

No Benefit of Fish Oil in Patients at High CVD Risk

Michael O'Riordan

May 08, 2013

MILAN, ITALY — The supplemental use of n-3 fatty acids does not reduce the risk of cardiovascular morbidity and mortality in patients with multiple cardiovascular-disease risk factors^[1].

These are the conclusions of the **Risk and Prevention Study Collaborative Group**, a collective of Italian researchers led by **Maria Carla Roncaglioni** (Mario Negri Institute of Pharmacological Research, Milan, Italy). In addition to having no effect on the study's primary end point in this group of patients with multiple cardiovascular risk factors or atherosclerotic disease, but no previous MI, the researchers did not observe any benefit on secondary end points, including death from coronary causes or sudden death from cardiac causes or major ventricular arrhythmias.

"Our findings provide no evidence of the usefulness of n-3 fatty acids for preventing cardiovascular death or disease in this population," write the researchers in the May 9, 2013 issue of the *New England Journal of Medicine*.

Dr James Stein (University of Wisconsin, Madison), who was not affiliated with the study, said in an email to **heartwire** that the results are disappointing but consistent with recent studies showing no significant effect of fish-oil supplements. "Especially interesting that there was no effect even in those with low baseline intake of omega-3 fats, those not on aspirin, and those not on statins," he commented.

In the analysis, the researchers did observe a significant interaction between the efficacy of n-3 fatty acids and sex ($p=0.04$), with women treated with fish oil having statistically significant 18% lower risk of the primary end point when compared with women treated with placebo. However, the investigators and Stein caution that the interaction should be interpreted cautiously and might simply be due to chance.

Fish Oil a No-Go, Nada Effect

The study included 12 513 patients, including 6244 randomly assigned to 1 g of n-3 fatty acids (polyunsaturated fatty-acid ethyl esters with eicosapentaenoic acid and docosahexaenoic acid content not less than 85%) and 6269 patients randomized to placebo. The primary end point of the trial was initially a composite that included death, nonfatal MI, and nonfatal stroke but was later revised at one year after a blinded assessment showed a very low event rate. The primary end point was revised to death from cardiovascular causes or hospital admissions for cardiovascular causes.

After a median follow-up of five years, the primary end point curves were virtually superimposable. The primary end point occurred in 11.7% of patients who received the fish oil and 11.9% who received the placebo. The rates of the secondary end points were also similar in both treatment groups.

Primary and Secondary End Points

Outcome	n-3 fatty acids, n=6239 (%)	Placebo, n=6266 (%)	p
Primary end point	11.7	11.9	0.64

Death from cardiovascular causes	2.3	2.2	0.80
Hospitalizations for cardiovascular disease	9.9	10.1	0.68
Death or nonfatal MI or stroke	7.8	7.5	0.64
Death from cardiovascular cause or nonfatal MI or stroke	4.6	4.4	0.59
Fatal or nonfatal coronary event	5.0	5.2	0.51
Death from coronary cause	1.3	1.2	0.66
Sudden death from cardiac cause or major ventricular arrhythmia	1.0	0.8	0.22
Sudden death from cardiac causes	0.8	0.6	0.36

Dr Dariush Mozaffarian (Harvard Medical School, Boston, MA), who was also not involved with the study, said that heart-disease death, rather than nonfatal heart disease or total cardiovascular disease, is the clinical end point most likely influenced by fish oil. For that reason, this trial is important because it is one that has large numbers of heart-disease deaths (158 deaths from coronary causes).

"The lack of any discernible effect on coronary death raises concerns about the real benefits of fish-oil supplements in patients at high risk for cardiovascular disease," said Mozaffarian. "Recommendations to eat fish, in the context of an overall healthy diet, increasing activity, and stopping smoking, should remain the priority for reducing risk."

Dr Eric Topol (Scripps Clinic, La Jolla, CA), editor in chief of theheart.org, posted a video blog on the site, noting that the dose of n-3 fatty acids used in the study was the same dose used in the **GISSI** and **GISSI-HF** trials, two studies that showed a benefit with regard to reducing sudden cardiac death, presumably through the ability to suppress ventricular arrhythmias.

"I have an awful lot of patients that come to me on fish oil, and I implore them to stop taking it," said Topol. The present study, with its efficacious dose, arms physicians with data to tell patients who have not had an MI and who don't have heart failure that n-3 fatty acid supplementation with fish oil is not effective. He called fish oil a "no-go," noting that if the supplement had no effect in this high-risk patient population, of whom just 40% were taking statins, it's hard to imagine n-3 fatty acids will provide any benefit in lower-risk subjects.

"Fish oil does nothing," continued Topol. "We can't continue to argue that we didn't give the right dose or the right preparation. It is a nada effect."

In contrast, Mozaffarian noted that the fish-oil supplement did not cause any harm to patients. In fact, more patients in the placebo arm stopped taking treatment than those who received the fish-oil supplements (17.9% in n-3 fatty acid group vs 19.4% in the placebo group). "So for patients who won't eat fish or wish to be sure they are getting their omega-3s, there is no reason to stop taking fish-oil supplements if they're already on them," he told **heartwire** .

Recently, the **Alpha Omega Trial** even showed that omega-3 fatty acids failed to have any benefit in post-MI patients. Another study, the **OMEGA** trial, found that omega-3 fatty acids provided no benefit in well-treated patients who had an acute MI.

References

1. Risk and Prevention Study Collaborative Group. n-3 fatty acids in patients with multiple cardiovascular risk factors. *N Engl J Med* 2013; 368: 1800-1808.

Heartwire © 2013 Medscape, LLC

Cite this article: No Benefit of Fish Oil in Patients at High CVD Risk. *Medscape*. May 08, 2013.