Inflammatory Marker Tied to CV Mortality

BY MITCHEL L. ZOLER
Philadelphia Bureau

TORONTO — An elevated serum level of a novel inflammatory marker, YKL-40, was linked with a significantly increased risk for all-cause death and cardiovascular death in a study of more than 4,000 patients with a history of myocardial infarctions or angina.

"This is the first time that YKL-40 levels were tested in patients with cardiovascular disease," Dr. Jens Kastrup said at the 14th World Congress on Heart Disease.

YKL-40 is produced by macrophages in early atherosclerotic lesions, and serum levels are elevated in patients with inflammation and tissue remodeling. Prior studies showed that serum levels of YKL-40 are high in patients with ST-elevation myocardial infarctions and in those with stable coronary artery disease. Elevated levels following a myocardial infarction eventually subside back close to normal. YKL-40 levels are also elevated in cancer patients, and results from other studies have suggested that YKL-40 may be a prognostic marker in cancer patients, said Dr. Kastrup, director of angiogenesis research at the Heart Centre of Rigshospitalet, Copenhagen.

YKL-40 is measured by an investigational immunoassay made by Quidel Corp. of San Diego. Quidel provided some of the assays used in the current study but did not provide any other research support. Dr. Kastrup said that he and his associates had no other financial relationship with the company and that Quidel had no role in the study.

Serum specimens were used from 4,298 patients with a diagnosis of myocardial infarction (about two-thirds of the patients) or angina who had been enrolled in an earlier trial that had compared the efficacy of 2 weeks of treatment with clarithromycin against placebo (BMJ 2006;332:22-7).

The median level of YKL-40 was 110 mcg/L, compared with a normal value of 30-40 mcg/L, Dr. Kastrup said at the congress, sponsored by the International Academy of Cardiology. The patients were divided into six groups based on their serum levels, ranging from the lowest (less than 110 mcg/L) to the highest (256 mcg/L or greater).

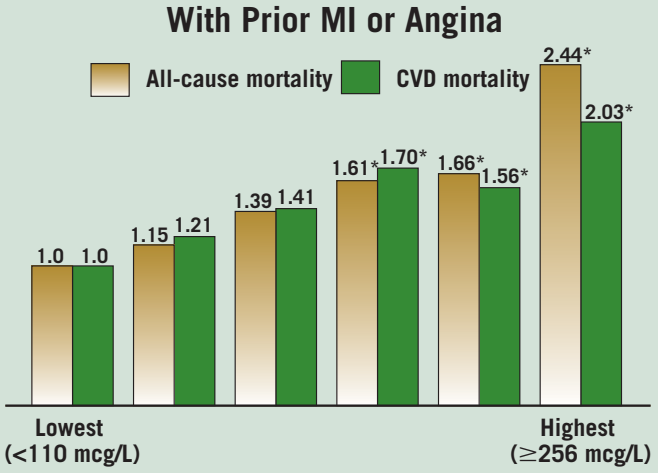
During an average follow-up of 2.6 years, the rate of all-cause death rose with the serum level of YKL-40, with the highest rate of death in patients in the subgroup with the highest serum level. After adjustment for baseline differences such as age, sex, smoking history, hypertension, and diabetes, patients with the highest level of YKL-40 were about 2.4-fold more likely to die than were patients in the subgroup with the lowest level of YKL-40, a statistically significant difference.

Similar analyses showed that patients with the highest levels of YKL-40 were also significantly more likely to have a cardiovascular disease death than were patients with the lowest level. (See box.) ■

'This is the first time that YKL-40 levels were tested in patients with cardiovascular disease.'

DR. KASTRUP

Relative Mortality Risk by YKL-40 in Patients With Prior MI or Angina



*Statistically significant difference relative to reference value.
Note: Relative risks adjusted for baseline differences in 4,298 patients in age, sex, smoking, hypertension, and diabetes.
Source: Dr. Kastrup

ELSEVIER GLOBAL MEDICAL NEWS

MINDFUL PRACTICE

Lowering Lipids the 'Natural Way'

BY JON O. EBBERT, M.D., AND ERIC G. TANGALOS, M.D.

The Problem

A 54-year-old man with a history of hypertension schedules an appointment with you for a routine medical examination. His blood pressure is well controlled on atenolol. His body mass index is 37 kg/m^2. His total cholesterol level is 258 mg/dL, with an HDL cholesterol level of 32 mg/dL and an LDL of 182 mg/dL; his triglyceride level is 220 mg/dL. According to the Adult Treatment Panel (ATP-III) guidelines, his LDL level should be less than 130 mg/dL. You inform him that he needs to lower his cholesterol to reduce his risk for cardiovascular disease. He tells you that he has been trying to diet and lose weight since you instructed him to do so last year, but his efforts have been unsuccessful because of his stressful job and significant travel. You offer to prescribe a statin, but he refuses and tells you that his brother was prescribed the same medication and had severe muscle and joint aches. He tells you that his brother stopped the medication and used dietary supplements to lower his cholesterol. He would like to do the same because he does not like to "take medication if he doesn't have to."

The Question

In patients with hypercholesterolemia who are not at therapeutic goal, do nonprescription cholesterol-lowering interventions reduce cholesterol as much as statins do?

The Search

You log on to PubMed (www.pubmed.gov) and enter "hypercholesterolemia AND dietary supplements." You find a relevant study. (See box at right.)

Our Critique

This study provides evidence that "alternative" (nonprescription) therapies may decrease cholesterol levels comparably to statin medications. However, the behavioral intervention delivered to the group receiving red yeast rice (which is available over the counter and contains naturally occurring lovastatin) and fish oil was astounding and not generalizable. We would have liked to have seen a third intervention arm that received red yeast rice/fish oil with the same counseling provided to the recipients of statins. With this arm, we could determine if, in the absence of a board-certified cardiologist and an intervention team providing 42 hours of counseling, we would observe any degree of cholesterol lowering with red yeast rice/fish oil and how that would compare with cholesterol profile changes with a prescribed statin.

Clinical Decision

You write down the preparations used in the study and discuss diet and exercise with your patient. You agree to check his cholesterol in 6 months. Otherwise, he is on his own.

DR. EBBERT *and* DR. TANGALOS *are with the Mayo Clinic in Rochester, Minn. They have no conflict of interest to report. To respond to this column or suggest topics for consideration, write to Dr. Ebbert and Dr. Tangalos at our editorial offices or e-mail them at imnews@elsevier.com.*

D.J. Becker et al.

Simvastatin vs. therapeutic lifestyle changes and supplements: Randomized primary prevention trial. Mayo Clin. Proc. 2008;83: 758-64.

► **Design and Setting:** Randomized, open-label clinical trial done at a cardiology practice in Philadelphia.

► **Subjects:** Men and women aged 18-80 years with either: LDL cholesterol level of 130 mg/dL or more with two or more cardiovascular risk factors, or LDL between 160 and 210 mg/dL with no or one cardiovascular risk factor. Cardiovascular risk factors include age (men older than 45 years, women older than 55 years or postmenopausal), hypertension requiring treatment, HDL less than 40 mg/dL, current cigarette smoking, diabetes mellitus, or family history of premature coronary artery disease. Potential subjects were excluded if they had known coronary artery disease or had undergone a procedure to treat such disease, triglyceride level over 400 mg/dL, use of warfarin, severe liver or kidney disease, an orthopedic condition preventing exercise, or other systemic disease.

► **Intervention:** Subjects were randomized to either a conventional treatment group that received simvastatin 40 mg/day with standard diet and exercise counseling; or to an alternative treatment group (AG) that received three capsules of fish oil daily, red yeast rice supplements (3.6 g per day if LDL was over 160 mg/dL or 2.4 g per day if LDL was 160 mg/dL or less), and a 12-week lifestyle program involving weekly 3.5-hour meetings taught by a board-certified cardiologist, a dietician, exercise physiologists, and relaxation practitioners.

► **Outcomes:** The primary outcome was the percentage change from baseline levels of LDL cholesterol. Secondary outcomes were the percentage change from baseline levels of HDL cholesterol and triglycerides at 12 weeks.

► **Results:** Of the 79 subjects who were randomized, 74 completed the study. No significant differences were observed between the two groups at baseline other than weight (AG 87.7 kg vs. 80.8 simvastatin group). Weight decreased by 4.7 ± 2.4 kg (–5.5%) in the AG and by 0.3 ± 2.2 kg (–0.4%) in the simvastatin group. BMI also decreased significantly more in the AG (mean difference –1.5). No significant differences were observed between the groups with respect to blood pressure or fasting glucose. In the AG, significant changes were observed in levels of total cholesterol (percent change –32.4 ± 11.8%), LDL (–42.4 ± 14.8%), and triglycerides (–29.2 ± 36.3%), but not in HDL. Significant changes were also observed in the statin group with declines in total cholesterol, LDL, and triglycerides, but no changes were seen in HDL. Triglyceride levels declined more in the AG than in the statin group (mean difference –36.4).