A 45-year-old man had an acute myocardial infarction and received urgent percutaneous coronary angioplasty with stenting to his left anterior descending artery. He had no family history of coronary artery disease. He was a non-smoker with no known history of hypertension. His LDL was 2.6 mmol/L and fasting glucose was 5.1 mmol/L. His body mass index was 23.6. New cardiovascular risk factors including hsCRP, homocysteine and Lp(a) were also normal. The patient kept on asking his cardiologist what was the contributing factor of his heart attack. The cardiologist could not give him a good explanation until he ordered an oral glucose tolerance test (OGTT) which showed that the patient had impaired glucose tolerance (IGT) with postprandial hyperglycaemia (PPHG); his fasting glucose was 5.6 mmol/l but the 2 hr pp glucose was 10.8 mmol/l. (Normal range <7.8 mmol/L).

Postprandial Hyperglycaemia and Cardiovascular Disease Risk

PPHG contributes to the development of cardiovascular disease (CVD). The damaging effects of PPHG on the cardiovascular system occur even in the nondiabetic range. A significant proportion of dysglycaemic individuals develop vascular damage during the prediabetes stage. Numerous epidemiological studies had demonstrated a strong correlation between PPHG and CV mortality. In a meta-analysis of 38 studies of nondiabetic subjects, the group with the highest postprandial blood glucose level (8.3-10.8 mmol/l) had a 27 percent greater CVD risk than the group with the lowest level (3.8-5.9 mmol/l). Postprandial glucose may be a better predictor of CVD than fasting glucose in several Asian populations. PPHG can now be considered an independent risk factor for CVD even prior to the development of diabetes. A number of experimental studies have also demonstrated the pro-atherogenic role of postprandial glycaemic peaks. Studies have consistently demonstrated the glucotoxic effects of PPHG on blood vessels. PPHG induces oxidative stress, induces endothelial dysfunction and attenuates flow-mediated vessel dilatation, increases carotid intima-media thickness and increases the production of inflammatory cytokines. International guidelines now recognise the link between PPHG and CVD, and highlight the need for integrated management of these conditions. There is an emphasis on identifying and controlling PPHG to reduce the risk of CVD.

Abnormal Glucose Metabolism in Patients with Coronary Artery Disease

The Euro Heart Survey collected data on European patients (n=3,444) with acute or stable coronary artery disease. Approximately one third of them (n=1,524) had known type 2 diabetes mellitus (T2DM) at study start. OGTT was performed in patients without known T2DM and revealed that fewer than half of those tested had normoglycaemia, 37% had IGT and 18% newly diagnosed T2DM. The China Heart Survey, similar to the design of the Euro Heart Survey, enrolled 3,513 Chinese patients with coronary artery disease. T2DM was known to be present in about one third of patients. Among the remaining 2,263 patients, OGTT diagnosed T2DM in 27% and prediabetes in another 37%. Together, the Euro and China Heart Surveys provided strong and universal evidence of a high prevalence of abnormal glucose metabolism among patients with CV disease, highlighting the need to improve strategies for glucometabolic screening and management.

Detecting Abnormal Glucose Metabolism in Patients with Cardiovascular Disease

A high proportion of patients with CVD have impaired glucose metabolism or PPHG which are often under-diagnosed. This condition often remains undiagnosed until a serious CV complication exposes the disease. Most physicians including cardiologists rely mainly on fasting glucose to diagnose abnormal glucose metabolism. A diagnosis based on fasting glucose alone would under-diagnose the prevalence of abnormal glucose metabolism in patients with coronary artery disease. The Euro Heart Survey reported that two-thirds of patients with positive OGTT would have remained undiagnosed if only fasting plasma glucose levels had been considered.

International guidelines recommend that all patients with CVD should be tested by OGTT if their glucometabolic condition is not already known. Routine use of OGTT in the cardiology setting is a simple, cost-effective approach to improve the detection and management of glucometabolic abnormalities in patients with CVD.

Secondary Prevention for Patients with CVD and PPHG
Early institution of glucose-lowering therapy has been shown to be beneficial in patients with CAD and newly diagnosed T2DM by the Euro Heart Survey on Diabetes and the Heart. Among patients with newly diagnosed T2DM who started on glucose-lowering drugs, none of these patients died during the first year follow-up but there were 25 deaths among those who did not receive such treatment. Among CV patients with IGT or PPHG, early institution of glucose-lowering therapy may also be beneficial apart from patient education and lifestyle counselling. So far, only one oral drug has been approved for the treatment of prediabetes and PPHG, the α-glucosidase inhibitor acarbose. Acarbose delays the absorption of carbohydrates from the gastrointestinal tract and lowers postprandial plasma glucose levels which is important for the atherogenic process. Results from the STOP-NIDDM study analysis indicated that the use of acarbose in subjects with IGT not only reduced glucose levels and delayed the onset of T2DM, but also provided benefits in CVD protection. In STOP-NIDDM, acarbose reduced the risk of CV events by 49% including a 91% reduction in the risk of clinical myocardial infarction in patients with IGT. In addition, in a subgroup analysis of these patients after an average time of 3.9 years, acarbose was also shown to slow the progression of carotid intima-media thickness. To assess the efficacy of acarbose in the secondary prevention of CV events among Asian patients with IGT and established CVD, the ACE (Acarbose Cardiovascular Evaluation) study has been started in multiple sites in China Mainland and Hong Kong. This is a randomised, placebo-controlled trial that investigates the effects of acarbose, with secondary prevention of cardiovascular morbidity and mortality as a primary end point. It will follow approximately 7,500 patients for a minimum of four years. There will be major implications on public health in Asia if the results are positive.

Conclusion

PPHG plays a pivotal role in the pathogenesis of CVD and is often neglected in clinical practice. Studies have provided cumulative evidence of high prevalence of PPHG in patients with CVD. Use of OGTT improves the diagnosis of abnormal glucose metabolism and PPHG in patients with CVD. Postprandial glucose should now be a therapeutic target to minimise CVD risks. Appropriate treatment may reduce the risk of further CV events in patients with established CVD. Collaboration between cardiologists and diabetologists is essential to achieve an early diagnosis, to increase awareness of the coexistence of these conditions, and to achieve therapeutic targets.

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