Cholesterol Lowering for Primary Prevention of Cardiovascular Events in Older Adults

Lemaitre RN, Psaty BM, Heckbert SR, et al. Therapy with hydroxymethylglutaryl-coenzyme A reductase inhibitors (statins) and associated risk of incident cardiovascular events in older adults: evidence from the Cardiovascular Health Study. Arch Intern Med 2002;162:1395–400.

Study Overview

Objective. To determine if statin use is associated with a reduction in the risk of first cardiovascular event or all-cause mortality in older adults.

Design. Prospective cohort study.

Setting and participants. Noninstitutionalized participants older than age 65 years were selected randomly from Medicare participation lists from communities in 4 states (North Carolina, California, Maryland, and Pennsylvania) beginning in 1989. The average age at entry was 72 years. Patients were excluded if they had had a myocardial infarction (MI) or stroke prior to the baseline examination. Additional African-American adults were recruited in 1992. The cohort was followed until 1997. The analysis only included patients for whom cholesterol-lowering therapy was recommended according to the 1993 National Cholesterol Education Program (NCEP) guidelines [1].

Main outcome measures. Cholesterol levels were measured at baseline and at the third year of follow-up. Statin and other cholesterol-lowering drug use was determined by survey and inspection of pill bottles at annual examinations. The primary outcomes were fatal and nonfatal MI, stroke, and coronary heart disease death; a secondary outcome was all-cause mortality. Outcomes were determined through semi-annual interviews with surviving participants or proxies and by review of medical records when the interview suggested a potential cardiovascular event. Deaths were confirmed using medical records, death certificates, and the Health Care Financing Administration (HCFA) database of health care utilization.

Main results. 1914 patients met all entry criteria. Median follow-up was 7 years 3 months. 251 patients were receiving drugs to lower cholesterol at baseline. Of those not treated with drugs at baseline, 717 patients had cholesterol levels that warranted drug therapy by NCEP guidelines, and 946 had levels that warranted dietary therapy by NCEP guidelines. 20% of the 1914 patients had cardiovascular events and 19% died. Compared with patients who did not take cholesterol-lowering drugs, the risk of cardiovascular events was lower for those taking any cholesterol-lowering drug (adjusted hazard ratio [HR], 0.53 [95% confidence interval {CI}, 0.36–0.76]) and for those taking statins in particular (HR, 0.44 [95% CI, 0.27–0.71]). Subgroups did not always achieve statistical significance and numeric data were not given for all of them. However, the risk estimates were reportedly similar for statin users above and below age 74 years at entry, with high-density lipoprotein (HDL) levels above or below 46 mg/dL at entry, and for men and women. Use of statins was associated with lower risk of all-cause mortality (HR, 0.56 [95% CI, 0.36–0.88]), as was use of non-statin drugs to lower cholesterol (HR, 0.43 [95% CI, 0.21–0.88]).

Conclusion. Statin use in elderly adults without prior MI or stroke is associated with decreased risk of cardiovascular disease and death. These observational data support the application of NCEP guidelines to adults in their seventies.

Commentary

Although the elderly experience higher rates of cardiovascular disease, until recently the precise role for the detection and treatment of high blood cholesterol for primary prevention in this group has been largely speculative for 2 reasons: in epidemiologic studies, the relative importance of elevated low-density lipoprotein (LDL) cholesterol in causing cardiovascular disease in the elderly appears to be lower than it is for middle-aged adults [1,2]; and the relevant clinical trials have included only a few older participants. Patients in the 2 large primary prevention trials using statins published to date

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tended to be in their late forties to early sixties and to have low HDL levels [3,4]. The current cohort study suggests that it is reasonable to apply the lessons learned from these trials to adults in their seventies and that the benefit of LDL lowering in the elderly will extend to those with and without low HDL.

Still, the cohort design cannot exclude important unmeasured confounders as the cause of the observed effects. Medication users may differ from nonusers in other important ways that influence health outcomes, and, as is being found in trials examining estrogen use for cardiovascular event reduction, controlled trials do not always yield the favorable results found in observational studies. In addition, this study does not examine side effects or tolerability of cholesterol-lowering drugs in the elderly. Though statins are generally well tolerated, the elderly as a group are more prone to the adverse effects of drugs in general, and this susceptibility could apply to the statins as well. Fortunately, preliminary results from the Heart Protection Study, a statin trial that contained a large number of persons up to age 80 years, suggest that benefits of cholesterol lowering in the elderly are similar to those found in other groups [2]; the study's publication will be welcome.

Applications for Clinical Practice

These results give further support to using a risk-based cholesterol treatment strategy for adults in their seventies for the primary prevention of cardiovascular events and stroke as is advocated by the NCEP [5]. More randomized trial data that include older patients will be helpful when they become available. There is still a paucity of information to guide cholesterol treatment for adults older than age 80 years.

–Review by Stephen D. Persell, MD

References

1. Summary of the second report on the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel II). JAMA 1993;269:3015–23.
2. Grundy SM. Statin therapy in older persons: pertinent issues [editorial]. Arch Intern Med 2002;162:1329–31.
3. Shepherd J, Cobbe SM, Ford I, et al. Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia. N Engl J Med 1995;333:1301–7.
4. Downs JR, Clearfield M, Weis S, et al. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: results of AFCAPS/TexCAPS. Air Force/Texas Coronary Atherosclerosis Prevention Study. JAMA 1998;279:1615–22.
5. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA 2001;285:2486–97.

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