

Time Since Diabetes Onset as a Determining Factor in Platelet Reactivity



Tiempo de evolución de la diabetes mellitus como factor determinante en la modificación de la reactividad plaquetaria

To the Editor,

We have read with interest the original article by Vivas et al.¹ The authors do a splendid job of evaluating the hypothesis that intensive glycemic control in patients with coronary artery disease modifies platelet reactivity after 1 year of treatment. The results of their study were negative, as there was no evidence of differences between this strategy and a conventional glycemic control strategy.

This report involves a different approach to a timely issue: the relationship between glycemic control and cardiovascular events, and we consider that a number of comments are warranted. One aspect that caught our attention was the heterogeneity of the study population (diabetic and nondiabetic patients), although hyperglycemia was detected in all of the participants during their hospital stay, which in some patients might be explained by stress-induced hyperglycemia. In addition, the authors do not mention whether occult diabetes was present in this population, a condition that has been reported in some series to have a prevalence of nearly 25% among presumably nondiabetic individuals.² Equally, the time since diabetes the onset in the population with known diabetes mellitus is not specified, a factor that is of major importance when assessing the reversibility of metabolic changes, including those produced in platelets. Moreover, the advanced mean age of the sample and the fact that 20% of the patients had noncoronary vascular disease or kidney disease and 73% were hypertensive leads us to consider that their profile is similar to that observed in the ACCORD trial,³ in which it was found that, in diabetic patients with this profile, intensive glycemic control provides no added value, and can even be harmful. The failure of the results in the report by Vivas et al¹ to demonstrate a difference could be in partial agreement with the findings of the ACCORD trial.³

It would be highly interesting to know whether early intensive glycemic control has reduced platelet reactivity in the population with occult or new-onset diabetes mellitus. Should this be the case, it might partially explain the long-term results of the UKPDS trial,⁴ in which intensive therapy in individuals with newly diagnosed diabetes reduced the risk of myocardial infarction and death from any cause. One of the possible explanations for these findings would be the metabolic memory phenomenon. Sustained hyperglycemia produces glycation of mitochondrial proteins, which form superoxides and advanced glycation end-products, a development that has been found to be one of the bases of diabetic vascular complications. It has been shown that if exposure to hyperglycemia can be delayed early in the process, we can, in turn, delay vascular complications. However, there comes a time (after years of exposure to hyperglycemia) in which glycemic control per se no longer impedes the glycated mitochondrial proteins from

continuing to produce superoxides.⁵ Thus, intensive glycemic control will be beneficial only if it is begun early.

In summary, we feel that, in a diabetic population, the time since onset of the disease^{6–8} is a key factor that could determine whether intensive glycemic control provides added value to the improvement in platelet reactivity, and this may explain the failure of the results of Vivas et al¹ to demonstrate a difference between the two therapeutic strategies. We encourage the authors to test the same hypothesis on early intensive glycemic control in a population with new onset diabetes, because we believe that it may be in these patients that the benefit is to be found.

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Available online 31 January 2014

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