

## **n-3 polyunsaturated fatty acids (PUFA) and vitamin E for morbidity and mortality reduction following myocardial infarction (MI)?**

GISSI-Prevenzione Investigators. Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI - Prevenzione trial. *Lancet* 1999; 354: 447-55

**Clinical Question:** Does supplementation with PUFA and/ or vitamin E reduce morbidity and mortality after MI?

**Background:** There is conflicting evidence on the benefits of foods rich in vitamin E, n-3 PUFA, and their pharmacological substitutes. The Greenland Eskimo population has a low incidence of coronary heart disease. It has been inferred that this attribute is related to their diet, which is high in fish oils (PUFA) and vitamin E. This controlled study investigates patients following MI looking at reductions in mortality and morbidity with fish oil and/ or vitamin E supplements.

**Population Studied:** From October, 1993, to September, 1995, 11324 Italian patients surviving recent (within the last 3 months) MI were enrolled. Patients with a poor short-term prognosis or who were unable to take the supplements due to allergies or coagulation defects were excluded from the study. 85% of the participants were male and 63% were aged 50-70. The patients were encouraged to follow a Mediterranean diet, use aspirin, beta-blockers, and an ACE-inhibitor. **Study Design and Validity:** This randomized, non-blinded study assigned the 11,324 patients to supplements of n-3 PUFA ( 1 g daily, n=2836), synthetic vitamin E (300 mg daily, n=2830), both (n=2830), or neither (control, n+2828) for 3-5 years.

**Outcomes measured:** The primary combined efficacy endpoint was death, non-fatal MI, and non-fatal stroke. Intention-to-treat analyses were done by treatment group.

**Results:** Treatment with n-3 PUFA (alone or in combination), but not vitamin E, significantly lowered the risk of the primary endpoint (PUFA alone: 12.3% -vs- 14.6%,  $P<0.05$ ; PUFA with vitamin E: 12.6% -vs- 13.9%,  $P<0.05$ ). Benefit was attributed to a decrease in the risk of death (8.3% -vs- 9.6%,  $P<0.05$ ), specifically cardiovascular death (5.1% -vs- 6.2%,  $P<0.05$ ). There was no significant decrease in non-fatal MI and stroke between the groups. No significant change in death or non-fatal events was noticed with vitamin E supplementation.

**Recommendations for Clinical Practice:** This study provides good evidence that dietary supplementation with n-3 PUFA reduces mortality in post-MI Italian patients who follow a Mediterranean diet and standard post-MI medical advice. It also provides good evidence that vitamin E supplementation has no effect on mortality in the same patient population. A similar investigation is warranted in other populations before this supplementation is implemented for all post-MI patients.