quently of a stroke, and autopsy found clusters of myotubes embedded in the scar tissue. There was no cardiomyogenic differentiation as reflected by the lack of gap junction formation.

Comment

This is the first study and follow-up by the Menashe group. This study addresses the feasibility of such an approach in patients with severe LV dysfunction. However, it is unknown at this time whether the transplanted cells contribute to the overall contractility of the ventricle or whether it is due to the overall improved contraction of the adjacent segments. Substantial work remains to evaluate the time course of survival of these transplanted cells and to determine whether they actually contribute to contraction. More sophisticated molecular imaging will be needed to test these hypotheses in the future. Of particular concern is the incidence of ventricular tachycardia post-transplantation. Whether this condition indicates the development of ventricular foci at the site of implantation, resulting in re-entry pathways, is still to be determined. ■

Statins

Statin Therapy and Timing

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Several decades of observational studies have revealed that cholesterol levels are directly related to the prevalence of coronary artery disease.[1,2] More recent large-scale randomized trials have taught us that lowering cholesterol with statin therapy reduces subsequent cardiac events for patients with chronic coronary artery disease.[3] However, several questions concerning the timing of therapy with statins in other clinical settings remain. Two recent reports attempt to address these issues.

Early Statin Initiation and Outcomes in Patients with Acute Coronary Syndromes

Newby LK, Kristinsson A, Bhapkar MV, et al.
JAMA. 2002;287:3087–3095.

To assess the value of initiating statin therapy early in patients with acute coronary ischemia, an observational study was conducted in 15,900 patients in two Sibrafiban vs Aspirin to Yield Maximum Protection from Ischemic Heart Events Post-acute Coronary Syndromes (SYMPHONY) trials. The trials were designed to determine the efficacy of using an oral glycoprotein IIb/IIIa platelet receptor inhibitor in patients with acute coronary syndromes.

The 12,365 patients who did not take a statin before the index coronary event were divided into those who started a statin early after the acute event (median, 2 days; n = 3952) and those who never received statin therapy and survived more than 5 days after the acute event (n = 8413).

The authors concluded that there was no relationship between early initiation of statin therapy and improved outcomes for patients with acute coronary syndromes.

The primary composite endpoint for the trial was death, recurrent myocardial infarction, or severe recurrent ischemia at 90 days.

The average age was 58 years, and 75% of the patients were men. Revascularization was performed in 32.8% of the patients who received early statin therapy and in 19.4% of patients who did not get the statin. Patients who received early statin therapy were more likely to be younger, to have a history of elevated cholesterol or infarction as the index event, to be receiving ß-blockers, heparin, or glycoprotein IIb/IIIa platelet receptor inhibitors, and to be living in North America. Early statin therapy was less likely to be initiated in patients with an S3 gallop sound, atrial fibrillation, hypertension, previous stroke, prior angiography or coronary revascularization, and in patients receiving aspirin and nitrates.

The 90-day and 1-year unadjusted mortality was 1.2% for patients who received early statins versus 2.1% for patients who received no statins. However, there was no difference in the composite endpoint between the groups after adjustment for statin propensity and covariates. Interestingly, there were significantly fewer strokes at 90 days in the early-statin group. Among the 2711 patients with available lipids, early statin therapy was associated with a higher adjusted risk for death or myocardial infarction at cholesterol levels below treatment guidelines, but was more favorable at higher levels. The authors concluded that there was no relationship between early initiation of statin therapy and improved outcomes for patients with acute coronary syndromes. The authors' subset analysis suggests, however, that early statin therapy may be of benefit for patients with elevated cholesterol levels.

These observational data, which are in contrast with promising data from the Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering (MIRACL) trial, must be interpreted with caution. In the absence of definitive proof of harm, the initiation of statin therapy for patients with acute coronary syndromes can be considered, awaiting the results of ongoing clinical trials.

Fluvastatin for Prevention of Cardiac Events Following Successful First Percutaneous Coronary Intervention: A Randomized Controlled Trial

Serruys PW, de Feyter P, Macaya C, et al.
JAMA. 2002;287:3215–3222.

To determine the efficacy of lowering lipids after percutaneous coronary intervention, 1677 patients who had undergone a successful procedure in Europe, Canada, or Brazil were randomized to early initiation of fluvastatin 40 mg twice daily or to placebo. Eligible patients had baseline total cholesterol levels between 135 and 270 mg/dL and fasting triglyceride levels of <400 mg/dL. The median follow-up was 3.9 years.

The incidence of the primary combined endpoint (cardiac death, nonfatal myocardial infarction, or repeat revascularization) was significantly lower among the fluvastatin recipients (21.4%) than among the placebo recipients (26.7%), and this result was unrelated to baseline cholesterol levels above or below the median. In addition, the benefit of fluvastatin was demonstrated in diabetic patients and patients with multivessel disease, and was independent of gender. Importantly, there were no adverse outcomes, including elevations in muscle enzymes or rhabdomyolysis, in the fluvastatin group. The authors concluded that fluvastatin initiated after successful percutaneous coronary intervention improves clinical outcomes.

This study, the first prospective evaluation of statin therapy following percutaneous coronary intervention, supports the intuitive use of lowering lipids early in this subset of revascularized patients.

This study, the first prospective evaluation of statin therapy following percutaneous coronary intervention, supports the intuitive use of lowering lipids in this subset of revascularized patients; it also confirms the importance of lowering lipids in patients with coronary artery disease. ■

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