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n-3 Fatty Acids Do Not Prevent Cardiovascular Events in High-Risk Patients

Clinical Question

Does supplementation with n-3 fatty acids prevent cardiovascular events in high-risk patients?

Bottom Line

There is no evidence that n-3 fatty acids prevent cardiovascular events or death in older adults who have cardiovascular disease (or who are at risk of it but have not had a myocardial infarction). (Level of Evidence = 1b)

Synopsis

Despite great enthusiasm and a wealth of disease-oriented evidence, the patient-oriented evidence to support n-3 fatty acids in cardiovascular prevention is sparse at best. In this study, 12,505 patients with known cardiovascular disease or at least four of the following risk factors were recruited: age 65 years or older, male, hypertension, hyperlipidemia, tobacco use, obesity, and a family history of premature cardiovascular disease. Patients with diabetes mellitus and at least one other risk factor were also included. Patients with a previous myocardial infarction, pregnant women, and those with a short expected lifespan were excluded. The study patients were randomly assigned, with concealed allocation, to receive a capsule containing 1 g of n-3 fatty acids or a placebo capsule

of olive oil. The mean age of participants was 64 years, 62% were male, and only one-third ate fish two or more times per week. Groups were balanced at the start of the study, and analysis was by intention to treat.

After a median follow-up of five years, the primary combined outcome of death, nonfatal myocardial infarction, or nonfatal stroke occurred in 11.7% of patients who received n-3 fatty acids and in 11.9% of those who received the placebo ($P = .58$). This was also true when a per-protocol analysis was used, as well as for individual outcomes including sudden cardiac death, cardiovascular death, hospitalization, myocardial infarction, and stroke. The only differences seen were fewer hospitalizations for heart failure (1.5% of patients receiving n-3 fatty acids vs. 2.3% of patients receiving placebo; $P = .002$; number needed to treat = 125 for five years) and a borderline reduction in the likelihood of death or first hospitalization for cardiovascular causes in women but not men. Given the large number of comparisons, these findings could easily have occurred by chance alone.

Study Information

Study design: Randomized controlled trial (double-blinded)

Funding source: Industry and government

Allocation: Concealed

Setting: Outpatient (any)

Reference: Roncaglioni MC, Tombesi M, Avanzini F, et al.; Risk and Prevention Study Collaborative Group. n-3 fatty acids in patients with multiple cardiovascular risk factors [published correction appears in *N Engl J Med*. 2013;368(22):2146]. *N Engl J Med*. 2013;368(19):1800-1808.

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