Sweet and sour coronary heart disease: results from the China Heart Survey

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This editorial refers to 'The relationship between coronary artery disease and abnormal glucose regulation in China: The China Heart Survey' by D.-Y. Hu et al., on page 2573

In 2002, Norhammar et al. published the results of the oral glucose tolerance testing (OGTT) of 181 consecutive patients admitted to the coronary care unit because of acute myocardial infarction (AMI) and without previously known diabetes. Among these patients, previously unknown diabetes and impaired glucose tolerance (IGT) were much more common than expected, 31 and 35%, respectively. Equally high prevalences were detected when the OGTT was repeated 3 months after the event. This finding was soon repeated in the large material of the Euro Heart Survey and also extended to the patients with stable coronary heart disease (CHD). Of the 923 patients with an acute CHD event, 22% had newly detected diabetes and 36% IGT. Among the 997 patients with stable CHD, 14% had newly detected diabetes and 37% IGT.

It should be noted that 31% of the Euro Heart Survey patients had previously known diabetes. When added to the figures revealed by the OGTT, this means that about half of the CHD patients had diabetes and, additionally, about a quarter had IGT. Similar findings have been reported from a smaller Austrian study among patients undergoing elective coronary angiography. An important feature of the Euro Heart Survey was that two-thirds of the patients with abnormal glucose regulation would have remained undiagnosed without the use of OGTT. The same group has recently provided additional evidence that using different cutpoints for the fasting blood glucose, or a combination of fasting blood glucose, glycosylated haemoglobin A1c and statistical modelling, is insufficient to overcome the problem and cannot reach the same diagnostic accuracy as OGTT.

The aforementioned studies have been limited to European populations and their generalizability to other ethnic groups has been uncertain. Another limitation is that almost a third of the eligible patients did not undergo OGTT in the Euro Heart Survey, which creates some uncertainty around the prevalence estimates of diabetes and IGT. Given these limitations, the new results from the China Heart Survey are an important confirmation and extension of the earlier European findings. Hu et al. report results that are remarkably similar to those of the Euro Heart Survey and demonstrate that in China as well, the usually sour CHD contains a sweet tinge. Among the 3513 patients hospitalized for CHD, 33% had previously known diabetes. After OGTT, the proportion of diabetic patients increased to 53%, and a further 24% had IGT. No difference was observed between patients hospitalized for acute CHD and stable CHD. Furthermore, 81% of patients with new diabetes and 87% of those with IGT would have remained undiagnosed if OGTTs had not been performed.

The acute CHD patients in the China Heart Survey as well as in the Euro Heart Survey are a selected subset of survivors of an acute event. A considerable proportion of CHD events are out-of-hospital sudden deaths or deaths in the emergency room. Since these patients do not survive long enough to have an OGTT, it should be considered whether this could bias the prevalence estimates obtained from these surveys. Data on glucose tolerance and sudden cardiac deaths are understandably scant, but available evidence suggests that diabetes and higher blood glucose levels predispose to sudden cardiac deaths. Furthermore, the fact that in both studies the prevalence of diabetes and IGT was similar in stable and acute manifestations of CHD makes a substantial survival bias unlikely.

An interesting feature of the Chinese study is that the patients were not obese by Western standards. The average body mass index was 24.2 kg/m² and the waist circumference 90 cm among men and 88 cm among women. In the Euro Heart Survey, these were 27.4 kg/m², 99 and 95 cm, respectively. It has been suggested earlier that the cutpoints for obesity, in particular for waist circumference, should be different for different ethnic groups, with Asians having lower thresholds than individuals of European origin. These Chinese data clearly support the need for ethnicity-specific cutpoints for obesity, but further research is warranted to find out whether there could be a common underlying pathology for CHD and impaired glucose regulation, independent of obesity.

The prevalence of diabetes is increasing all over the world. There are, however, no data on the prevalence trends of diabetes and IGT among patients with CHD. It can be hypothesized that with better control of other risk factors, such as high cholesterol, high blood pressure, and smoking, and with simultaneously increasing obesity, the
A proportion of CHD cases due to diabetes and abnormal glucose regulation could be increasing quite dramatically. In Olmsted County, Minnesota, the odds of prevalent diabetes among patients with incident myocardial infarction increased 3% with each increasing year between 1979 and 1998. This suggests that besides substantially improved diagnostics with the use of OGTT, another factor that may have contributed to the findings of the China Heart Survey and the Euro Heart Survey could have been an increasing trend in the prevalence of abnormal glucose regulation among patients with CHD.

The findings of Hu et al. have both clinical and research implications. The obvious clinical implication is that OGTT should be considered for all CHD patients who do not have previously known diabetes. The China Heart Survey and the Euro Heart Survey have shown that OGTT is safe and feasible to perform before hospital discharge when the patient is in stable condition. Since the prevalence of abnormal glucose regulation was the same in both stable and acute CHD patients, it seems logical to consider OGTTs for ambulatory CHD patients as well. The resulting correct classification of glucometabolic state could help to prevent them from getting acute manifestations of CHD, some of which may be fatal within minutes. Patients with type 2 diabetes are known to have increased mortality and recurrence rate after an AMI. Furthermore, a follow-up of the patients included in the GAMi (Glucose tolerance in patients with Acute Myocardial Infarction) study has shown that the newly detected abnormal glucose tolerance is a strong predictor of recurrent, major cardiovascular events with a hazard ratio of 4.18.

Much can be done to reduce the excess risk among CHD patients with abnormal glucose regulation. In diabetic patients, good metabolic control of blood glucose level at the acute stage of myocardial infarction is associated with lower long-term mortality. In stable CHD, the current prevention and treatment guidelines advise particularly strict risk factor control in patients with diabetes or IGT. These guidelines are of course impossible to follow if diabetes is not adequately diagnosed, which seems to be possible only with the more widespread use of OGTT. Among patients with IGT, the development of full-blown diabetes can be prevented or postponed with intensive lifestyle intervention directed towards weight reduction and increased exercise or with the use of medications. Although these studies were not powered to examine the effect of diabetes prevention on CHD endpoints, it seems logical to assume that, in the long run, the development of CHD events will be retarded as well.

As to the research implications, it would obviously be useful to know whether these findings in Europeans and Chinese represent a universal phenomenon, i.e. would be valid also in other ethnic groups. Epidemiological studies should produce better estimates for the prevalence of diabetes and IGT in normal populations to enable better comparisons of CHD patients and unselected control populations. This would also enable the calculation of the aetiological fraction of CHD because of abnormal glucose regulation. Data on trends over time would be particularly valuable for assessing whether the proportion of CHD patients with abnormal glucose regulation is still increasing. Finally, these findings should spark the search for a common biological background for the pathogenesis of impaired glucose regulation and CHD. Obesity and sedentary lifestyle certainly play a role, but there may be other metabolic and genetic factors that are common to these disorders. These factors may represent very basic biological mechanisms, since they have similar effects in at least Asian and European populations and predispose people to the deleterious effects of ‘Western’ lifestyle, which now seems to have spread to China as well.

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References


