Improvement in the function of hibernating myocardium in a patient with heart failure due to coronary artery disease receiving high-dose simvastatin

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We report the case of a 70-year-old man with a history of myocardial infarction and coronary artery bypass grafting, presenting with signs and symptoms of heart failure. Cardiac magnetic resonance imaging demonstrated a small amount of scarring in the anteroseptal wall, moderate left ventricular enlargement, and a left ventricular ejection fraction of 26%. Patient was started on simvastatin 20 mg daily, gradually increased to 80 mg daily, which were maintained for another 4 weeks. Twelve weeks after the initial presentation, the patient experienced a marked improvement in his symptoms. Repeat cardiac magnetic resonance imaging showed global improvement in left ventricular contractility, with ejection fraction of 36% and end-diastolic volume decreasing from 230 to 153 ml. We speculate that high-dose statin therapy had a significant role in improving the ventricular function in our patient by improving the endothelial flow. This hypothesis is presently being tested in a larger prospective trial.

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A 70-year-old man with a history of asthma, myocardial infarction and three-vessel coronary artery bypass grafting 15 years prior to this visit presented with dyspnea on exertion. His medications included fosinopril, diltiazem and nitrates. Patient could not tolerate beta-blockers due to his severe reactive airway disease. Physical exam revealed a blood pressure of 154/86 mmHg, heart rate of 96 b/min, elevated jugular venous pressure, a third heart sound and mild ankle edema. Total and LDL-cholesterol at that time were 225 and 150 mg/dl, respectively. Adenosine stress myocardial perfusion imaging with Tc-99 sestamibi and Tl-201 showed a large area of reversible ischemia involving the inferior, inferoseptal and inferoapical walls with regional motion abnormalities in the apex.

The patient refused coronary angiography and cardiac magnetic resonance imaging (MRI) was obtained. Delayed contrast-enhanced MRI using gadolinium demonstrated only a small amount of scarring in the anteroseptal wall (Fig. 1). Cine-MRI demonstrated moderate left ventricular (LV) enlargement, with an LV ejection fraction (LVEF) of 26%. There was severe hypokinesis of the anteroseptal wall with moderate hypokinesis of the remaining walls (Fig. 2).

As part of a protocol evaluating the effects of high-dose simvastatin on wall motion abnormalities in patients with coronary artery disease using MRI, the patient was started on simvastatin 20 mg daily. This dose was gradually increased over the next 8 weeks to 80 mg daily, which were maintained for another 4 weeks. One week after the initial visit, the dose of diltiazem was decreased from 240 to 120 mg daily, and 3 weeks later torsemide 10 mg daily and spironolactone 25 mg daily were added to control his blood pressure.

Twelve weeks after the initial presentation, the patient experienced a marked improvement in his symptoms and repeat cine-MRI (Fig. 3) showed a global improvement in LV contractility. The LVEF increased to 36% and the LV end-diastolic volume decreased from 230 to 153 ml. His total and LDL-cholesterol after 12 weeks decreased to 146 and 72 mg/dl, respectively.

At the end of the study, patient agreed to undergo coronary angiography that showed near total occlusion in all major coronary

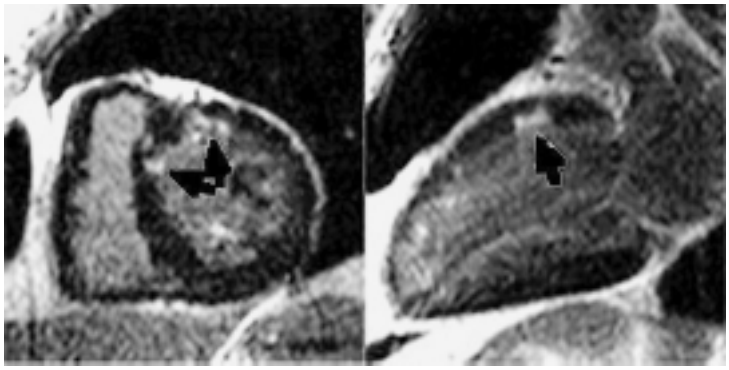

Figure 1. *Delayed contrast-enhanced magnetic resonance imaging in the short-* (left panel) *and long-axis views* (right panel). *Only a small amount of hyperenhancement, depicting myocardial scarring, is seen* (arrows).

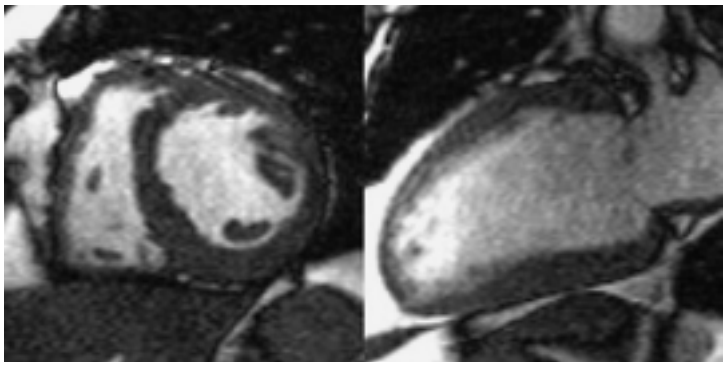

Figure 2. *Corresponding cine-magnetic resonance imaging views demonstrate near akinesis of the anteroseptal wall with moderate hypokinesis elsewhere.*

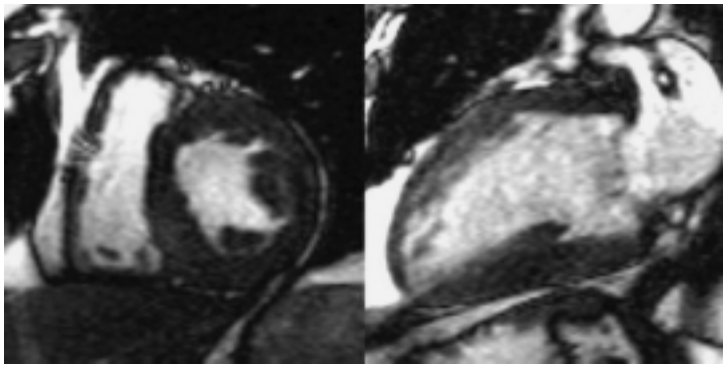

Figure 3. *Repeat cine-magnetic resonance imaging following 12 weeks of high-dose simvastatin demonstrates global improvement in contractility with a significant decrease in left ventricular chamber dimensions. Both sets of cine-images were taken using the same field-of-view.*

arteries and in one of the previous grafts, with minimal occlusion of the other two grafts.

It is known that treatment with HMG-CoA reductase inhibitors improves coronary blood flow in patients with coronary artery disease, probably as a result of the beneficial effects on the endothelial function[1,2]. Indeed, endothelial function can improve after a single lowering of LDL by apheresis[3]. A recent study has shown that inflammatory cytokines, known to have negative inotropic and apoptotic effects, decreased, while the LVEF increased, in patients with idiopathic dilated cardiomyopathy treated with simvastatin[4].

Increasing the blood flow in regions of hibernating myocardium and/or possible cytokine inhibition may have resulted in improvement in the wall motion abnormalities and LVEF seen in our patient. Although is possible that a change in medications be associated

with an improvement in LV function, to our knowledge, there is no published evidence that a decrease in the diltiazem dose or addition of a diuretic will increase the LVEF. Therapies associated with an improvement in LVEF, such as ACE-inhibitors, beta-blockers or aldosterone antagonists usually take 6-12 months to show this effect. In our case, the patient was on spironolactone for only 8 weeks.

Nonetheless, it is tempting to speculate that high-dose statin therapy had a significant role in improving the LVEF in our patient. The hypothesis that LV function can improve in patients with hibernating myocardium due to coronary artery disease with high-dose simvastatin is presently being tested in a larger prospective trial.

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