# Evidence Conflicts on Fish Oil's Heart Effects

#### BY KATE JOHNSON Montreal Bureau

BOSTON — New studies showing conflicting results on the effect of fish oil on the heart add weight to the notion that perhaps age and health status influence whether omega-3 fatty acids prevent or promote cardiac arrhythmias, according to Dr. Anthony Aizer.

His study, which he presented at the annual meeting of the Heart Rhythm Society, linked increased fish consumption with a higher risk of developing atrial fibrillation (AF) in healthy male physicians (aged 40-84 years) who were enrolled in the previously reported Physicians' Health Study (N. Engl. J. Med. 1989;321:129-35).

The findings corroborate recently published results from the Danish Diet, Cancer, and Health study (Am. J. Clin. Nutr. 2005;81:50-4), but contrast with data from the Cardiovascular Health study (Circulation 2004;110:368-73), said Dr. Aizer, who is an electrophysiologist at New York University Medical Center. He said one explanation for the conflicting findings could be that fish oil may have profibrillatory effects in healthy individuals but antifibrillatory effects in subjects with preexisting cardiovascular disease (CVD).

"One hypothesis is that omega-3 fatty acids have some effects on the autonomic nervous system—in particular, by increasing parasympathetic tone. In generally healthy individuals without CVD, it is sometimes thought that an increase in autonomic tone may play a role in the development of AF," he said in an interview. "In contrast, in older, less healthy individuals it's possible that other effects are more significant. In certain individuals, the effect of omega-3 fatty acids that enhance cardiac tissue refractoriness may have a more significant impact, thereby preventing AF."

Dr. Aizer's analysis of the Physicians' Health Study included 17,679 men who had completed a fish consumption questionnaire in 1983 and of whom 7% reported AF 15 years later. He found that men who reported eating five or more fish meals per week had a 55% higher rate of AF, compared with men who ate fish only once a month.

But two other smaller studies that were presented as posters at the meeting reported the cardiac benefits of omega-3 fatty acids.

A prospective study of six patients with paroxysmal AF showed that an infusion of 100 mL of omega-3 fatty acids resulted in an increase in atrial refractoriness, a reduction in AF inducibility, and a prolongation of fibrillatory cycle length, reported Dr. Hercules E. Mavrakis, from Heraklion University Hospital in Crete, Greece.

And another study of 26 patients with inducible ventricular tachycardia (VT) at 3 or more months post MI showed strong benefits of oral omega-3 fatty acid capsules (180 mg eicosapentaenoic acid and 120 mg docosahexaenoic acid) daily, compared with placebo, over a 40-day treatment period, reported Dr. Glenn D. Young from the Cardiovascular Research Centre in Adelaide, Australia.

At the end of the study, VT was no longer inducible in 5 of the 12 treated patients, and 5 of the remaining 7 patients required more aggressive stimulation to induce arrhythmia. By contrast, in the 14 control patients, VT was no longer inducible in only 1 patient, and 3 of the remaining 13 patients required more aggressive inducement.

"Statistically, it was a very significant result. There seems to be a direct effect of fish oil in preventing ventricular tachycardia," said Dr. Young in an interview. "People can achieve that level with only [two or three] oily fish meals a week."

Dr. Aizer's finding of a higher incidence of AF with increased fish consumption cannot be interpreted as causal. "This wasn't a randomized, controlled trial [of fish consumption]—there could always be an association of fish with some other factor that's causing the atrial fibrillation," he said.

## High-Carb, Low–Glycemic Index Diet Cuts Weight, Cardiac Risk

#### BY MARY ANN MOON Contributing Writer

A high-carbohydrate, low-glycemic index diet both decreases fat mass and maximizes cardiovascular risk reduction, compared with three other weight-loss diets, reported Joanna McMillan-Price of the University of Sydney (Australia) and her associates.

A low-fat, high-carbohydrate diet is still considered the "best practice" among physicians. In contrast, high-protein and low–glycemic index diets have caught on with the public, but "clinicians and health professionals remain skeptical, calling for greater scientific evidence on which to base" their advice to patients who want to lose weight, the researchers said.

They conducted a 12-week, randomized, controlled trial of four weight-loss diets that all aimed for the same fat content (30% of total energy intake), the same moderate fiber content (30 g/day), and the same daily caloric goals (1,400 kcal for women and 1,900 kcal for men). The carbohydrate and protein contents of the four eating plans varied. The participants comprised 129 overweight young adults. The 98 women and 31 men were aged 18-40 years and had a body mass index (kg/m<sup>2</sup>) of 25 or more.

Diet 1 was a conventional weight-loss eating plan: a high-carbohydrate (55% of energy intake) and average protein (15% of energy intake) diet that relied on high–glycemic index whole grains, such as fiber-rich breakfast cereals and breads. Diet 2 was a high-carbohydrate but low–glycemic index eating plan, which had the same proportions of protein and carbohydrates but relied on low– instead of high–glycemic index carbohydrates.

Diet 3 was a high-protein (25% of energy intake), low-carbohydrate (45% of energy intake) eating plan that relied on lean red meats and high–glycemic index whole grains. Diet 4 had the same proportions of protein and carbohydrates but relied on low– rather than high–glycemic index carbohydrates.

All four diets reduced weight by 4%-6%, and all reduced fat mass and waist circumference. Weight

loss of 5% or more occurred in 31% of subjects on diet 1, in 56% on diet 2, in 66% on diet 3, and in 33% on diet 4.

All four groups reduced fat intake, but the highcarbohydrate groups ate the most fiber and consumed less fat overall, less saturated and polyunsaturated fats, and less cholesterol than did the high-protein groups. Thus, diet 2 produced "the best clinical outcomes, reducing both fat mass and LDL-cholesterol levels," Ms. McMillan-Price and her associates said (Arch. Intern. Med. 2006;166:1466-75).

"Our findings suggest that dietary glycemic load, not just overall energy intake, influences weight loss and postprandial glycemia. ... Diets based on low–glycemic index whole-grain products (in lieu of whole grains with a high glycemic index) maximize cardiovascular risk reduction" as well as weight loss.

In an accompanying editorial, Dr. Simin Liu of the department of epidemiology at University of California, Los Angeles, said that physicians should encourage patients' use of "glycemic index" and "glycemic load" concepts along with caloric count and nutrient composition, because these designations are superior to the "simple" or "complex" carbohydrate classifications in predicting glucose and insulin responses.

"We need to teach our patients to identify low-glycemic index foods within different food groups. Typically, foods with a low degree of starch gelatinization, such as pasta, and those containing a high level of viscous soluble fiber, such as whole grain barley, oats, and rye, have slower rates of digestion and lower glycemic index values," Dr. Liu noted (Arch. Intern. Med. 2006;166:1438-9).

"Without any drastic change in regular dietary habits, for example, one can simply replace high–glycemic index grains with low–glycemic index grains, and starchy vegetables with less starchy ones, and cut down on soft drinks that are often poor in nutrients yet high in glycemic load," Dr. Liu added.

### Low HDL Increases Complication Rate in Stent Recipients With ACS

ATLANTA — Low baseline HDL-cholesterol levels in patients who receive a drug-eluting stent for acute coronary syndrome appears to be an independent risk factor for adverse short- and long-term clinical outcomes, Dr. Roswitha M. Wolfram said at the annual meeting of the American College of Cardiology.

The most likely hypothesis to explain this finding is that HDL cholesterol plays an important role in dampening the inflammatory response to percutaneous intervention, according to Dr. Wolfram of Washington Hospital Center.

She presented an observational study in 1,032 consecutive patients who got a drug-eluting stent when they presented at the center with acute coronary syndrome. Of them, 550 had low baseline HDL levels, defined as less than 40 mg/dL in men or 45 mg/dL in women. The other 482 were categorized as having high HDL. Ninety-eight percent of patients in both groups were on statin therapy during follow-up.

The 30-day rates of mortality and a composite end point consisting of target lesion revascularization and/or major cardiac adverse events were significantly higher in stented patients with low HDL. The same was true during days 31-365. (see box.)

Patients with low baseline HDL were more likely to be diabetic, had higher body mass index and triglyceride levels, and had lower total cholesterol than those with high HDL. Upon adjusting for these potential confounders in a multivariate analysis, two independent predictors of death at 1 year emerged: a history of diabetes, which conferred a 3.8-fold increased risk, and a high baseline HDL, which was associated with a 70% relative risk reduction.

—Bruce Jancin

#### **Outcomes for Drug-Eluting Stent Patients Baseline HDL Cholesterol Level** High Low (n = 550) (n = 482)**Mortality** Days 0-30 0% 3.0% Days 31-365 3.8% 14.3% **TVR/MACE\*** Days 0-30 0.3% 3.2% Days 31-365 12.0% 26.7%

\*TVR/MACE: composite end point of target lesion revascularization and/or major cardiac adverse events. Source: Dr. Wolfram