

Omega-3 Fatty Acids & Atrial Arrhythmias

Human Studies

N-3 Fatty acids for the prevention of atrial fibrillation after coronary artery bypass surgery: a randomized, controlled trial.

Calo L, Bianconi L, Colivicchi F, Lamberti F, Loricchio ML, de Ruvo E,
J Am Coll Cardiol 2005;45:1723-8.

OBJECTIVES: The aim of this study was to assess the efficacy of preoperative and postoperative treatment with n-3 polyunsaturated fatty acids (PUFAs) in preventing the occurrence of atrial fibrillation (AF) after coronary artery bypass graft surgery (CABG). **BACKGROUND:** Postoperative AF is a common complication of CABG. There is growing clinical evidence that PUFAs have cardiac antiarrhythmic effects. **METHODS:** A total of 160 patients were prospectively randomized to a control group (81 patients, 13 female, 64.9 +/- 9.1 years) or PUFAs 2 g/day (79 patients, 11 female, 66.2 +/- 8.0 years) for at least 5 days before elective CABG and until the day of discharge from the hospital. The primary end point was the development of AF in the postoperative period. The secondary end point was the hospital length of stay after surgery. All end points were independently adjudicated by two cardiologists blinded to treatment assignment. **RESULTS:** The clinical and surgical characteristics of the patients in the two groups were similar. Postoperative AF developed in 27 patients of the control group (33.3%) and in 12 patients of the PUFA group (15.2%) ($p = 0.013$). There was no significant difference in the incidence of nonfatal postoperative complications, and postoperative mortality was similar in the PUFA-treated patients (1.3%) versus controls (2.5%). After CABG, the PUFA patients were hospitalized for significantly fewer days than controls (7.3 +/- 2.1 days vs. 8.2 +/- 2.6 days, $p = 0.017$). **CONCLUSIONS:** This study first demonstrates that PUFA administration during hospitalization in patients undergoing CABG substantially reduced the incidence of postoperative AF (54.4%) and was associated with a shorter hospital stay.

[Effect of omega-3 fatty acids on the prevention of atrial arrhythmias] [Article in Italian]

Biscione F, Totteri A, De Vita A, Lo Bianco F, Altamura G.
Ital Heart J Suppl 2005;6:53-9.

BACKGROUND: The effects of omega-3 fatty acids on membrane stabilization are well known. Reduction of ventricular arrhythmias and sudden death has been reported; fewer data exist regarding the effects on atrial arrhythmias. The object of this report is to evaluate the reduction of atrial arrhythmia-fibrillation after treatment with omega-3, in patients with dual-chamber pacemakers. **METHODS:** We have examined 40 patients with paroxysmal atrial tachyarrhythmia recorded at the periodic pacemaker controls. At the study entry, all patients were treated with omega-3 (1 g/die); no changes in the device programming and in the previous pharmacological therapy were allowed. The devices were interrogated after 4 months of treatment to evaluate the number of episodes and the burden of atrial tachyarrhythmia. At this time, the treatment was discontinued and the patients were reevaluated 4 months later. **RESULTS:** Two patients discontinued the treatment complaining of adverse gastroenteric effects. The episodes of atrial tachyarrhythmia in the pre-treatment period resulted 444 +/- 1161, and the burden 3.89% of time; in the treatment period resulted respectively 181 +/- 436 (-59%, $p = 0.037$) and 1.06% (-67%, $p = 0.029$). After drug withdrawal, the episodes of atrial tachyarrhythmia raised to 552 +/- 1717 ($p = 0.065$) and the burden to 2.69% ($p = 0.003$). **CONCLUSIONS:** Our data suggest a powerful effect of omega-3 fatty acids in the reduction of atrial tachyarrhythmia-fibrillation in these patients, without significant adverse effects.

n-3 Fatty acids consumed from fish and risk of atrial fibrillation or flutter: the Danish Diet, Cancer, and Health Study.

Frost L, Vestergaard P
Am J Clin Nutr 2005 Jan;81(1):50-4.

BACKGROUND: Experimental studies have shown that n-3 polyunsaturated fatty acids in fish may have antiarrhythmic properties. **OBJECTIVE:** We examined the association between consumption of n-3 fatty acids from fish and risk of atrial fibril-

lation or flutter. DESIGN: In a prospective cohort study of 47 949 participants (mean age: 56 y) in the Danish Diet, Cancer, and Health Study, we investigated the relation between the consumption of n-3 fatty acids from fish estimated from a detailed semiquantitative food questionnaire and risk of atrial fibrillation or flutter. The subjects were followed up in the Danish National Registry of Patients for the occurrence of atrial fibrillation or flutter and in the Danish Civil Registration System (vital status and emigration). The consumption of n-3 fatty acids from fish was analyzed as sex-specific quintiles with the use of Cox proportional hazards models. RESULTS: During follow-up (x: 5.7 y), atrial fibrillation or flutter had developed in 556 subjects (374 men and 182 women). When the lowest quintile of n-3 fatty acids consumed from fish was used as a reference, the unadjusted hazard rate ratios in quintiles 2, 3, 4, and 5 were 0.93, 1.11, 1.10, and 1.44, respectively (P for trend = 0.001). The corresponding adjusted hazard rate ratios were 0.86, 1.08, 1.01, and 1.34 (P for trend = 0.006). Inclusion of information on the frequency of fatty fish consumption did not alter these associations. CONCLUSIONS: Consumption of n-3 fatty acids from fish was not associated with a reduction in risk of atrial fibrillation or flutter. We cannot exclude the possibility of residual confounding caused by a lack of information on intake of fish-oil tablets.

Fish intake and risk of incident atrial fibrillation.

Mozaffarian D, Psaty BM, Rimm EB, Lemaitre RN, Burke GL, Lyles MF, Lefkowitz D, Siscovick DS. *Circulation* 2004 Jul 27;110(4):368-73. Epub 2004 Jul 19.

BACKGROUND: Atrial fibrillation (AF) is the most common arrhythmia in clinical practice and is particularly common in the elderly. Although effects of fish intake, including potential antiarrhythmic effects, may favorably influence risk of AF, relationships between fish intake and AF incidence have not been evaluated. METHODS AND RESULTS: In a prospective, population-based cohort of 4815 adults \geq age 65 years, usual dietary intake was assessed at baseline in 1989 and 1990. Consumption of tuna and other broiled or baked fish correlated with plasma phospholipid long-chain n-3 fatty acids, whereas consumption of fried fish or fish sandwiches (fish burgers) did not. AF incidence was prospectively ascertained on the basis of hospital discharge records and annual electrocardiograms. During 12 years' follow-up, 980 cases of incident AF were diagnosed. In multivariate analyses, consumption of tuna or other broiled or baked fish was inversely associated with incidence of AF, with 28% lower risk with intake 1 to 4 times per week (HR=0.72, 95% CI=0.58 to 0.91, P=0.005), and 31% lower risk with intake \geq 5 times per week (HR=0.69, 95% CI=0.52 to 0.91, P=0.008), compared with $<$ 1 time per month (P trend=0.004). Results were not materially different after adjustment for preceding myocardial infarction or congestive heart failure. In similar analyses, fried fish/fish sandwich consumption was not associated with lower risk of AF. CONCLUSIONS: Among elderly adults, consumption of tuna or other broiled or baked fish, but not fried fish or fish sandwiches, is associated with lower incidence of AF. Fish intake may influence risk of this common cardiac arrhythmia.

Animal Studies

Dietary fish oil protects against stretch-induced vulnerability to atrial fibrillation in a rabbit model

Nino DM, Murphy KJ, Howe PR, Saint DA. *Circulation* 2005;116:1189-94.

INTRODUCTION: Dietary fish oil is thought to reduce sudden cardiac death by suppressing ventricular arrhythmias but little is known about its impact on atrial arrhythmias. We examined the effect of dietary fish oil on the rabbit model of stretch-induced vulnerability to atrial fibrillation (AF). METHODS AND RESULTS: Six-week-old rabbits were fed standard rabbit pellets supplemented with 5% tuna fish oil (n = 6) or supplemented with 5% sunflower oil (n = 6) for 12 weeks. Six rabbits raised on the standard diet were used as controls. In Langendorff-perfused hearts intraatrial pressures were increased in a stepwise manner and rapid burst pacing applied to induce AF at increasing intraatrial pressures until AF was sustained ($>$ 1 minute). Atrial refractory periods were recorded at each pressure. Increased atrial pressure resulted in a reduction in atrial refractory period and a propensity for induction of sustained AF. Higher pressures were needed to induce and sustain AF in the fish oil group compared with the sunflower oil and control groups. The stretch-induced drop in refractory period was also less marked in the fish oil group. Red blood cell, atrial, and ventricular omega-3 fatty acid levels were significantly higher in the fish oil group. The ratio of atrial n-6/n-3 polyunsaturated fatty acids was 13 \pm 0.9 with sunflower oil and 1.5 \pm 0.01 with fish oil (P $<$ 0.001). CONCLUSIONS: Incorporation of dietary omega-3 fatty acids into atrial tissue reduces stretch-induced susceptibility to AF

Laboratory Studies

Termination of asynchronous contractile activity in rat atrial myocytes by n-3 polyunsaturated fatty acids.

Jahangiri A, Leifert WR, Patten GS, McMurchie EJ.
Mol Cell Biochem 2000;206:33-41.

A protective effect of the n-3 polyunsaturated fatty acids (PUFAs) in preventing ventricular fibrillation in experimental animals and cultured cardiomyocytes has been demonstrated in a number of studies. In this study, a possible role for the n-3 PUFAs in the treatment of atrial fibrillation (AF) was investigated at the cellular level using atrial myocytes isolated from young adult rats as the experimental model. Electrically-stimulated, synchronously-contracting myocytes were induced to contract asynchronously by the addition of 10 microM isoproterenol. Asynchronous contractile activity was reduced following acute addition of the n-3 PUFAs docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) at 10 microM, compared with no fatty acid addition (from 99.0+/-1.0% to 30.7+/-5.2% (p < 0.05) for DHA and 23.8+/-2.8% (p < 0.01) for EPA), while the saturated fatty acid, docosanoic acid (DA) and the methyl ester of DHA (DHA m.e.) did not exert a significant effect on asynchronous contractile activity. Asynchronous contractile activity was also reduced to 1.7+/-1.7% in the presence of the membrane fluidising agent, benzyl alcohol (p < 0.001 vs no fatty acid addition). Cell membrane fluidity was determined by steady state fluorescence anisotropy using the fluorescent probe, TMAP-DPH. Addition of DHA, EPA or benzyl alcohol significantly increased sarcolemmal membrane fluidity (decreased anisotropy, r(ss)) of atrial myocytes compared with no addition of fatty acid (control) (from r(ss) = 0.203+/-0.004 to 0.159+/-0.004 (p < 0.01) for DHA, 0.166+/-0.001 (p < 0.01) for EPA and 0.186+/-0.003 (p < 0.05) for benzyl alcohol, while DA and DHA m.e. were without effect. It is concluded that the n-3 PUFAs exert anti-asynchronous effects in rat atrial myocytes by a mechanism which may involve changes in membrane fluidity.

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