Coronary slow flow has been long recognized as an aspecific angiographic pattern in different cardiac conditions. Among the others, it is often observed in patients with normal coronary arteries. Several studies have suggested that increased sympathetic outflow to the cardiovascular system may be responsible for both symptoms and electrocardiographic changes (1-3) that occur in patients with angina pectoris, positive exercise test and angiographically smooth coronary arteries (cardiac syndrome X). Because the autonomic nervous system plays a pivotal role in the regulation of coronary blood flow, increased sympathetic activity could account for both primary reduction of coronary blood flow (4) and reduced vasodilator reserve, which is observed in some patients with syndrome X (5). In these patients, beta-blockade with atenolol has been previously shown to normalize QT interval and dispersion, 2 markers of sympathetic activity (6). However, despite beta-blockade with traditional agents has been previously shown to yield several favourable effects (7), some pharmacological properties of conventional beta-blockers could make them not ideal in patients with syndrome X, especially in those patients exhibiting increased arteriolar resistance. In fact, apart from reducing sympathetic activity, most selective beta-blockers decrease insulin sensitivity, increase blood lipid levels and reduce endothelial function (8-12). More specifically, endothelial dysfunction could be the cause of reduced progression of the angiographic dye (coronary slow flow) observed in some patients with angina and normal coronary arteries. Since endothelial dysfunction (13) and slow flow (14) have been associated to worse prognosis, the identification of more appropriate therapies for these clinical syndromes would be envisaged.

In the present issue of the Anatolian Journal of Cardiology, Güneş and colleagues have evaluated the effects of a new generation beta-blocker, nebivolol, in a population of patients with coronary slow flow (15), undergoing coronary angiography because of suspected coronary artery disease (angina and/or positive exercise testing). In this study, 3 months treatment with nebivolol has been shown to improve atrial indexes of autonomic nervous control and Doppler left ventricular filling pattern. The hypothesis is that these functional and electrophysiological improvements depend on the beneficial effects exerted by nebivolol in terms of prevention of myocardial ischemia, through a mixed anti-adrenergic and endothelial function improvement mechanism.

This is an interesting study for two distinct reasons. First, it confirms the negative electrophysiological effects of an often underestimated angiographic pattern, the so-called "coronary slow-flow phenomenon". Turkish cardiologists have been traditionally very active in studying various clinical contexts in which this angiographic pattern is evidenced and investigating several clinical characteristics associated to its occurrence (16-24). Nevertheless, coronary slow flow is often (worldwide) dismissed as a trivial and benign angiographic finding, even though substantial evidence seems to indicate the contrary (14, 25-26). In fact, this phenomenon has been also associated with serious arrhythmic risk (27), and, despite several therapies have been proposed for its treatment, no systematic studies in this sense have been performed so far. This is indeed the second reason of interest of Güneş et al. study (15), where the effects of nebivolol, a new generation beta-blocker, have been evaluated in a population of patients with coronary slow flow. The observed beneficial electrophysiological and functional effects of nebivolol in these patients are not surprising, if one takes into consideration the pathophysiology of coronary slow flow and the mechanism of action of this new beta-blocker. In fact, apart from the highly selective antagonism of β₁-adrenergic receptors, nebivolol also dilates arteries by mechanisms involving nitric oxide (NO) (28). The mechanism of vasodilator action of nebivolol is attributed largely to activation of endothelial NO synthase in vascular endothelial cells (28), which seem to be strongly involved in the pathogenesis of microvascular dysfunction (29-30). Therefore, the paper of Güneş et al. suggests that nebivolol can be considered an effective new therapeutic tool in the management of patients with angina, angiographical normal
coronary arteries and coronary slow flow who, on the other hand, are often very symptomatic and may carry a prognosis not as good as that of similar patients not presenting slow flow. However, further studies are warranted to evaluate the long-term prognostic implications of coronary slow flow and the potential clinical effects of nebivolol in this context.

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References