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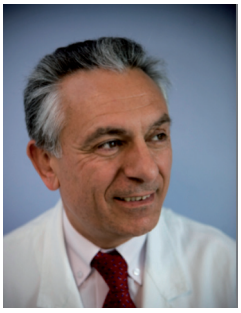
Cardiovascular events in diabetics: a great challenge and an unsolved problem



Mario Marzilli, MD, PhD
Cardiovascular Medicine Division, Cardiothoracic Department, University of Pisa, Pisa, Italy

Correspondence: Professor Mario Marzilli, Cardiovascular Medicine Division, University of Pisa, Via Paradisa, 2, 56100 Pisa, Italy
E-mail: mario.marzilli@med.unipi.it

The prevalence of diabetes in adults worldwide was estimated to be 2.8% in 2000 and is expected to grow to 4.4% by the year 2030, with the number of adults with the disease rising from 171 million to 366 million within that time frame.[1] The greatest relative increase will occur in the Middle Eastern Crescent, sub-Saharan Africa, and India. In developing countries, the majority of people with diabetes are relatively young, currently 45-64 years of age, in contrast to the diabetic population in developed countries, where most are at least 65 years of age. This pattern is likely to be accentuated by the year 2030. In association with increasing diabetes prevalence, increasing proportions with cardiovascular disease–related morbidity and mortality will inevitably result. The risk of myocardial infarction (MI) in diabetic patients with no previous MI is similar to nondiabetic patients that have a history of MI. Indeed, whereas the 7-year incidence rate of MI in nondiabetics with a history of MI at baseline is 18.8% (vs 3.5% in nondiabetics with no prior MI; $P<0.001$), the rate in diabetics with no prior MI is 20.2% (vs 45% in diabetics with prior MI at baseline; $P<0.001$).[2]

Notably, vascular atherosclerotic disease in diabetics differs in several aspects from disease in nondiabetics. In diabetics, atherosclerotic involvement of arteries tends to be more diffuse, to extend to smaller vessels, and to develop earlier. Also, plaques exhibit a larger lipid-rich atheroma, greater macrophage infiltration, and more thrombosis. Furthermore, clinical manifestations of vascular atherosclerotic disease occur more frequently, present with greater severity, and carry a worse prognosis than in nondiabetics.

Accordingly, diabetes is regarded as a major risk factor for cardiovascular adverse events and a key target in preventive strategies.[3] Unfortunately, as it clearly emerges from articles in this issue of *Heart and Metabolism*, data so far are less than encouraging. Standard antidiabetic therapies offer no protection from cardiovascular events, aggressive antidiabetic therapies are no better than standard therapies, and revascularization procedures leave diabetics at much greater risk of adverse events than nondiabetics.

A better understanding of the mechanisms of myocardial ischemia in diabetics appears necessary and urgent if we are to improve this disappointing scenario. Diabetics have an increased prothrombotic milieu, they present with diffuse and severe microvascular dysfunction, and they have an abnormal cardiac energy metabolism: these mechanisms may all contribute to precipitate ischemia and worsen the prognosis. Given this complexity of the pathogenesis of myocardial ischemia, it is naive to expect major improvements in clinical outcomes to result from inno-

vations in catheter-based techniques or from better control of plasma glucose levels.

A more comprehensive approach to ischemic heart disease is necessary, one that takes into consideration nonatherosclerotic and nonvascular mechanisms contributing to myocardial ischemia, including agents that optimize cardiac energy metabolism (ie, trimetazidine). ■

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