

# Lipid Ratio Flags Heart Disease Risk in Elderly

Study suggests that for patients at least 70, a statin won't help if baseline HDL is over 45 mg/dL.

BY MITCHEL L. ZOLER  
Philadelphia Bureau

NEW YORK — In elderly people, the ratio of LDL cholesterol to HDL cholesterol was the most powerful measure of cardiovascular disease risk in a retrospective analysis of data collected in a trial with almost 6,000 patients.

The analysis also suggested that elderly patients—those who are at least 70 years old—will not benefit from statin therapy if their serum level of HDL cholesterol at baseline is greater than 45 mg/dL.

"We need to study this more, but that's what our new analysis suggests," said Chris J. Packard, Ph.D., at an international symposium on triglycerides and HDL.

The results of several previous studies have shown that an elevated level of LDL cholesterol is not a risk factor for cardiovascular disease in the elderly. Despite this, the results from a large trial that were first reported in 2002 showed that during a follow-up period that averaged 3.2 years, a regimen of 40 mg pravastatin/day cut the risk of new cardiovascular disease events by a statistically significant 15%, compared with placebo, in patients aged 70-82 who had either established vascular disease or elevated risk factors for vascular disease (*Lancet* 2002;360:1623-30).

This finding from the Prospective Study of Pravastatin in the Elderly at Risk (PROSPER) trial raised the question of why statins were effective at lowering risk in patients with an average age of 75 who are usually not harmed by high LDL cholesterol levels, said Dr. Packard, a biochemist and research director at Glasgow Royal Infirmary, Scotland.

One element of the new analysis was to assess the impact of pravastatin treatment by quintile of HDL cholesterol level. This assessment showed that all of the benefit of pravastatin treatment was confined to the two quintiles with the lowest levels of HDL cholesterol at baseline. In these patients, whose levels were all less than 45 mg/dL, pravastatin treatment was associated with a 33% reduction in cardiovascular events, compared with the group treated with placebo. Among the other 60% of patients, who all started the study with an HDL cholesterol level of more than 45 mg/dL, pravastatin treatment was not linked with any reduction in events, compared with the placebo group.

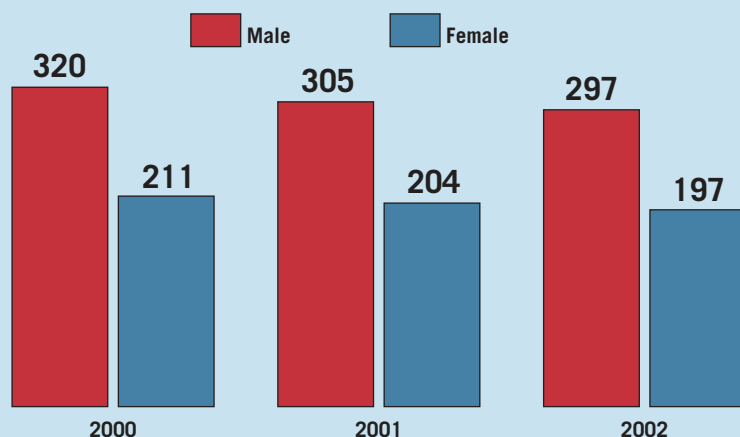
The impact of statin treatment on HDL cholesterol levels was greatest in the 25% of patients whose HDL cholesterol levels were the lowest at baseline. In this group, pravastatin treatment was linked with an average increase of 10.7%. In contrast, among the 25% who started with the highest HDL cholesterol levels, statin treatment was linked with a 4.8% increase. But further analysis showed that the change in HDL cholesterol level, by itself, was not linked to the change in risk, said Dr. Packard at the symposium, sponsored by the Giovanni Lorenzini Medical Foundation. Nor was the change in risk linked with changes in serum levels of C-reactive protein.

But significant reductions in risk were linked with changes in the ratio of LDL to HDL cholesterol. Elderly patients who had a significant reduction in this ratio had, on average, a statistically significant reduction in their cardiovascular disease risk, Dr. Packard said. ■

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## DATA WATCH

### Heart Disease Death Rates on the Decline



Note: Based on deaths per 100,000 people.

Source: Centers for Disease Control and Prevention

KEVIN FOLEY, RESEARCH

# Non-HDL Cholesterol Predictive Of First Heart Attack in Women

BY DIANA MAHONEY  
New England Bureau

NEW ORLEANS — Measuring non-HDL cholesterol level may be a better primary screen for risk of first nonfatal myocardial infarction in women than measuring the level of LDL cholesterol, reported Wildon R. Farwell, M.D.

LDL cholesterol has long been considered the most atherogenic lipoprotein, but recent studies have implicated other types of cholesterol, including triglyceride-rich very low-density-lipoprotein cholesterol and intermediate-density-lipoprotein cholesterol—both of which are included in the non-HDL measure, Dr. Farwell said at the annual meeting of the Society of General Internal Medicine.

He and his colleagues at Brigham and Women's Hospital, Boston, analyzed data from a cohort of nearly 19,000 women from the Women's Health Study who neither had a diagnosis of hyperlipidemia nor took cholesterol medication. They performed direct-measurement assays for lipid parameters and collected baseline self-reported risk factors at enrollment. They confirmed 118

self-reported cases of first nonfatal MI and used Cox proportional hazards models to compare the independent associations of non-HDL cholesterol and LDL cholesterol with MI risk, adjusting for cardiovascular risk factors.

The mean values of LDL and non-HDL cholesterol in the 118 MI patients were 116.3 mg/dL and 147.5 mg/dL, respectively. Non-HDL cholesterol level was a more significant predictor of risk than LDL cholesterol level. "The hazard ratio for the highest tertile [of non-HDL cholesterol] was 2.91, compared with 1.51 for LDL," Dr. Farwell said. Similarly, the hazard ratios for the middle non-HDL and LDL tertiles were 1.81 and 0.92, he reported.

The non-HDL tertile measures were defined as less than 130.1 mg/dL, from 130.1 to 159.4 mg/dL, and greater than 159.4 mg/dL. For LDL cholesterol, the tertile measures were defined as less than 102.1 mg/dL, from 102.1 to 126.6 mg/dL, and greater than 126.6 mg/dL.

"While LDL cholesterol is important, non-HDL cholesterol may be the more important predictor, at least in some groups of people," Dr. Farwell said. ■

# Treatment Target Needed for HDL Cholesterol, Expert Says

BY MITCHEL L. ZOLER  
Philadelphia Bureau

NEW YORK — It's time to set a target for high-density lipoprotein cholesterol in the U.S. lipid guidelines, Ernst J. Schaefer, M.D., said at the Second International Symposium on Triglycerides and HDL.

"We should try to target patients to raise their HDL cholesterol, especially if they have established heart disease. We have as much data today for HDL as we had in 1988 when we were asked to set guidelines for LDL," said Dr. Schaefer, professor of medicine at Tufts University, Boston.

But another lipid expert who spoke at the symposium disagreed. "The time is not yet right for firm HDL guidelines," said Antonio M. Gotto Jr., M.D., dean of the Weill Medical College of Cornell University in New York. "Results from clinical trials must confirm the benefit of treating patients with agents that primarily target HDL cholesterol."

"It's important to treat beyond LDL cholesterol," said Dr. Schaefer, who is also director of the lipid and heart disease prevention clinic and laboratory at Tufts-New England Medical Center. "Changes in HDL cholesterol and HDL-inclusive parameters are the strongest predictors of risk. A substantial fraction of patients don't get treated to increase their HDL. But for every 1% increase in HDL, there is about a 1%-3% reduction in coronary heart disease risk."

Dr. Schaefer said that he was unsure of the best target level for HDL chole-

sterol. One option is to recommend raising levels to at least 40 mg/dL for men and 50 mg/dL for women. Another option is to set a minimum goal of more than 40 mg/dL or more than 45 mg/dL for everyone. The existing lipid goals of the National Cholesterol Education Program, the Adult Treatment Panel III, do not set a treatment strategy for patients based on their serum HDL cholesterol level.

Dr. Schaefer reviewed the evidence that documents the prognostic importance of a low level of HDL cholesterol and the risk reduction that occurs when the level of HDL cholesterol is raised. For example, in the Framingham study the strongest predictor of a person's cardiovascular risk was total cholesterol divided by HDL cholesterol. Existing guidelines in both Canada and Europe say that patients with existing coronary disease should be treated until this ratio drops below 4.0.

The results of treatment trials have documented the efficacy of several drugs to raise serum levels of HDL cholesterol and reduce the risk of cardiovascular disease events. These have included studies using cholestyramine, gemfibrozil, simvastatin, and niacin, Dr. Schaefer at the symposium, which was sponsored by the Giovanni Lorenzini Foundation.

"There is a consistent pattern that's much stronger statistically [for raising HDL cholesterol] than for [lowering] LDL cholesterol. Increasing HDL cholesterol by even a small amount may benefit patients," Dr. Schaefer said. ■