiming at cholesterol levels <5 mmol/L and low-density lipoprotein <1.8 mmol/L.

- **Glucose lowering drugs.** Intensify treatment to reach an HbA1c target of <7% (53 mmol/mol). Considering recent evidence of reduced cardiovascular outcomes with the GLP1-receptor agonists (liraglutide, semaglutide, or albiglutide), in patients with type 2 diabetes and established cardiovascular disease, the addition of one of these agents to metformin and insulin glargine is appropriate. Although their mechanism of action is not fully elucidated, these drugs seem to have a positive impact on several cardiovascular risk factors, including a small reduction in systolic blood pressure, weight loss as well as direct protective vascular and cardiac effects, which may improve the prognosis of our patient.

- **Antiplatelet therapy.** Dual antiplatelet therapy (DAPT) is given up to 1 year after a myocardial infarction (MI). Based on recent findings from the COMPASS and PEGASUS-TIMI 54 trials, prolonged DAPT may be beneficial in patients with previous MI and type 2 diabetes. The addition of very low-dose rivaroxaban (2.5 mg b.i.d.) or ticagrelor (60 mg b.i.d.) up to 3 years to low-dose aspirin should thus be considered.

Unsatisfactory management of patients with type 2 diabetes and CAD as described here is a common clinical scenario. Excellent treatment options warranting the reduction of cardiovascular risk are available but remain underused. Although the data from cardiovascular outcome trials have to various degree been integrated into clinical practice more work is needed to encourage physicians to adopt the evidence-based, cardioprotective therapies in patients with type 2 diabetes who have or are at risk for cardiovascular disease. To focus on individualized

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**Table 1** Characteristics at baseline, 1-year follow-up, and guideline targets

| Variables                          | Admission | 1-year follow-up | Guideline targets |
|-----------------------------------|-----------|------------------|-------------------|
| **Physical examination/demography** |           |                  |                   |
| Age                               | 45        | 46               |                   |
| Gender                            | Male      | —                |                   |
| Smoking                           | Yes       | No               | Quit smoking      |
| Height (cm)                       | 178       | 178              |                   |
| Weight (kg)                       | 118       | 114              | Weight stabilization/reduction |
| BMI (kg/m²)                       | 37        | 36               |                   |
| Heart rate (b.p.m.)               | 72, SR,   | No murmurs      |                   |
| Blood pressure (mmHg)             | 180/105   | 155/95          | ≤130/80           |
| Exercise test                     | Normal    |                  |                   |
| Echocardiography                  | Normal LVEF|                |                   |
| **Laboratory analysis**           |           |                  |                   |
| Haemoglobin; g/L (mg/L)           | 15.1 (151)|                  |                   |
| Troponin T; µg/L                  | <0.02     |                  |                   |
| CK-MB; µg/L                       | 3.7       |                  |                   |
| S-CRP mg/L                        | <5        |                  |                   |
| Cholesterol; mmol/L (mg/dL)       | 7.5 (290) | 5.5 (213)       | ≤5.0 (193)        |
| LDL; mmol/L (mg/dL)               | 5.5 (213) | 3.1 (120)       | <1.8 (70)         |
| Admission fp-glucose; mmol/L (mg/dL) | 12.6 (227)| 8.3 (150)   | <7.0 (126)        |
| HbA1C; mmol/mol (% DCCT)          | 70 (8.6)  | 57 (7.4)        | ≤53 (<7)          |
| **Pharmacological therapy**       |           |                  |                   |
| Aspirin                           | —         | 100 mg          |                   |
| Plavix                             | —         | 75 mg           | — or -1           |
| Atorvastatin                      | —         | 40 mg           | 80 mg             |
| Carvedilol                        | —         | 25 mg           | —                 |
| Ramipril                          | —         | 10 mg           | —                 |
| Insulin glargine                  | —         | 52 IU           | — or -1           |
| Metformin                         | —         | 800 mg *2       | — or | |

Straight arrow indicates continue and upward arrow indicates increase dose. Straight line with block indicates stop treatment. BMI, body mass index; CK-MB, creatinine-kinase myoglobin binding; CRP, C reactive protein; DCCT, diabetes control and complications trial; HbA1c, glycated haemoglobin A1C; LDL-C, low-density lipoprotein cholesterol; LVEF, left ventricular ejection fraction.
target achievement is the lesson given by this real-world clinical case.

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