Is There a Statin Effect on Arrhythmia and Survival in Patients With Nonischemic Cardiomyopathy?

Goldberger et al. (1), authors of “Effects of Statin Therapy on Arrhythmic Events and Survival in Patients With Nonischemic Dilated Cardiomyopathy”, note that the data “strongly suggests that statins may improve mortality in patients with nonischemic cardiomyopathies.” Although an association has been demonstrated between statin use and survival, it will take more data before an effect can be attributed to statin therapy. The fact that there is no significant difference in the number of appropriate implantable cardioverter-defibrillator (ICD) shocks between patients treated with statins and those not treated with statins does not support the concept that statins have a pleiotropic antiarrhythmic effect.

Another factor that needs to be considered is whether statin therapy in this study is just a marker for a better prognosis. Although data are not presented, it is presumed that patients on statin therapy had higher cholesterol. Studies (2,3) have shown that higher serum total cholesterol is independently associated with a better prognosis in patients with heart failure. Patients without statin therapy may have had poor nutrition or some other type of medical problem related to poor survival (4). It would be interesting to know the albumin levels or other measures of general nutrition in the statin and nonstatin groups.

The investigators (1) note in the limitations section of their study that it is highly implausible to assume that hypercholesterolemia selects a patient population at markedly lower risk. Rather than dismissing this relationship, the inverse relationship between heart failure mortality and cholesterol level should be considered in any future study of possible statin effect.

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Reply

Drs. Coplan and Ramos reemphasize several important points from our study (1). First, because this was a retrospective analysis of a randomized clinical trial, the results must be properly tested in a prospective clinical trial before firm conclusions can be drawn regarding the effects of statins on survival in nonischemic cardiomyopathy. Regarding the mechanism for the observed survival benefit related to statin use in the DEFINITE (DEFiBrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation) substudy, Drs. Coplan and Ramos again correctly point out that the data do not support a pure antiarrhythmic effect, as discussed in our study.

With regard to our interpretation regarding the implausibility that statin use incidentally identified a low-risk population, it should be noted that the subgroup treated with statins was older and had a higher incidence of diabetes. As noted by the investigators and discussed in our study, low cholesterol has been reported to be associated with increased mortality, raising the possibility that absence of treatment with statins represents a selection bias for a high-risk group, perhaps due to poor nutrition. Although cholesterol or albumin levels were not obtained on all participants, there was no difference in body mass index between patients treated with statins and those not treated.

Interestingly, subsequent to publication of the DEFINITE substudy, Go et al. (2) reported reduction in mortality associated with statin use in a large cohort study in which cholesterol levels were only slightly lower in the group not treated with statins.

Finally, Drs. Coplan and Ramos correctly point out that future studies should consider the potential inverse relationship between heart failure mortality and cholesterol level. However, we believe it is implausible that the excess mortality in this DEFINITE substudy was related to low cholesterol in the group not treated with statins.

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