

# Effects of Omega-3 Fatty Acids in Cardiac Arrhythmias

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**Abstract:** *Although epidemiological studies provide strong evidence for an inverse relationship between omega-3 polyunsaturated fatty acids (n-3 PUFAs) and cardiac mortality, inconsistent and often conflicting results have been obtained from both animal studies and clinical prevention trials. Circulating (acute administration) n-3 PUFAs affect ion channels directly while incorporation (long-term supplementation) of these lipids into cell membranes indirectly alter cardiac electrical activity via alteration of membrane properties. 2) n-3 PUFAs reduce baseline HR and increase HRV via alterations in intrinsic pacemaker rate rather than from changes in cardiac autonomic neural regulation. 3) n-3 PUFAs may be only effective if given before electrophysiological or structural remodeling has begun and have no efficacy against atrial fibrillation. 5) Despite initial encouraging results, more recent clinical prevention and animal studies have not only failed to reduce sudden cardiac death but actually increased mortality in angina patients and increased rather than decreased malignant arrhythmias in animal models of regional ischemia. 6) Given the inconsistent benefits reported in clinical and experimental studies and the potential adverse actions on cardiac rhythm noted during myocardial ischemia, n-3 PUFA must be prescribed with caution and generalized recommendations to increase fish intake or to take n-3 PUFA supplements need to be reconsidered.*

**Keywords:** Omega-3 fatty acids, polyunsaturated fatty acids, fish oil, cardiac arrhythmias

## 1. Introduction

Omega-3 fats are a key family of polyunsaturated fats. There are three main omega-3s: Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) come mainly from fish, so they are sometimes called marine omega-3s. Alpha-linolenic acid (ALA), the most common omega-3 fatty acid in most Western diets, is found in vegetable oils and nuts (especially walnuts), flax seeds and flaxseed oil, leafy vegetables, and some animal fat, especially in grass-fed animals. The human body generally uses ALA for energy, and conversion into EPA and DHA is very limited. CHD is caused by atherosclerosis, a long-term process in which fatty deposits of plaque build up on the inside of the coronary arteries, the blood vessels that supply the heart muscle with oxygen and nutrients. Eventually, the coronary arteries become so narrow that the flow of blood to the heart muscle is decreased or easily blocked by plaque or a blood clot. CHD can produce chest pain, called angina; heart attack; or both. Atherosclerosis begins when the inside wall of an artery is damaged by high levels of cholesterol and triglycerides, another form of fat in your blood, and by inflammation. A diet high in fat, particularly saturated fat, increases cholesterol and triglycerides. Artery damage can also be caused by high blood pressure, tobacco smoke, or diabetes. To help prevent heart disease, you should keep your cholesterol and triglycerides at or below recommended levels. According to the National Heart, Lung, and Blood Institute, that means a total cholesterol level of less than 200 mg/dL and a triglyceride level of less than 150 mg/dL

## 2. Source of Omega-3 Fatty Acids

Fish oil is the most concentrated source of the omega-3 fatty acids EPA and DHA. These fatty acids are present in cold-water fish such as wild salmon, halibut, and mackerel, as well as in fish oil supplements. Existing data suggest that a dose of fish oil that delivers approximately 1,400–2,000 mg of EPA plus 1,000–1,500 mg of DHA is likely to yield heart

rhythm benefits. This dose is similar to that used in the GISSI-Prevenzione trial that yielded a substantial reduction in cardiovascular events.

A secondary source of omega-3 fatty acids is alpha-linolenic acid (ALA) found in flaxseed, walnuts, and canola oil. Less than 10% of the alpha-linolenic acid ingested, however, is converted into active EPA or DHA, since much of it is simply burned for calories. These sources should be viewed as second choices in your quest to obtain adequate levels of omega-3 fatty acids necessary for optimal health. Nonetheless, emerging experiences are suggesting that alpha-l

## 3. Side effects and Warnings of Omega-3 Acids

Omega-3 is considered likely safe when taken as a supplement in recommended doses for up to 2-3.5 years, or when included in the diet (1-2 fish meals per week). The U.S. Food and Drug Administration (FDA) has ruled that the use of EPA and DHA, the primary omega-3 fatty acids found in fish, as dietary supplements is safe and lawful, as long as daily intakes do not exceed three grams per person daily from food and supplement sources. Omega-3 is considered possibly safe when taken by mouth in amounts found in foods during pregnancy and breastfeeding. There is not enough information at this time regarding the safety of fish oils when used in amounts greater than those found in foods during pregnancy and breastfeeding. Up to 20 grams of fish may be well tolerated by most adults, although some experts warn that high doses may cause bleeding complications.

Omega-3 may also cause abnormal heart rhythm, abnormally high urination, acid reflux, anemia, anorexia, bad breath, bad taste in the mouth, bloating, bloody urine, blurred vision, burping, cancer, changes in energy and physical activity (in infants whose mothers received supplementation), changes in homocysteine levels, the

common cold, constipation, diarrhea, dizziness, excess fat in the stool, fainting (in pregnant women at birth), a feeling of ants crawling on the skin, a feeling of burning or prickling, a feeling of lifelessness, fever, fishy hiccups, gas, headache, heart attack, hospitalization (chest pain, congestive heart failure, or nervous system problems), increased risk of stroke, indigestion, intolerance to capsule number or size, mania, memory problems, muscle pain or swelling, nausea, the need for surgery (coronary revascularization), nervous system toxicity, nosebleed, restlessness, sleep problems, sudden cardiac death, skin problems (irritation, itching, rashes), stomach pain, throat pain, tiredness, vomiting and weight gain

#### 4. Benefits of Omega-3 Fatty Acids on Cardiovascular System

The cardiovascular benefits of dietary omega-3 polyunsaturated fatty acids (n-3 PUFA) have been actively investigated for nearly 40 years. Beginning with the pioneering studies of Bang and Dyerberg (Dyerberg et al., 1978; Bang et al., 1980), epidemiological data provide strong evidence for an inverse relationship between fatty fish consumption and cardiac mortality (Kromhout et al., 1985; Daviglus et al., 1997). In contrast to these observational studies, interventional studies using n-3 PUFAs for the secondary prevention of adverse cardiovascular events in patients with heart disease have yielded conflicting results. Some studies have reported reduced sudden cardiac death or mortality (Burr et al., 1989; Marchioli et al., 2002), while other more recent studies have reported that n-3 PUFAs either had no effect on cardiac arrhythmias [either ventricular arrhythmias/sudden death (Brouwer et al., 2006; Yokoyama et al., 2007; GISSI-HF Investigators, 2008; Kromhout et al., 2010; Rauch et al., 2010) or atrial fibrillation (Kowey et al., 2010; Mozaffarian et al., 2012; Sandesara et al., 2012)] or actually increased adverse cardiac events (Burr et al., 2003; Raitt et al., 2005). Not surprisingly, meta-analysis of these studies have yielded similar conflicting results (Hooper et al., 2004; Jenkins et al., 2008; Brouwer et al., 2009; Leon et al., 2009; Zhao et al., 2009; Filion et al., 2010) with the most recent study finding that omega-3 fatty acids were neutral, neither increasing nor decreasing the risk for arrhythmias (Rizos et al., 2012). Similar conflicting results have been obtained from animals models (McLennan et al., 1988; Billman et al., 1994; Coronel et al., 2007; Billman et al., 2012). Of particular note, dietary n-3 PUFAs increased rather than decreased susceptibility to arrhythmias induced by regional myocardial ischemia in isolated hearts (Coronel et al., 2007) and provoked ventricular fibrillation in conscious animals previously shown to be at a low risk for malignant arrhythmias (Billman et al., 2012). Despite these inconsistent findings, the American Heart Association and the American College of Cardiology continue to recommend fish oils for the secondary prevention of coronary artery disease (Kris-Etherton et al., 2003; Smith et al., 2006). Based in part upon these recommendations, consumer demand for n-3 PUFA products (both nutritional supplements and foods enriched with these lipids) has exploded. It has been estimated that 5–10% of the adult US population use fish oil supplements and sales are projected to exceed 7 billion dollars by the end of 2011. Despite the intensive marketing of fish oil products, a scientific

consensus on the effects of n-3 PUFA on cardiac rhythm has yet to be reached. It is the purpose of this book to stimulate a discussion on the putative benefits of n-3 PUFAs on cardiac rhythm. The book contains both state-of-the art reviews of the literature and original research articles that address various aspects of the effects of n-3 PUFAs on cardiac rhythm. The book is divided into three sections. The first section addresses the effects of n-3 PUFAs on heart rate variability. The second section provides comprehensive reviews of the effects of n-3 PUFAs on ventricular arrhythmias/sudden death and on atrial fibrillation. The third and final section evaluates the cellular mechanisms by which n-3 PUFAs can influence arrhythmia formation. By understanding how n-3 PUFAs affect the cardiac rhythm, the author hopes that this brief monograph will provide an education sufficient to keep at least one heart from breaking.

#### 5. Conclusion

Omega-3 fatty acids act as pleiotropic agents on the cardiovascular system with diverse range of effects, most of which are beneficial. Although findings from several studies have suggested a mechanistic possibility of an antiarrhythmic effect, those from clinical studies have not convincingly supported this mode of action. Chronic and severe deficiency of the omega-3 fraction of fats from the American diet may be major causative factor behind cardiovascular events, particularly life threatening heart arrhythmias. Fish oil rich in omega-3 fatty acids may help treat the basics nutritional deficit that underlies many rhythm disorders.

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