n-3 polyunsaturated fatty acids reduced mortality and morbidity after recent myocardial infarction


QUESTION: In patients with recent myocardial infarction (MI), are n-3 polyunsaturated fatty acids (PUFAs) and vitamin E, singly or in combination, effective for reducing morbidity and mortality?

Design
Randomised (allocation concealed*), blinded (outcome assessors),† controlled trial with 42 month follow-up.

Setting
Centres in Italy.

Patients
11 324 patients (51% ≤60 y of age, 85% men) with recent MI (within previous 3 mo) who had no contraindications to the study dietary supplements and no conditions with unfavorable short-term prognoses. Follow-up was 99.9%.

Intervention
Patients were allocated to n-3 PUFAs (n = 2836), vitamin E (n = 2830), n-3 PUFAs and vitamin E (n = 2830), or no supplement (n = 2828). n-3 PUFAs was given in 1 gelatin capsule containing eicosa-pentaenoic acid, 850–882 mg, and docosahexaenoic acid as ethylsters in the mean ratio of 1:2, respectively. Vitamin E, 300 mg, was given as 1 capsule of synthetic α-tocopherol.

Main outcome measures
The combined outcome of all-cause mortality, non-fatal MI, and non-fatal stroke and the combined outcome of cardiovascular death, non-fatal MI, and non-fatal stroke.

Main results
Analysis was by intention to treat. Both combined outcomes were reduced by n-3 PUFAs at 42 months (p = 0.023 for death and non-fatal MI and stroke; and p = 0.008 for cardiovascular death, non-fatal MI, and non-fatal stroke. p = 0.03)(table). Vitamin E did not lead to a difference between groups (table). Combined n-3 PUFAs and vitamin E led to a reduction in the combined outcome of death, non-fatal MI, and non-fatal stroke (p = 0.03)(table).

Conclusions
In patients with recent myocardial infarction (MI), n-3 polyunsaturated fatty acids led to a reduction in the combined outcome of all-cause death, cardiovascular death, non-fatal MI, and non-fatal stroke. Vitamin E alone did not show an effect.

†See glossary.
† p value calculated from data in article.

COMMENTARY
Although many plausible reasons exist to explain why vitamin E should reduce the adverse consequences of coronary artery disease, it does not seem to do so. I suspect that the positive results of epidemiological studies of vitamin E simply reflect its use among people with healthier lifestyles and do not show a cause-and-effect relation. This study reinforces the necessity of properly done randomised controlled trials (RCTs) to determine whether interventions truly work.

Are the results of this study at odds with those of other RCTs? No, because vitamin E supplementation resulted in a mix of good and bad results. In the α-Tocopherol, β-Carotene (ATBC) trial,† a slight decrease in the risk for nonfatal acute MI was counterbalanced by a slight increase in fatal coronary artery disease. In the Cambridge Heart Antioxidant Study (CHAOS),‡ the combined outcome of cardiovascular death and non-fatal acute MI decreased significantly while cardiovascular and total deaths increased slightly. The Heart Outcomes Prevention (HOPE) trial apparently shows a neutral effect. Therefore, vitamin E cannot be recommended for prophylaxis.

Marine oils and PUFAs, found in fish and marine mammals, have been shown to reduce triglyceride levels; to reduce the interaction between the platelet and vessel wall; and in 1 trial, to reduce the risk for death.¶

Unless one has the ability or desire to ingest 100 g/day of fatty fish (about 5 meals/wk), the use of n-3 PUFAs seems to be beneficial.

David Massel, MD
Victoria Hospital
London, Ontario, Canada


 Sources of funding: Bristol-Myers Squibb; Pfizer; Pharmacia-Upjohn; Società Prodotti Antibiotici.

For correspondence: Dr R Marchioli, GISSI-Prevenzione Coordinating Centre, Consorzio Mario Negri Sud, Via Nazionale, 66030 Santa Maria Imbaro, Italy. Fax: +39-0872-578240.