NUMEROUS studies have demonstrated that treatment of hypercholesterolemia in high-risk persons by 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (statins) reduces cardiovascular morbidity and mortality in elderly persons (1–17). The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) (NCEP III) guidelines recommend that the serum low-density lipoprotein (LDL) cholesterol be reduced to \( \leq 100 \) mg/dl in patients with coronary heart disease (CHD), other clinical forms of atherosclerotic vascular disease, diabetes mellitus, the metabolic syndrome, and with multiple risk factors that confer a 10-year risk for CHD \( \geq 20\% \), regardless of age (18). Should these guidelines be modified because of data published since these guidelines were recommended?

The Heart Protection Study included 20,536 persons aged 40 to 80 years (5806 persons aged 70 to 80 years at study entry and aged 75 to 85 years at follow-up) with a serum total cholesterol of 135 mg/dl or higher and prior myocardial infarction (8510 persons), other CHD (4876 persons), or no CHD (7150 persons) (4). Of the 7150 persons without CHD, 1820 had cerebrovascular disease, 2701 had peripheral arterial disease, and 3982 had diabetes mellitus. Although treated hypertension was present in 8457 persons, only 237 persons were included on the basis of hypertension alone. Patients were randomized to simvastatin 40 mg daily or to placebo. Mean follow-up was 5 years.

Compared with placebo, simvastatin caused significant reductions in all-cause mortality by 13\%, in any vascular death by 17\%, in major coronary events by 27\%, in any stroke by 25\%, in coronary or noncoronary revascularization by 24\%, and in any major vascular event by 24\% (4). In the 3500 persons with an initial serum LDL cholesterol of \( <100 \) mg/dl, reduction of the serum LDL cholesterol from 97 mg/dl to 65 mg/dl by simvastatin caused a similar reduction in risk as did treatment of patients with higher serum LDL cholesterol levels (4). Simvastatin significantly reduced all-cause mortality, vascular death, major coronary events, coronary or noncoronary revascularization, and any major vascular event regardless of initial levels of serum lipids, age, or gender (4). On the basis of these data, the Heart Protection Study Investigators recommended treating patients at high risk for vascular events with statins, regardless of the initial levels of serum lipids, age, or sex (4).

At 3-year follow-up of 1410 persons, mean age 81 years, with prior myocardial infarction and a serum LDL cholesterol of 125 mg/dl or higher, reducing the serum LDL cholesterol by statins to \( \leq 90 \) mg/dl was associated with a 20\% incidence of new coronary events, whereas reducing the serum LDL cholesterol to 90–99 mg/dl was associated with a 48\% incidence of new coronary events (6). Statins reduced the incidence of new coronary events in persons older than 90 years (6).

In this study, the incidence of new stroke was 7\% if the serum LDL cholesterol was reduced to \( \leq 90 \) mg/dl and 16\% if the serum LDL cholesterol was reduced to 90–99 mg/dl (7). The incidence of new stroke was reduced in persons up to age 90 years but not in persons older than 90 years (7).

In the Lipid Lowering Arm of the Anglo-Scandinavian Cardiac Outcomes trial, 10,305 persons (6570 older than 60 years) with hypertension and at least 3 other cardiovascular risk factors with no history of CHD and a mean serum LDL cholesterol of 133 mg/dl were randomized to atorvastatin 10 mg daily or to placebo (11). At 3.3-year follow-up, the serum LDL cholesterol was 90 mg/dl in patients treated with atorvastatin (11). At 3.3-year follow-up, atorvastatin significantly reduced the incidence of fatal CHD and nonfatal myocardial infarction by 34\% in persons aged 60 years and younger and by 36\% in persons older than 60 years (11).

In the Reversal of Atherosclerosis With Aggressive Lipid Lowering (REVERSAL) study, intravascular ultrasound was used to measure progression of atherosclerosis in 502 patients, mean age 57 years, with CHD randomized to pravastatin 40 mg daily or atorvastatin 80 mg daily (19). The serum LDL cholesterol was reduced to 110 mg/dl in the pravastatin group and to 79 mg/dl in the atorvastatin group. At 18-month follow-up, compared with baseline values, patients treated with atorvastatin had no change in atheroma burden, whereas patients treated with pravastatin showed progression of coronary atherosclerosis (19).
In 4162 patients, mean age 58 ± 11 years, hospitalized for an acute coronary syndrome (29% with unstable angina pectoris and 71% with an acute myocardial infarction), the median serum LDL cholesterol was 95 mg/dl in patients randomized to pravastatin 40 mg daily versus 62 mg/dl in patients randomized to atorvastatin 80 mg daily (14). At 2-year follow-up, the primary end point of death from any cause, myocardial infarction, documented unstable angina pectoris requiring rehospitalization, coronary revascularization (performed at least 30 days after randomization), and stroke was 26.3% in the pravastatin group versus 22.4% in the atorvastatin group, a 16% reduction in favor of atorvastatin (p = .005) (14).

These data favor modification of the NCEP III guidelines in elderly and younger persons. Elderly or younger patients at high risk for cardiovascular events should be treated with a statin, regardless of initial serum lipid levels. In addition, the serum LDL cholesterol goal should be <70 mg/dl, not <100 mg/dl. The most potent statins for achieving these serum LDL cholesterol goals are atorvastatin and rosuvastatin (20,21).

ACKNOWLEDGMENT

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