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**

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

**Setting**

Centers 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 PPUA was given in 1 gelatin capsule containing eicosapentaenoic acid, 850 to 882 mg, and docosahexaenoic acid as ethyl asters 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, nonfatal MI, and nonfatal stroke and the combined outcome of cardiovascular death, nonfatal MI, and nonfatal 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 nonfatal MI and stroke; and P = 0.008 for cardiovascular death, nonfatal MI, and nonfatal stroke) (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, nonfatal MI, and nonfatal 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, nonfatal MI, and nonfatal stroke. Vitamin E alone did not show an effect.

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*See Glossary.
†P value calculated from data in article.

<table>
<thead>
<tr>
<th>Outcomes at 42 mo</th>
<th>Supplement type</th>
<th>Supplement</th>
<th>No Supplement</th>
<th>RRR (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death, MI, and stroke</td>
<td>n-3 PUFAs</td>
<td>12.6%</td>
<td>14.6%</td>
<td>14% (2 to 25)</td>
<td>48 (26 to 332)</td>
</tr>
<tr>
<td></td>
<td>Vitamin E</td>
<td>13.1%</td>
<td>14.6%</td>
<td>10% (–2 to 21)</td>
<td>Not significant</td>
</tr>
<tr>
<td></td>
<td>Combined</td>
<td>12.7%</td>
<td>14.6%</td>
<td>13% (1 to 24)</td>
<td>52 (27 to 610)</td>
</tr>
<tr>
<td>Cardiovascular death, MI, and stroke</td>
<td>n-3 PUFAs</td>
<td>9.2%</td>
<td>11.4%</td>
<td>19% (5 to 30)</td>
<td>47 (27 to 177)</td>
</tr>
<tr>
<td></td>
<td>Vitamin E</td>
<td>10.1%</td>
<td>11.4%</td>
<td>11% (–3 to 24)</td>
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</tbody>
</table>

†Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article. MI and stroke refer to nonfatal events.

**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 epidemiologic studies of vitamin E simply reflect its use among persons with healthier lifestyles and do not show a cause-and-effect relation. This study reinforces the necessity of properly done randomized 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 (1), 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) (2), the combined outcome of cardiovascular death and nonfatal acute MI decreased significantly while cardiovascular and total deaths increased slightly. The Heart Outcomes Prevention (HOPE) trial (3) 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 (4). Unless one has the ability or desire to ingest 100 g/d of fatty fish (about 5 meals/wk), the use of n-3 PUFAs seems to be beneficial.

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**References**