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Should you still recommend omega-3 supplements?

Probably not. A new meta-analysis adds to a growing body of evidence that omega-3 fatty acids do little to protect against heart disease.

PRACTICE CHANGER

Stop recommending omega-3 fatty acid supplements for cardiovascular protection. They have no significant impact on all-cause mortality, acute myocardial infarction, sudden death, or stroke.[1]

STRENGTH OF RECOMMENDATION

A: Based on a meta-analysis of randomized controlled trials (RCTs).

Rizos E, Ntzani E, Bika E, et al. Association between omega-3 fatty acid supplementation and risk of major cardiovascular disease events: a systematic review and meta-analysis. *JAMA*. 2012;308:1024-1033.

ILLUSTRATIVE CASE

A 59–year-old patient who had a myocardial infarction (MI) 3 years ago is taking an ACE inhibitor, a statin, and a β-blocker. He asks you whether he should also take omega-3 fatty acid supplements to further decrease his risk of heart disease. What should you tell him?

Coronary artery disease (CAD) kills more than 500,000 Americans every year,[2] and medical and dietary therapies for primary and secondary cardiovascular protection are paramount. Omega-3 polyunsaturated fatty acid (PUFA) supplementation is one such therapy. Omega-3 PUFAs are precursors to certain prostaglandins that decrease the proinflammatory state in patients with CAD. They also lower triglyceride levels and produce an antiarrhythmic effect by promoting electrical stability.

But do PUFA supplements provide cardioprotection?

The American Heart Association's Nutrition Committee recommends either omega-3 PUFA supplementation with 250 to 500 mg eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) per day or 2 servings of oily fish per week for both primary and secondary prevention of CAD.[3] The European Society of Cardiology also encourages increased consumption of oily fish.[4]

These recommendations are based on primary and secondary prevention studies, performed between 1989 and 2007, that found a 15% to 29% decrease in all-cause mortality and nonfatal cardiovascular events associated with regular intake of omega-3 fatty acids.[5-7] The systematic review and meta-analysis detailed below revisited the effect of omega-3 supplementation on major cardiovascular outcomes.[1]

STUDY SUMMARY

Omega-3 supplements don't lower cardiovascular risk

This meta-analysis included 20 RCTs with a total of 68,680 patients. The median age was 68 years, with a range from 49 to 70 years. Thirteen of the studies evaluated omega-3 PUFAs for secondary prevention of cardiovascular outcomes, 4 assessed both primary and secondary prevention, and 3 looked at outcomes in patients with implantable cardioverter defibrillators. All lasted longer than

one year, and most were high quality, with a low risk of bias.

The median treatment duration was 2 years, with a maximum of 6.2 years. The mean omega-3 PUFA dose evaluated in the studies was 1.5 g per day, with the exception of 2 studies in which patients received omega-3 PUFAs through dietary sources. Twelve studies used a dose of 1 g or more per day. Half of the included trials were performed during the period when statins were routinely prescribed for cardiovascular risk modification (1998 or later).

Outcomes included all-cause mortality (17 studies), cardiac death (13 studies), sudden death (7 studies), MI (13 studies), and stroke (9 studies).

This meta-analysis found trends toward a decrease in all-cause mortality, cardiac death, sudden death, and MI in patients taking omega-3 PUFAs, but no statistically significant association between any of the outcomes and omega-3 PUFA supplementation. The relative risk for all-cause mortality was 0.96 (95% confidence interval, 0.91-1.02; *P*=.17). Prespecified subgroup analysis found no association between treatment effect and omega-3 fatty acid dose.

Are dietary sources of omega-3s more effective?

In the 2 trials involving dietary supplementation with omega-3 PUFAs, the results for all-cause mortality and cardiac death were conflicting, with one showing an increase in all-cause mortality and cardiac death and the other showing a decrease in both outcomes compared with the control group.

No harmful effects of omega-3 PUFAs were found in either the supplement- or diet-based studies.

WHAT'S NEW

More evidence of little benefit

The meta-analysis by Rizos et al is the most up-to-date, comprehensive look at the value of omega-3 fatty acids for primary and secondary prevention of cardiovascular events. It differs from previous reviews in that most included studies were well-done RCTs. In addition, the studies were performed in both primary and secondary cardiovascular disease prevention settings and involved different forms of omega-3 PUFA supplementation, including dietary sources and supplements. The trials were predominantly larger than those included in previous systematic reviews, as well. The baseline risk for cardiovascular disease in the newer studies (7 of the 20 RCTs were completed after 2007) may be different from that of previous studies because of increased use of certain medications, such as statins.

In recent years, other studies of omega-3 PUFAs have had similar results. A meta-analysis of 14 RCTs found that omega-3 PUFA supplementation offered no benefit for the secondary prevention of cardiovascular disease.[8] The FORWARD trial—published earlier this year—showed that omega-3 PUFAs did not decrease the recurrence of atrial fibrillation in patients with a history of confirmed paroxysmal atrial fibrillation.[9] And an earlier (2006) analysis of RCTs and cohort studies found no benefit from omega-3 fatty acids for primary prevention of cardiovascular disease or cancer.[10]

CAVEATS

No significant help, and no harm

While this meta-analysis found no statistically significant benefits from omega-3 PUFAs, there is no evidence of harm from PUFA intake, whether from dietary sources or supplements. There is no need to tell patients who wish to take omega-3 supplements not to do so. But we should not promote their use for the sole purpose of cardiovascular disease prevention.

CHALLENGES TO IMPLEMENTATION

Changing minds won't be easy

Despite recent findings indicating that omega-3 PUFAs provide little primary or secondary protection against cardiovascular events, advertising from supplement manufacturers may make it hard to change patients' minds. Because diets and supplements containing these fatty acids do not cause apparent harm, patients and physicians may decide that a small potential benefit is worth the expense.

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CONTINUED

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PRACTICE OPPORTUNITIES