n-3 fatty acids and cardiovascular events after myocardial infarction.

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BACKGROUND: Results from prospective cohort studies and randomized, controlled trials have provided evidence of a protective effect of n-3 fatty acids against cardiovascular diseases. We examined the effect of the marine n-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) and of the plant-derived alpha-linolenic acid (ALA) on the rate of cardiovascular events among patients who have had a myocardial infarction.

METHODS: In a multicenter, double-blind, placebo-controlled trial, we randomly assigned 4837 patients, 60 through 80 years of age (78% men), who had had a myocardial infarction and were receiving state-of-the-art antihypertensive, antithrombotic, and lipid-modifying therapy to receive for 40 months one of four trial margarines: a margarine supplemented with a combination of EPA and DHA (with a targeted additional daily intake of 400 mg of EPA-DHA), a margarine supplemented with ALA (with a targeted additional daily intake of 2 g of ALA), a margarine supplemented with EPA-DHA and ALA, or a placebo margarine. The primary end point was the rate of major cardiovascular events, which comprised fatal and nonfatal cardiovascular events and cardiac interventions. Data were analyzed according to the intention-to-treat principle, with the use of Cox proportional-hazards models.

RESULTS: The patients consumed, on average, 18.8 g of margarine per day, which resulted in additional intakes of 226 mg of EPA combined with 150 mg of DHA, 1.9 g of ALA, or both, in the active-treatment groups. During the follow-up period, a major cardiovascular event occurred in 671 patients (13.9%). Neither EPA-DHA nor ALA reduced this primary end point (hazard ratio with EPA-DHA, 1.01; 95% confidence interval [CI], 0.87 to 1.17; P=0.93; hazard ratio with ALA, 0.91; 95% CI, 0.78 to 1.05; P=0.20). In the prespecified subgroup of women, ALA, as compared with placebo and EPA-DHA alone, was associated with a reduction in the rate of major cardiovascular events that approached significance (hazard ratio, 0.73; 95% CI, 0.51 to 1.03; P=0.07). The rate of adverse events did not differ significantly among the study groups.

CONCLUSIONS: Low-dose supplementation with EPA-DHA or ALA did not significantly reduce the rate of major cardiovascular events among patients who had had a myocardial infarction and who were receiving state-of-the-art antihypertensive, antithrombotic, and lipid-modifying therapy. (Funded by the Netherlands Heart Foundation and others; ClinicalTrials.gov number, NCT00127452.)

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