The endothelium plays a fundamental role in regulating circulatory homeostasis through the secretion of substances with vasoactive effects, such as nitric oxide, prostacyclin, and endothelin, the expression of surface molecules that modulate the adhesion and activation of leukocytes and platelets, and the release of regulatory factors that control cell proliferation. Endothelial dysfunction is one of the initial events in the development of atherosclerosis—and of ischemic heart disease in particular—and could play a causal role in the onset and progression of the disease. In support of this potential influence, it is a well-known fact that endothelial function is altered in most of the situations in which there is risk of atherosclerosis, such as advanced age, smoking, hypertension, diabetes, and menopause, and that certain changes in lifestyle or pharmacological interventions that reduce the incidence of cardiovascular events also improve endothelial function. Moreover, there is a large body of laboratory data indicating that the endothelium influences leukocyte chemotaxis, lipoprotein oxidation, and thrombogenesis, all of which are key aspects in the development and progression of atherosclerosis.

The method most widely utilized to assess coronary endothelial function is the analysis of the response to intracoronary infusion of acetylcholine, which, under normal conditions, produces vasodilation mediated by the release of nitric oxide, whereas in patients with risk factors or established coronary artery disease, it frequently triggers a vasoconstrictor response. In healthy individuals, acetylcholine infusion also induces an increase in coronary blood flow and a decrease in distal vascular resistance, and these effects are considered to be indicators of microvascular endothelial function. The ultrasound analysis of the changes in the diameter of the brachial artery during reactive hyperemia and venous occlusion plethysmography are less aggressive and more widely available techniques for the study of endothelial function, the results of which, in expert hands, correlate quite well with those of coronary angiography with acetylcholine. Finally, determinations in blood or urine of substances released by normal or dysfunctional endothelium, such as nitric oxide metabolites, von Willebrand factor, certain inflammatory markers, or the soluble forms of a number of adhesion molecules, have also been utilized for the indirect evaluation of endothelial function.

Endothelial function deteriorates in acute myocardial infarction. In experimental models, hypoxia and acidosis change the function of endothelial cells in culture, and during reperfusion following prolonged coronary artery occlusion, there is a reduction in the coronary vasodilator response to acetylcholine and in microvascular function, both in the infarct-related artery, and in more remote regions. There are a number of mechanisms involved in posts ischemic endothelial dysfunction, from the oxidative stress that occurs during the initial minutes of reperfusion to the leukocyte and platelet deposition that takes place over the following hours and days, with the ultimate release of vasoconstrictor substances by these cells. In patients with acute myocardial infarction, a decrease in the coronary vasodilator response has been reported, both in the infarct-related artery and more remote regions. A few years ago, Íráculis et al observed, in 16 patients with acute myocardial infarction successfully treated with thrombolytic agents at Hospital Universitario de Bellvitge in Barcelona, Spain, that the infusion of acetylcholine into the infarct-related artery 9 (2) days after the infarction produced a more marked vasoconstrictor response, which was significantly greater than that observed in a control group of patients with stable ischemic heart disease, and the magnitude of which was correlated with the size of the infarct. The examination was repeated 1 year later in those patients in whom it was possible, and a considerable improvement in the response to acetylcholine was observed.

The question as to whether the different reperfusion strategies applicable in acute myocardial infarction can produce distinct effects on coronary endothelial function...
The same could be said for the potential clinical implications of the drug-eluting stents in endothelial function soon after the infarction, taking into account the fact that there are large series comparing the incidence of ischemic events, the need for revascularization and even mortality, and the situations in which thrombolysis continues to be preferable are quite well defined. As a consequence, the fact that the deterioration of endothelial function in the infarct-related artery is less marked following reperfusion with a metallic stent than after thrombolytic therapy will probably have little influence when it comes to choosing one reperfusion strategy or another.
of serious clinical events with one type of stent or the other, that identify the major predictors of complications associated with drug-eluting stents.\textsuperscript{17}

If it were demonstrated that post-infarction endothelial dysfunction independently predicted the development of adverse events, including those related to the stents, its evaluation—especially if it could be done as noninvasively as possible—could be highly useful, as pointed out by González-Costello et al, in terms of individualizing the management of the patients. In the mean time, our therapeutic decisions in acute myocardial infarction must be based on the large body of clinical information available. Recent trials with drugs like estrogens,\textsuperscript{18} antioxidants,\textsuperscript{19} or L-arginine\textsuperscript{20} oblige us to take certain precaution when it comes to drawing clinical implications from the studies of endothelial function, as it is seen that endothelial function and the prognosis of the patients do not always follow parallel paths.

REFERENCES