The prevalence of abnormal glucose regulation in patients with coronary artery disease across Europe

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This editorial refers to “The prevalence of abnormal glucose regulation in patients with coronary artery disease across Europe: The Euro Heart Surgery on diabetes and the heart” by M. Bartnik et al. on page 1884

Coronary artery disease (CAD) accounts for over 60% of deaths in people with diabetes, which is at least twice that of the non-diabetic population. In addition, impaired glucose metabolism (IGM), comprising impaired glucose tolerance (IGT) and impaired fasting glycaemia (IFG), is also associated with an increased risk of CAD.

The paper by Bartnik et al. [1] in this issue of the Journal reports the findings of the Euro Heart Survey on Diabetes and the Heart. In a cohort of 4961 people from 110 countries throughout Europe presenting with CAD, only 29% of people with acute CAD and 34% of people with stable CAD were normoglycaemic. In other words, in people presenting to hospital with CAD, it was abnormal to have normal glucose tolerance.

Abnormal glucose tolerance is common in the general population. In Australian men and women aged 65 years, similar to the mean age of the Euro Heart Survey population, approximately 8% had undiagnosed diabetes and 25% had IGM [2]. Therefore, although both undiagnosed diabetes and IGM are common, they are even more common in people presenting with CAD.

Although there are some uncertainties with respect to the representativeness of the Euro Heart Survey population and that not all subjects had an oral glucose tolerance (OGTT), the results have significant implications for clinical practice. People with diabetes have a worse prognosis after a myocardial infarction and strict glucose control improves survival [3].

These data provide strong evidence that people without known diabetes who present with CAD should be screened for undiagnosed diabetes and IGM. But how and when should this be done?

The WHO criteria for classification of glucose metabolism are shown in Table 1 [4]. In an asymptomatic person, diabetes can be diagnosed on the basis of measurement of fasting plasma glucose (FPG) or the 2h plasma glucose (2h PG) during an OGTT. IGT, the more common form of IGM, can only be diagnosed by the 2h PG during an OGTT, whereas IFG is diagnosed on the FPG alone. In Caucasian populations, approximately 50% of undiagnosed diabetes can be diagnosed by an elevated FPG and 50% on the 2h PG. In the Euro Heart Survey, FPG identified only one third of people with previously undiagnosed diabetes or IGM. Therefore, an OGTT is required in a substantial percentage of the population to detect undiagnosed diabetes or IGM. It should be noted that measurement of glycated haemoglobin alone performs poorly as a screening test for diabetes and IGM.

The OGTT is a major barrier to screening for abnormalities of glucose tolerance. It is considered inconvenient to both patients and health professionals and there is concern about its reproducibility. In 555 people without known diabetes participating in the Hoorn study, repeat OGTTs were performed over a 2-6 week period. The reproducibility of normal glucose tolerance was 91%, 48% for IGT and 78% for new diabetes. Most of the movement was in the IGT category with people moving from IGT to normal. Only one person moved from the
diabetic to normal category [5]. Similar findings have been reported in a Chinese population [6]. Such studies show fewer individuals with abnormal glucose tolerance on the second test, possibly related to a change in stress levels due to familiarity with the test procedure or because of self imposed lifestyle changes between tests. However, biological variation is also a significant contributor. Cummings and Fraser [7] reported a biological variation of 11% in their study of 14 healthy people aged 23–48 years who each had 10 OGTTs repeated at approximately one week intervals. Despite these shortcomings, Barrett-Connor [8] concluded in a balanced editorial revisiting the OGTT, that although it is disappointing that we do not have an easier method for screening for IGM, the OGTT remains our most valuable tool for the early recognition of persons with diabetes or who are at increased risk for diabetes and heart disease.

The second issue is when should people be tested? It has been a commonly held view that testing glucose tolerance in the peri-infarct period is inaccurate because of the potential confounding effects of acute stress, left ventricular dysfunction and inflammatory dysfunction [9]. However, the recent study by Norhammer et al. [10] has questioned this and suggests that undiagnosed diabetes and IGM can be detected before hospital discharge following an acute myocardial infarction. They assessed 181 people (mean age 63.5 years) without known diabetes admitted with an acute myocardial infarction with an OGTT prior to discharge and again three months after discharge. At discharge, 34% had normal glucose tolerance, 35% IGM, and 31% new diabetes. After three months the results were similar with the corresponding results being 35%, 40% and 25%, but it should be noted that the degree of concordance was not reported.

In view of the clear and accumulating evidence that glucose tolerance should be routinely assessed in all people without known diabetes who present with CAD, how should people be tested? There is no universally accepted answer to this question which requires a balance between waiting to make a definitive diagnosis and implementing aggressive glucose lowering therapy in the peri-infarct period. Until further study information becomes available, the following is a suggested practical approach. A capillary blood glucose should be measured as soon as possible after admission. If the result is \( \geq 11\) mmol/l, a diagnosis of diabetes should be presumed and can be substantiated by an elevated glycated hemoglobin and aggressive blood glucose lowering therapy should be implemented. All other people should have measurement of FPG on the first day after presentation. An FPG \( \geq 7.0\) mmol/l is consistent with a diagnosis of diabetes and treatment should be commenced. All others should have an OGTT prior to discharge. Many of the concerns related to the OGTT being burdensome to arrange and perform do not apply in the hospital environment.

The Euro Heart Survey has highlighted how common abnormal glucose tolerance is in people presenting with CAD. Its detection is therefore, paramount given the accumulating evidence of the prognostic importance of treating hyperglycaemia in the peri-infarct period. In addition, for people with impaired glucose metabolism, there is the opportunity to implement strategies to prevent or delay the development of diabetes and the specific diabetes-related complications. The results of the Euro Heart Survey provide strong evidence that testing people with acute CAD for abnormal glucose tolerance should be considered routine good clinical practice. Conversely, failing to test has potential medico-legal implications.

### References