

# Omega-3 polyunsaturated fatty acids and cardiac rhythm: an introduction

[Health & Medicine](#)



“ Sine doctrina, vita est quasi mortis imago” [Without, education, life is but the image of death] Dionysius Cato (Roman author, Fl. 4th c. AD).

“ If I can stop one heart from breaking, I shall not live in vain” Emily Dickinson (American poet, 1830–1886).

The effective management of cardiac arrhythmias, either of atrial or of ventricular origin, remains a major challenge for the cardiologist. Sudden cardiac death most frequently due to ventricular tachyarrhythmias ( [Hinkle and Thaler, 1982](#) ; [Bayes de Luna et al., 1989](#) ; [Greene, 1990](#) ) remains the leading cause of death in industrially developed countries, accounting for between 300, 000 and 500, 000 deaths each year in the United States ( [Abildstrom et al., 1999](#) ; [Zheng et al., 2001](#) ). In a similar manner, atrial fibrillation is the most common rhythm disorder ( [Kannel et al., 1998](#) ; [Lakshminarayan et al., 2006](#) ), accounting for about 2. 3 million cases in the United States and has been projected to increase by 2. 5-fold over the next half century ( [Anonymous, 1998](#) ). Indeed, the prevalence of this arrhythmia increases with each decade of life (0. 5% patient population between the ages of 50 and 59 years climbing to almost 9% at age 80–89 years) and contributes to approximately one-quarter of ischemic strokes in the elderly population ( [Kannel et al., 1998](#) ; [Lakshminarayan et al., 2006](#) ). The economic impact associated with the morbidity and mortality resulting from cardiac arrhythmias is enormous [incremental cost per quality-adjusted life-year as much as US \$558, 000 ( [Byrant et al., 2005](#) )].

Despite the enormity of this problem, the development of safe and effective anti-arrhythmic agents remains elusive. Several anti-arrhythmic drugs have

actually been shown to increase, rather than to decrease, the risk for arrhythmic death in patients recovering from myocardial infarction ( [Echt et al., 1991](#) ; [Waldo et al., 1996](#) ) while even “ optimal” pharmacological therapy fails to suppress these arrhythmias completely ( [Buxton et al., 1999](#) ). For example, the one-year mortality is 10% or higher, with sudden death accounting for approximately one-third of the deaths, in post-myocardial infarction patients treated with  $\beta$ -adrenergic receptor antagonists ( [Buxton et al., 1999](#) ). Implantable cardioverter defibrillators (ICDs) have been shown to reduce cardiac mortality, providing a better protection from sudden death than current pharmacological therapy in certain high-risk patient populations ( [Buxton et al., 1999](#) ; [Connelly et al., 2000](#) ). However, these devices are expensive to use and maintain ( [Groeneveld et al., 2006](#) ), negatively affect the patient's quality of life ( [Groeneveld et al., 2006](#) ), have a significant risk for inappropriate shock delivery ( [Poole et al., 2008](#) ), are ineffective in females patients ( [Henyan et al., 2006](#) ), and, perhaps most importantly, only extend life by a mean of 4. 4 months ( [Connelly et al., 2000](#) ). Given the adverse outcomes associated with ICDs and many anti-arrhythmic medications, as well as the partial protection afforded by even the best agents (e. g.,  $\beta$ -adrenergic receptor antagonists and ICDs), it is obvious that more effective anti-arrhythmic therapies must be developed.

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 ( <https://assignbuster.com/omega-3-polyunsaturated-fatty-acids-and-cardiac-rhythm-an-introduction/>

[Kromhout et al., 1985](#) ; [Daviglius 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 [ [www.marketresearch.com](http://www.marketresearch.com), product reports].

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 (chapters 2–4). The second section provides comprehensive reviews of the effects of n-3 PUFAs on ventricular arrhythmias/sudden death (chapters 5–8) and on atrial fibrillation (chapters 8–10). The third and final section (chapters 11–16) 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.

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