Although there is increasing evidence of benefit in using statins to treat patients with non-ischaemic heart failure, it is not yet possible to recommend the routine use of these drugs in all heart failure patients, irrespective of the aetiology.
namely through the so-called pleiotropic effects, is gaining increased strength. For example, the reduction in coronary events observed in a timeframe of just 16 weeks is too short to ascribe to the positive effects of cholesterol lowering alone. Statins may retard the progression of chronic heart failure through effects that may directly impact on coronary ischaemia, namely restoration of endothelial function and stabilisation of plaque, but also by additional properties such as effects on myocardial function, downregulation of AT-1 receptor, and inhibition of proinflammatory cytokines.

In animal models of ischaemic heart failure after myocardial infarction, fluvastatin has been found to decrease left ventricular cavity dilation, myocyte hypertrophy, interstitial fibrosis and animal mortality. Although the initial phenomenon inducing heart failure was ischaemic in nature, the progression of the disease, which was significantly altered, was not dependent on further ischaemic events, supporting the non-coronary actions of these drugs in the myocardium.

Furthermore, evidence in favour of the therapeutic benefits of statin treatment in patients with non-ischaemic heart failure, irrespective of serum cholesterol values or atherosclerotic disease, has been recently provided by several authors. In a study published by Node et al., including 63 patients with idiopathic dilated cardiomyopathy randomly assigned to treatment with simvastatin or placebo for 14 weeks, the authors observed an improvement in left ventricular fraction, a reduction in plasma concentrations of TNF-α, interleukin-6 and brain natriuretic peptide and an improvement in flow-mediated brachial artery vasodilatation. Multivariate analysis of changes in LDL cholesterol values showed that serum cholesterol was not a significant predictor of statin-induced improvement in endothelium-dependent vasodilatation in patients with heart failure. These findings suggest that statins may improve cardiac function, in part, by modulating the inflammatory state.

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These beneficial effects may also be observed in patients with heart failure and a normal ejection fraction—that is, diastolic heart failure—as shown in a preliminary study published by Fukuta et al. These authors evaluated a cohort of symptomatic patients with an ejection fraction > 50% during a mean follow-up period of 21 (SD 12) months and found that, after adjustment for differences in baseline clinical variables, statin treatment was associated with lower mortality and improved survival. In a retrospective study in a cohort of elderly patients between 66–85 years with newly diagnosed heart failure, statin use within 90 days following the diagnosis was associated with a lower risk of death. More recently, Sola et al. evaluated the effects of randomly assigned atorvastatin 20 mg or placebo during a 12 month period in 108 patients with non-ischaemic heart failure and reduced left ventricular ejection fraction. These authors found that atorvastatin treatment was associated with an increase in left ventricular ejection fraction and reduced left ventricular end-diastolic diameter and end-systolic diameter. There was also an increase in erythrocyte superoxide dismutase activity and a decrease in serum concentrations of high sensitivity C-reactive protein, interleukin-6 and TNF-α receptor II.

Similar results in systemic inflammation were reported in a randomised, placebo-controlled, crossover study using atorvastatin 10 mg for 16 weeks in patients with non-ischaemic heart failure. However, in another study by Blanke BR et al. these authors found a neutral effect of high dose (80 mg) atorvastatin for 12 weeks on 15 patients on markers of inflammation and endothelial activation like high sensitivity C-reactive protein, TNF-α soluble receptor, TNF-α, intercellular adhesion molecule-1, P-selectin, and FMD. It has been proposed that differences in heart failure severity and statin dose used among studies might explain the distinct responses observed.

**CONCLUSION**

Although there is increasing evidence in favour of a beneficial effect of statin treatment in patients with non-ischaemic heart failure, the studies performed so far are limited by the reduced number of patients enrolled and the short period of follow-up. Thus, at the present time it is not possible to recommend the routine use of this class of drugs in all heart failure patients irrespective of the aetiology. Fortunately there are ongoing studies like CORONA (Controlled Rosuvastatin Multinational Trial in Heart Failure), GISSI-HF (Gruppo Italiano per lo Studio della Sopravvivenza nell’a Insufficienza Cardiaca) or UNIVERSE (Rosuvastatin Impact on Ventricular Remodeling Lipids and Cytokines) that may help us clarify these issues in the near future.

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