Fish oil and atrial fibrillation after cardiac surgery: a meta-analysis of randomized controlled trials
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CRD summary
This review concluded that brief perioperative fish oil supplementation appeared to be safe and well tolerated but did not significantly reduce the incidence of postoperative atrial fibrillation or length of hospitalisation after surgery. This conclusion appears to be reliable.

Authors' objectives
To evaluate the effect of fish oil supplementation on postoperative atrial fibrillation (POAF) incidence after cardiac surgery.

Searching
PubMed, EMBASE and The Cochrane Library databases were searched from inception to November 2012 without language restrictions. Search terms were reported and reference lists of retrieved articles were examined to identify further relevant studies.

Study selection
Published prospective randomised controlled trials with a parallel design investigating the effects of fish oil supplementation (oral or intravenous) on the prevention of POAF in adults (at least 18 years of age) undergoing cardiac surgery were eligible for inclusion.

Most of the studies included patients without previous atrial fibrillation who underwent coronary artery bypass graft and/or valve surgery and received oral supplementation of fish oil. Mean ages ranged from 62.7 to 67.0 years. Concurrent medications included beta-blockers, angiotensin converting enzyme inhibitors, angiotensin II receptor blockers and statins in all studies; amiodarone was permitted in one study. Mean doses of fish oil ranged from 1.72 to 4.60g/day. Ratios of EPA (eicosapentaenoic acid) to DHA (docosahexaenoic acid) ranged from 0.5 to 1.4. Supplementation began between half a day and 21 days before surgery. Follow-up ranged from intensive care unit discharge to 14 days after surgery. Comparators were olive oil, free fatty acids, sunola (a sunflower oil), corn oil or no treatment.

Two reviewers independently selected studies for inclusion. Disagreements were resolved by consensus.

Assessment of study quality
Two reviewers independently assessed quality using both the Jadad Scale and the Cochrane Risk of Bias tool.

Data extraction
Data were extracted on study characteristics. Dichotomous outcome data were calculated as relative risks with 95% confidence intervals. Continuous outcomes were calculated as weighted mean differences and related 95% confidence intervals.

Two reviewers independently extracted data. Discrepancies were resolved by consensus.

Methods of synthesis
Statistical heterogeneity was examined using the Cochran Q test and the $I^2$ statistic. In the absence of statistically significant heterogeneity ($Q$ test $p>0.10$ or $I^2\leq50\%$), studies were pooled using a fixed-effect model; a random-effects model was used where heterogeneity was significant.

The possible influence of participant and study characteristics on outcomes was assessed using meta-regression and subgroup analyses. Potential publication bias was assessed using Egger's test and funnel plots.
Results of the review
Eight RCTs (2,687 patients, range 93 to 1,516) were included in the review. Trials scored between 2 and the maximum possible 5 points on the Jadad scale; four studies reported adequate methods of random sequence generation and only two reported allocation concealment. Two studies were of an open-label design and were considered to have a high risk of bias due to the lack of blinding.

Perioperative supplementation of fish oil did not significantly reduce incidence of POAF (RR 0.86, 95% CI 0.71 to 1.03; I²=50%) or length of hospitalisation after surgery (WMD 0.10 days, 95% CI -0.48 to 0.67 days; I²=69%). No studies reported serious adverse events associated with fish oil supplementation and there was no significant effect on perioperative mortality, incidence of major bleeding or length of stay in the intensive care unit.

Meta-regression and subgroup analyses suggested possibly larger benefits with higher doses of docosahexaenoic acid (DHA): fish oil significantly reduced incidence of POAF in trials of supplements with DHA above 1g/day but not in trials with lower doses of DHA.

Authors’ conclusions
Meta-analysis did not support the preventative effects of perioperative fish oil supplementation for the incidence of POAF, although fish oil appeared to be safe and well tolerated and did not significantly affect the perioperative mortality, incidence of major bleeding or hospital and intensive care unit stays.

CRD commentary
This review used appropriate methods to identify and synthesise the relevant randomised evidence for the effects of fish oil supplementation on POAF. The authors made efforts throughout to minimise potential for errors and bias.

From the presented evidence, the authors' main conclusion – that fish oil supplementation appeared to be safe and well tolerated but did not significantly reduce the incidence of POAF – appears to be reliable. Readers should be aware that the duration of treatment and follow-up in the included studies was generally very short and so the included evidence may not be applicable to long-term use of fish oil supplementation.

The possible relationship observed between DHA dose and efficacy might have been due to the lack of blinding in several studies that used a higher dose of DHA; the authors appropriately highlighted this as an area that needed to be confirmed in future trials.

Implications of the review for practice and research
Practice: The authors stated that there was insufficient evidence to recommend fish oil as a preventative measure for postoperative atrial fibrillation.

Research: The authors stated that the influence of pretreatment with cardiac medications and use of on-pump cardiac surgeries should be investigated in future studies as well as the relative amounts of docosahexaenoic acid and eicosapentaenoic acid in fish oil.

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