

Simvastatin Reduces Graft Vessel Disease and Mortality After Heart Transplantation: A Four-Year Randomized Trial

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Introduction.—The most critical long-term complication of heart transplantation is accelerated graft vessel disease (GVD). It is possible that progressive coronary vascular disease is the result of posttransplantation hypercholesterolemia. The efficacy of primary antihypercholesterolemia with simvastatin was compared with that of general dietary therapy in a 4-year prospective, randomized trial of 72 patients who underwent orthotopic heart transplantation.

Methods.—The goal was to maintain posttransplant low-density lipoprotein (LDL) cholesterol levels at below 120 mg/dL. All patients received triple immunosuppression therapy. Patients were randomized to an active treatment group that received a low-cholesterol diet and simvastatin (10 mg/day initially, depending on their LDL cholesterol level, then increased to 10 mg/day at 6 weeks if needed) or a control group that was treated with dietary measures alone.

Results.—During the course of the trial, the mean serum cholesterol level in the simvastatin group was significantly lower than that of the control group (Fig 1). Patients in the simvastatin group also had significantly better long-term survival (Fig 2) and a decreased incidence of GVD in coronary angiographic findings (16.6% vs. 42.3%). At 4 years, 88.6% of patients in the simvastatin group and 70.3% of patients in the control group were alive. There were no significant between-group differences in the occurrence of graft rejections, but there was a decreased tendency toward serious rejections in the simvastatin group, compared with the control group (2.8% vs. 13.5%). In a subgroup of 10 patients from the simvastatin group and 17 patients from the control group, patients with an LDL cholesterol level less than 110 mg/dL had significantly less intimal thickening and a significantly lower intimal index than patients with higher cholesterol levels.

Conclusion.—Compared with dietary measures alone, patients in a treatment group of simvastatin and diet who underwent heart transplan-

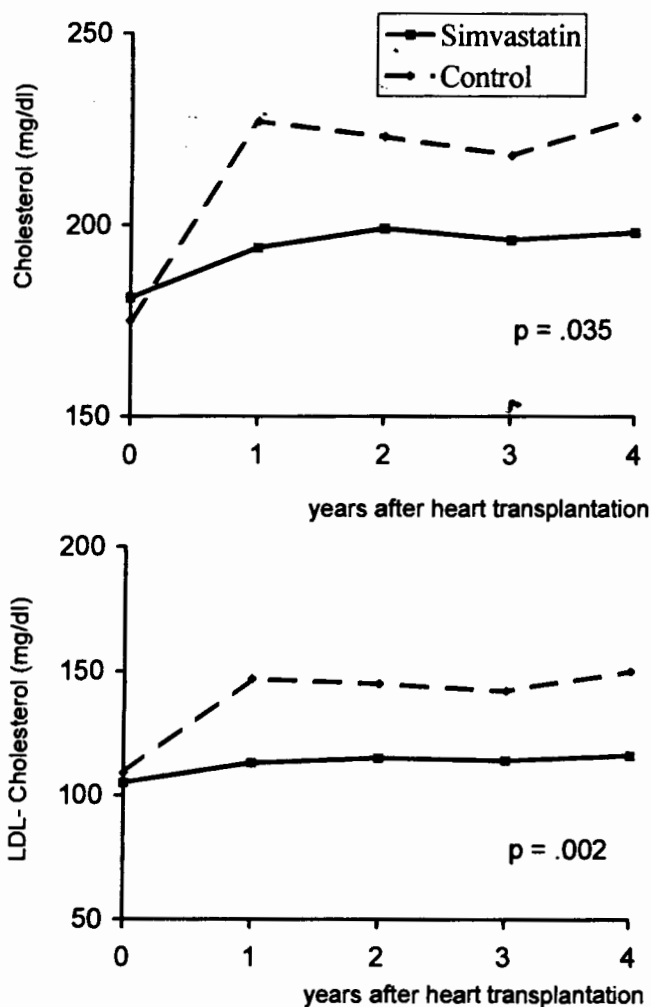


FIGURE 1.—Mean \pm SD cholesterol and LDL cholesterol levels during 4 years after heart transplantation (to convert values to mmol/L, multiply by 0.02586). (Courtesy of Wenke K, Meiser B, Thiery J: Simvastatin reduces graft vessel disease and mortality after heart transplantation: A four-year randomized trial. *Circulation* 96:1398–1402, 1997. Reproduced by permission of *Circulation*. Copyright 1997 American Heart Association.)

tation had a significant reduction in cholesterol levels, a significantly higher long-term survival rate, and a lower incidence of GVD.

► These data strongly suggest that simvastatin or a similar antihypercholesterolemic drug should be used in patients following cardiac transplantation.

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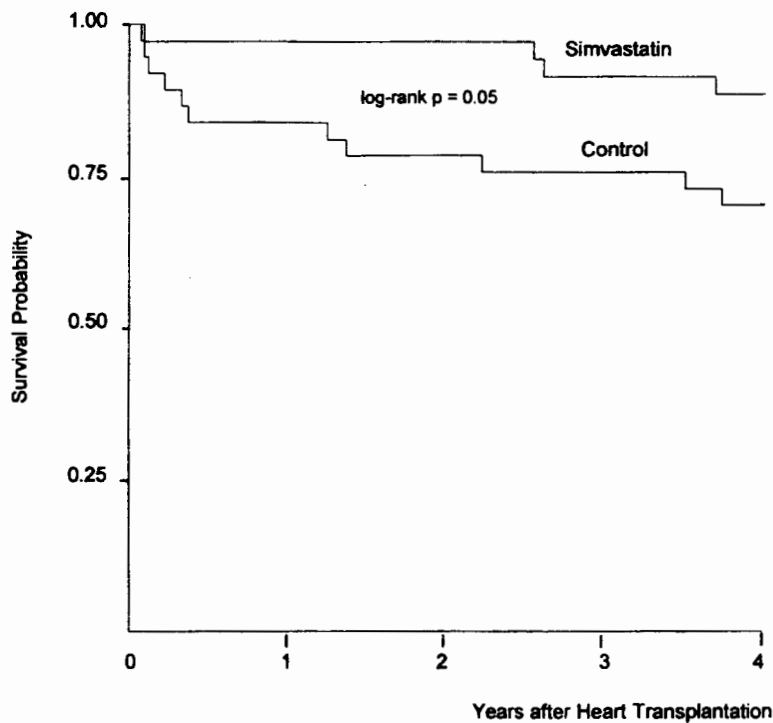


FIGURE 2.—Kaplan-Meier curves for survival 4 years after heart transplantation in the study patients. (Courtesy of Wenke K, Meiser B, Thiery J: Simvastatin reduces graft vessel disease and mortality after heart transplantation: A four-year randomized trial. *Circulation* 96:1398–1402, 1997. Reproduced by permission of *Circulation*. Copyright 1997 American Heart Association.)