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Articles

# Effects of eicosapentaenoic acid on major coronary events in hypercholesterolaemic patients (JELIS): a randomised open-label, blinded endpoint analysis

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## Summary

### Background

Epidemiological and clinical evidence suggests that an increased intake of long-chain n-3 fatty acids protects against mortality from coronary artery disease. We aimed to test the hypothesis that long-term use of eicosapentaenoic acid (EPA) is effective for prevention of major coronary events in hypercholesterolaemic patients in Japan who consume a large amount of fish.

### Methods

18 645 patients with a total cholesterol of 6.5 mmol/L or greater were recruited from local physicians throughout Japan between 1996 and 1999. Patients were randomly assigned to receive either 1800 mg of EPA daily with statin (EPA group; n=9326) or statin only (controls; n=9319) with a 5-year follow-up. The primary endpoint was any major coronary event, including sudden cardiac death, fatal and non-fatal myocardial infarction, and other non-fatal events including unstable angina pectoris, angioplasty, stenting, or coronary artery bypass grafting. Analysis was by intention-to-treat. The study was registered at [ClinicalTrials.gov](http://ClinicalTrials.gov), number [NCT00231738](https://clinicaltrials.gov/ct2/show/study/NCT00231738).

### Findings

At mean follow-up of 4.6 years, we detected the primary endpoint in 262 (2.8%) patients in the EPA group and 324 (3.5%) in controls—a 19% relative reduction in major coronary events ( $p=0.011$ ). Post-treatment LDL cholesterol concentrations decreased 25%, from 4.7 mmol/L in both groups. Serum LDL cholesterol was not a significant factor in a reduction of risk for major coronary events. Unstable angina and non-fatal coronary events were also significantly reduced in the EPA group. Sudden cardiac death and coronary death did not differ between groups. In patients with a history of coronary artery disease who were given EPA treatment, major coronary events were reduced by 19% (secondary prevention subgroup: 158 [8.7%] in the EPA group *vs* 197 [10.7%] in the control group;  $p=0.048$ ). In patients with no history of coronary artery disease, EPA treatment reduced major coronary events by 18%, but this finding was not significant (104 [1.4%] in the EPA group *vs* 127 [1.7%] in the control group;  $p=0.132$ ).

### Interpretation

EPA is a promising treatment for prevention of major coronary events, and especially non-fatal coronary events, in Japanese hypercholesterolaemic patients.

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