Short-Term Statin Therapy and Cardiac Function and Symptoms in Patients With Idiopathic Dilated Cardiomyopathy

To the Editor:

With great interest we read the article by Node et al.1 concerning short-term statin therapy in patients with idiopathic dilated cardiomyopathy (IDC). The demonstrated improvement of left ventricular ejection fraction (LVEF) by simvastatin therapy is intriguing. The authors speculated on several possible mechanisms, including a decrease in plasma cytokines and neurohormones. Although this may certainly have played a role, we think that another potential mechanism should have been discussed. We hypothesize that improvement of LVEF by simvastatin in the present study might be caused by the beneficial effects on myocardial blood flow (MBF) reserve.

In healthy subjects with hypercholesterolemia, statin treatment improves MBF reserve, as measured by positron emission tomography.2 In patients with IDC, MBF reserve is impaired in proportion to the severity of heart failure.3,4 Therefore, it is very likely that a decrease of cholesterol levels in patients with IDC will also lead to an improvement of MBF reserve. Whether such an improvement in MBF reserve in patients with IDC automatically translates into an increase in LVEF may be disputed. Nevertheless, recent work from our institution using positron emission tomography has demonstrated that regional impairment of MBF reserve is associated with decreases in contractile reserve and LVEF.4 The observed improvement in LVEF in the study by Node et al.1 may well have been caused by improvement of MBF reserve leading to increased LVEF.

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Response

We are pleased that Dr van Veldhuisen and colleagues found our study of interest.1 Although we speculated in our paper that the beneficial effects of statins on cardiac function in patients with idiopathic dilated cardiomyopathy may be due to improvements in endothelial function, neurohormonal imbalance, and inflammation, we agree that another potential mechanism may be due to improvement in myocardial blood flow (MBF) reserve. In experimental animals, we have found that statins upregulate coronary vascular endothelial nitric oxide production2 and decrease myocardial oxygen consumption.3 These effects could be the basis for the observed improvement in MBF reserve in hypercholesterolemic subjects with idiopathic dilated cardiomyopathy treated with statins.

We would like to emphasize, however, that improvements in cardiac function with statin treatment probably occur independently of cholesterol lowering. Indeed, we have recently found that statins increase myocardial capillary density in normal and cardiomyopathic Syrian hamsters without significant alterations in serum cholesterol levels.4 This may reflect a preservation of the coronary microvasculature due to a direct vascular protective effect of statins and is consistent with recent studies demonstrating direct angiogenic effect of statins on ischemic limb vasculature.5 The ability of statins, therefore, to positively affect the coronary microvasculature may contribute, in part, to the observed improvements in MBF reserve and myocardial function in patients with heart failure.

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