

Review: n-3 polyunsaturated fatty acids reduce fatal myocardial infarction, sudden death, and overall mortality in coronary artery disease

Bucher HC, Hengstler P, Schindler C, et al. N-3 polyunsaturated fatty acids in coronary heart disease: a meta-analysis of randomized controlled trials. *Am J Med* 2002 Mar;112:298-304.

QUESTION: In patients with coronary artery disease (CAD), is dietary or supplemental intake of n-3 polyunsaturated fatty acids more effective than a control diet or placebo for reducing fatal and non-fatal myocardial infarction (MI) and overall mortality?

Data sources

Studies in any language were identified by searching Medline, EMBASE/Excerpta Medica, Pascal BioMed, and Index Medicus from 1966 to August 1999; by searching the *Cochrane Library*; and by scanning bibliographies of relevant publications.

Study selection

Studies were selected if they were randomised controlled trials (RCTs) that compared dietary or supplemental intake of n-3 polyunsaturated fatty acids with a control diet or placebo, reported fatal or non-fatal MI and overall mortality, and followed patients with MI or angiographically established CAD for ≥ 6 months. Studies with angiographic primary end points were eligible if they reported data on MI and mortality. Studies of restricted patients who had had coronary bypass surgery or heart transplantation were excluded.

Data extraction

Data were extracted on intervention and control regimens, patients (number; age; history of MI; treatment with antiplatelet therapy; and total cholesterol, low density lipoprotein cholesterol, and triglyceride concentrations), follow up, study quality, and outcomes. Main outcomes were non-fatal MI, fatal MI, sudden death, and overall mortality.

Main results

11 RCTs (n=15 806, mean age range 49 to 66 y, mean follow up of 20 mo) met the selection criteria: 2 trials were of dietary intake and 9 were of supplemental intake of n-3 polyunsaturated fatty acids. Meta-analysis showed that dietary or supplemental intake of n-3 polyunsaturated fatty acids was more effective than a control diet or

placebo for reducing fatal MI, sudden death, and overall mortality (table). Groups did not differ for non-fatal MI (table).

Conclusions

In patients with coronary artery disease, dietary or supplemental intake of n-3 polyunsaturated fatty acids reduces fatal myocardial infarction, sudden death, and overall mortality more than a control diet or placebo. Groups do not differ for non-fatal myocardial infarction.

COMMENTARY

Observational studies have reported an inverse association between fish consumption and risk for CAD. Since the initial reports over 20 years ago, evidence has accumulated that fish oil fatty acids decrease the risk for CAD. In the meta-analysis by Bucher *et al*, the results from secondary CAD prevention trials analysing intake of fish, omega-3 fish oil supplements, and α -linolenic acid (a plant-based omega-3 fatty acid) were pooled to estimate the effect of these fatty acids on recurrent CAD events and total mortality. Consumption of omega-3 fatty acids in these trials conferred approximately a 20% to 30% reduction in CAD events and total mortality. Only 1 study examined the effect of α -linolenic acid, which, along with such other dietary changes as increased consumption of fruit, vegetables, and fibre, resulted in a 72% reduction in the risk for non-fatal MI and death from CAD over 46 months of follow up.¹ On average, the magnitude of the reported benefit from the omega-3 fatty acids is similar to that seen from statins. Fish oil fatty acids have beneficial effects on platelet aggregation, lipids, endothelial function, inflammation, and the risk for sudden death.

Current recommendations for non-pregnant healthy adults are to eat ≥ 2 servings of fish per week,² which may lower the relative risk for CAD by $\geq 50\%$. For patients with known CAD, the daily consumption of fatty fish (eg, herring, mackerel, and salmon) or approximately 1 g of a fish oil supplement may be recommended to decrease the risk for recurrent events.²

Joel A Simon, MD, MPH
San Francisco Veterans Affairs Medical Center
University of California, San Francisco
San Francisco, California, USA

- de Lorgeril M, Salen P, Martin J-L, *et al*. Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon Diet Heart Study. *Circulation* 1999;99:779-85.
- Krauss RM, Eckel RH, Howard B, *et al*. AHA Dietary Guidelines: revision 2000: a statement for healthcare professionals from the Nutrition Committee of the American Heart Association. *Circulation* 2000;102:2284-99.

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For correspondence:
Dr H C Bucher, Institut
für Klinische
Epidemiologie,
Kantonsspital Basel,
Basel, Switzerland.
hbucher@uhbs.ch.

Dietary or supplemental n-3 polyunsaturated fatty acids (n-3) v control diet or placebo (control) in coronary artery disease*

Outcomes at mean 20 months	Number of trials	Weighted event rates		RRR (95% CI)	NNT (CI)
		N-3	Control		
Non-fatal MI†	9	3.6%	4.3%	20% (-22 to 47)	Not significant
Fatal MI	8	4.5%	5.5%	27% (16 to 36)	96 (63 to 197)
Sudden death	5	2.1%	2.8%	31% (14 to 45)	133 (82 to 345)
Overall mortality	9	8.1%	9.5%	19% (10 to 27)	73 (49 to 147)

*MI = myocardial infarction. Other abbreviations defined in glossary; RRR, NNT, and CI calculated from meta-analysed data in article.

†A random effects model was used because heterogeneity existed.