Clinical case

The role of new cardiovascular risk factors in the assessment of silent coronary artery disease in diabetic patients: when attending guidelines may not be enough

Summary
Silent coronary artery disease (CAD) is common among diabetic patients. The presence of silent CAD is considered a powerful predictor of future cardiovascular events and early death, particularly in diabetic patients. Early identification of diabetic patients with silent CAD can permit their early treatment and consequent improvement of the cardiovascular prognosis. Recent studies showed new powerful predictors of silent CAD in diabetic patients. These predictors are: lipoprotein(a), homocysteine, insulin-resistance and, above all, erectile dysfunction. The case suggests that these new predictors could be effectively used in clinical practice, in order to early identify diabetic patients with silent CAD.

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A 51 years old man attended our outpatients diabetes clinic on september 2001 because of the recent onset of type 2 diabetes mellitus. He had fasting glycemia: 199 mg/dl, hemoglobin A1c: 9.5%, total cholesterol: 253 mg/dl, HDL: 39 mg/dl, triglycerides: 257 mg/dl. LDL was calculated according to the Friedewald formula and was 163 mg/dl. Systolic blood pressure was 165 mmHg and diastolic blood pressure 95 mmHg. These values of blood pressure were similar to those measured in several previous occasions. His waist circumference was 116 cm. According to the National Cholesterol Education Program (NCEP) criteria, the patient had metabolic syndrome. A hypocaloric and hyposodic diet was prescribed. Mild to moderate physical activity was suggested. Therapy with metformin (1500 mg/die) was started.
To better stratify his global cardiovascular risk and to verify the presence of possible complications, the patient was required to perform several laboratory and instrumental checks. Some of the so-called new cardiovascular risk factors, such as homocysteine, Lipoprotein(a) and Homeostasis Model Insulin-resistance Assessment (HOMA) index were also suggested. As any diabetic male, the patient was screened for the presence of erectile dysfunction
Silent CAD is an important life-threatening condition that is particularly common in diabetic patients. Asymptomatic CAD is a strong predictor of future coronary events and early death, especially in diabetic patients. The early identification and treatment of subjects with silent CAD is very important since in this way it is possible to improve greatly their prognosis. ADA recommends screening for silent CAD in diabetic patients either with complications or ECG abnormalities at rest or in the presence of two or more cardiovascular risk factors among those listed in Table 1. Nevertheless, the most recent American Heart Association guidelines are much more conservative in their recommendations for CAD screening in diabetes. Indeed they conclude that screening is not recommended on a routine basis at this time because it would not change management or lead to improvement in ou-
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Outcomes\(^1\). However, the Adult Treatment Panel III of the National Cholesterol Education Program has recently suggested that in people at very high cardiovascular risk, such as diabetic patients with CAD, an LDL goal of <70 mg/dl is a reasonable clinical strategy\(^1\). In high risk persons, such as diabetic patients without evidence of CAD, the recommended LDL goal is <100 mg/dl\(^1\). The identification of subjects with asymptomatic CAD may help to decide the therapeutic option\(^1\).

Increasing evidence is accumulating about the importance of new cardiovascular risk factors in the identification of people at elevated risk for silent CAD. Indeed, we showed that Lipoprotein(a) levels, homocysteine levels and apo(a) phenotypes can be reliable markers of asymptomatic CAD has been shown in diabetic patients\(^1\). Moreover, in these patients a significant association of ED and HOMA index with asymptomatic CAD has been recently reported\(^2,3\). ED has been even proposed as an “atypical” sign of silent CAD\(^4\). Taken together, the above studies seems to show that “new” cardiovascular risk markers, such as genetic risk factors, insulin-resistance and ED may be included into a “global risk panel” in order to better identify subjects to screen for the presence of silent CAD. In addition, among these new cardiovascular risk factors, the presence of ED should be regarded as an atypical sign of silent CAD, especially in diabetic patients with additional traditional cardiovascular risk factors.

In our diabetic patient silent CAD was not diagnosed at the moment of the screening for CAD, but when symptoms occurred. All guidelines have been followed; nonetheless silent CAD was not identified by using usual first-line screening testing. On the basis of the recent evidence of the literature, the present case suggests the importance to the so-called “new” risk factors in the assessment of global cardiovascular risk in diabetic patients. Indeed, in our patient three “non traditional” risk factors were present (high Lipoprotein(a) levels, ED and high HOMA index) in addition to other cardiovascular risk factors reported in Table 1. Moreover, abnormalities of resting ECG were present. Therefore the risk for silent CAD in our patient appeared to be extremely high. In particular the presence of ED strongly predicted the presence of asymptomatic CAD. Exercise ECG is the most widely used screening approach in general practice. Although a negative exercise testing at high workload provides reassurance that severe CAD is not present, standard exercise testing has limitations, including a relatively low sensitivity for the detection of moderate CAD. Therefore, cardiac assessment should require further testing in selected diabetic patients at very high risk of silent CAD. Important additional information can be given by stress myocardial perfusion imaging or stress echocardiography, that are able to increase sensitivity and specificity of exercise ECG. This approach may permit the identification of a higher proportion of subjects with silent CAD and their earlier treatment with possible improvement of cardiac prognosis.

| Table 1. Risk factors to be considered for a possible indication for exercise testing in uncomplicated diabetic patients according to the American Diabetes Association guidelines |
|-----------------|-----------------|-----------------|
| • Total cholesterol >240 mg/dl, LDL >160 mg/dl, or HDL <35 mg/dl |
| • Blood pressure >140/90 mmHg |
| • Smoking |
| • Family history for CAD |
| • Micro or macroalbuminuria |

References


4. Stern S. Symptoms other than chest pain may be important in the diagnosis of “silent ischemia”, or “the sounds of silence”. Circulation 2005; 111:e435-e437.