

## Oral Glucose Tolerance Test and Acute Coronary Syndrome

### To the Editor,

We read with great interest the article recently published in your journal about the importance of the magnitude of the variation in glycemia in the risk assessment of patients with the acute coronary syndrome (ACS).<sup>1</sup> The authors provide another variant of glucose measurement to those already proposed elsewhere,<sup>2</sup> and which may help us determine the risk in our patients.

The relation between diabetes mellitus and coronary heart disease is unquestioned; indeed, this is the main cause of death in diabetic patients. The prevalence of diabetes mellitus is growing and it will become even greater due to the increase in life expectancy and the prevalence of obesity in our population.<sup>3</sup> The percentage of patients seen in cardiology services who have diabetes and coronary disease may well now reach 50% in the real world.

However, we believe that it still remains unclear whether stress hyperglycemia in the ACS is a marker or a risk factor, that is, whether it is a mere spectator of ACS or whether it plays a true role in myocardial damage. Irrespectively, what remains to be resolved is whether glucose lowering treatment is beneficial in this context,<sup>4</sup> and relevant clinical studies are currently under way to elucidate this aspect.

As treatment of stress hyperglycemia has failed to show any conclusive results, we believe that the true emphasis should be on the detection of early stages of abnormal glucose regulation, mainly occult diabetes mellitus (ODM). This latter situation has already

been shown to have a prognostic impact in coronary patients,<sup>3</sup> and starting early glucose lowering treatment seems to improve the events during follow-up.<sup>5</sup> Furthermore, we can improve secondary prevention and adapt it to the objectives of the diabetic coronary patient (low-density lipoproteins <70 mg/dL and blood pressure <130/80 mm Hg). Consequently, performing an oral glucose tolerance test (OGTT) would be advisable to diagnose ODM, even though we recognize its variable reproducibility<sup>6</sup> and the scarce additional information provided by ODM in particular situations, such as coronary interventional procedures.<sup>7</sup>

In summary, we feel that, whilst glucose measurement is useful in patients with the ACS, we should insist on detecting ODM by means of an OGTT (Class I indication, level of evidence: B, in the European guidelines),<sup>8</sup> because in this setting we really will be able to help our patients with demonstrated efficacy.

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Manuel F. Jiménez-Navarro,<sup>a</sup>

Jesús M. de la Hera-Galarza,<sup>b</sup> María J. Molina-Mora,<sup>a</sup>

and Ernesto Hernández-Martín<sup>b</sup>

<sup>a</sup>Área del Corazón, Hospital Clínico Universitario Virgen de la Victoria,  
Malaga, Spain

<sup>b</sup>Área del Corazón, Hospital Universitario Central de Asturias, Oviedo,  
Asturias, Spain

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## Response

### To the Editor,

First of all, we would like to thank the authors of the 2 very interesting letters your journal published regarding our paper,<sup>1</sup> where we presented data on a new parameter to evaluate metabolic control in acute coronary syndrome (ACS) patients: magnitude of glycemia variation during hospitalization, which proved to be an independent predictor of long-term morbidity in non-diabetic, but not in diabetic patients.

Hyperglycemia in non-diabetics is more often a marker of stress response due to more extensive myocardial damage. A higher degree of stress is necessary to achieve the hyperglycemic state, because metabolic control in these persons is usually normal; in contrast, elevated glycemia after ACS in diabetics may be only a surrogate for poor glycemic control, not related with myocardial disease severity.

However, an important number of patients with no history of diabetes who develop hyperglycemia in stressful situations are true diabetics or have impaired glucose tolerance, and represent a higher risk cohort,<sup>2-4</sup> as abnormal glucose regulation is very common in patients with coronary artery disease. Indeed, it was noted that patients with known or newly detected diabetes mellitus were at a particularly high risk for death and other cardiovascular events.

However, a recent study<sup>5</sup> showed that two-thirds of ACS patients who had no previous diagnosis of diabetes had abnormal glucose tolerance by oral glucose tolerance test (OGTT) one week after the ACS, regardless of admission glucose levels, and admission hyperglycemia in non-diabetics did not represent previously undiagnosed abnormal glucose tolerance.

In accordance with European Society of Cardiology recommendations,<sup>6</sup> in our coronary care unit ACS patients with no previous history of diabetes undergo an OGTT on day 5 of hospitalization. In a recent evaluation of our data (including 843 patients), we

found that 246 patients (29.7%) had had a previous diagnosis of diabetes (type 2 diabetes in 90.1%), but after OGTT only 128 patients (15.2%) were found to have normal glucose metabolism (unpublished data). Of the remaining 715 (84.8%) patients, 27 were type 1 diabetics (3.8%), 425 (59.4%) had type 2 diabetes, 58 (8.1%) had impaired glucose tolerance and 205 (28.7%) impaired fasting glucose. Based on these results in a similar population from our coronary care unit, we can hypothesize that a large proportion of non-diabetic patients could be redefined as diabetics after OGTT results.

Nevertheless, our data on magnitude of glycemia variation clearly separated 2 ACS populations, depending on their prognosis: (long-term) diabetics and non-diabetics (or short-term/pre-diabetics – up to 78% of this patient population, based on our previous OGTT data).

If magnitude of glycemia variation were only a surrogate for undiagnosed diabetes, then its prognostic impact should be similar in both populations, given the high prevalence of undiagnosed diabetes and pre-diabetes in the population not previously known to be diabetic.

Available data on admission hyperglycemia and magnitude of glycemia variation seem to point to the existence of different responses to ACS stress by long-term diabetics and other patients (not known to be diabetic prior to ACS). Is there a “metabolic preconditioning” in long-term diabetics?

In order to answer this important question properly, we have to readdress the issue of OGTT data in “non-diabetic” ACS patients, as suggested in your letters. We are therefore in the process of retesting our non-diabetic ACS population with

OGTT post-discharge, and will share the results with the scientific community as soon as they become available, thus contributing further to the clarification of the complex relationships between metabolism, cardiac ischemia and prognosis.

Sílvia Monteiro, Pedro Monteiro, Mário Freitas,  
and Luís A. Providência  
Cardiology Department, Coimbra University Hospital,  
Coimbra Medical School, Coimbra, Portugal

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