OMEGA-3 FATTY ACIDS AND CARDIOVASCULAR HEALTH

According to the American Heart Association, approximately one in three deaths in the U.S. result from cardiovascular disease (CVD), with more than 2,100 people dying from it each day.[1] Although the treatment of CVD has improved markedly in the last decade, other factors such as hypertension, smoking, type 2 diabetes, physical inactivity and poor diet contribute substantially to an individual's chance of CVD mortality. Because diet contributes importantly to CVD, high blood pressure, diabetes and obesity and can be improved, this paper focuses on the contribution of dietary long-chain omega-3 polyunsaturated fatty acids (omega-3 PUFAs) to reducing the risk of CVD.

Long-chain omega-3 PUFAs come primarily from seafood or marine algae and consist mainly of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), with small amounts of docosapentaenoic acid. They are chiefly responsible for the association between regular fish consumption and a significantly lower risk of dying from CVD or coronary heart disease (CHD) in older adults,[2,3] in patients who survived a myocardial infarction (heart attack),[4] those on hemodialysis[5] and other patients.[6,7] Some recent clinical trials, however, reported no significant reduction in CVD mortality in patients at high risk of CVD who consumed EPA and DHA.[8-10] Reasons for the discrepancy between earlier trials and more recent ones may relate to the lower risk of mortality in patients now receiving state-of-the-art medical care,[7] insufficient statistical power in the study design[11] and a background of increased consumption of fish or omega-3 supplements.[12-14] Further, the use of several combined endpoints, such as fatal and nonfatal cardiac events, to evaluate the effect of omega-3 PUFAs increases the likelihood of observing no significant effect.[15,16] In contrast to studies claiming no benefit from omega-3 PUFAs in reducing the risk of heart disease mortality, other recent trials have documented a significantly lower risk of CVD mortality with higher consumption or blood levels of EPA and DHA.[2,17,18] Providing greater amounts of omega-3 PUFAs in CVD patients also warrants additional investigation. Evaluation of controversial studies requires an overview of the big picture before rejecting decades of credible findings and the more sophisticated understanding of CVD we now have.[15,19]

Omega-3 PUFAs, especially EPA, may be beneficial for individuals with heart failure. In this condition, the heart's ability to pump blood is impaired, leaving the tissues short of oxygen and a person feeling tired and short of breath. Heart failure affects more than 5 million Americans above the age of 20 years and carries a high risk of mortality.[20] Approximately half of patients with heart failure die within five years of diagnosis.[21] However, greater consumption of fish or omega-3 PUFAs or higher levels of EPA in the blood are associated with a lower risk of heart failure and reduced mortality from it.[22-24] Treatment of heart failure patients with omega-3 PUFAs may also improve ventricular function.[25-27] In another study, survivors of acute myocardial infarction (heart attack) who were treated with both a statin and omega-3 PUFAs experienced a significantly longer survival without heart failure compared with patients who received only the statin medication.[28] Others reported that patients with chronic heart failure and major depressive disorder who had higher plasma levels of omega-3 PUFAs or EPA had significantly longer survival compared with patients with the lowest levels of omega-3 PUFAs.[29] A review and meta-analysis of seven clinical trials in patients with heart failure concluded that fish oils are associated with improved cardiac performance, remodeling and functional capacity.[30]

Consumption of omega-3 PUFAs from marine sources has antithrombotic and anti-inflammatory effects and may have antiarrhythmic effects.[31,32] These fatty acids inhibit platelet aggregation and decrease thrombin formation, which discourages artery-blocking blood clot formation.[33-35] However, the ability of omega-3 PUFAs to increase the time for blood to clot has led to concerns about the risk of increased bleeding. A recent investigation of this issue concluded that because of their multiple beneficial effects on hemostasis, there was no need to stop consuming omega-3 PUFAs prior to surgery or when consuming other agents that control blood clotting.[36] In addition, the consumption of omega-3 PUFAs is associated with increased heart rate variability[37] and lower heart rate at rest, during stress and in myocardial ischemia.[38,39] These effects contribute to cardioprotection. Other important vascular effects of omega-3 PUFAs include a modest reduction in blood pressure,[40-42] increased dilation of the coronary arteries[43] and improved endothelial function.[44]

The anti-inflammatory effects of marine omega-3 PUFAs are being intensely investigated in healthy individuals and those with various clinical conditions. Inflammation underlies the major chronic conditions, including CVD, type 2 diabetes, metabolic syndrome, obesity and many autoimmune diseases, namely rheumatoid arthritis, asthma, colitis, psoriasis and some allergies. In fact, inflammation is the link between insulin resistance, obesity and type 2 diabetes, each of which increases the risk of CVD.[45] Atherosclerosis—the accumulation of lipids, immune cells and other substances as plaque in the arteries—contributes to and aggravates CVD and reducing the inflammation associated with it has become the target of medical therapies.[45,46] Through their effects on the endothelial cells lining the arteries, various immune cells and gene expression, omega-3 PUFAs reduce the excessive inflammatory activity observed in CVD.[44,47] Relatively recently, a new class of omega-3 PUFA derivatives has shown potent ability to limit and terminate overactive inflammatory responses. These agents include resolvins, protectins, lipoxins and maresins.[48]

One of the most important and consistent effects of omega-3 PUFAs is the reduction of blood triglyceride levels.[48] Hypertriglyceridemia occurs frequently in type 2 diabetes, obesity and several types of dyslipidemia and increases the risk of CVD by as much as 25%.[49] Very high levels of triglycerides increase the risk of pancreatitis as well. The triglyceride-lowering effect of omega-3 PUFAs is observed in individuals with normal blood lipid levels, but is dramatic in those with elevated triglycerides.[50,51] Omega-3 PUFAs may be used alone or in conjunction with other therapies for the treatment of elevated triglycerides and have the advantage of minimal, if any, side effects.[52]

This article has highlighted some of the main physiologic benefits of omega-3 PUFA consumption in CVD. Other effects beyond the scope of this paper include increased adiponectin levels, which are associated with increased fatty acid oxidation, improved insulin sensitivity and adipocyte function;[53] reduced oxidative stress;[54,55] increased plaque stability;[56] and changes in membrane structure, signaling proteins and gene expression, all of which contribute to the ways omega-3 PUFAs protect cardiovascular health and extend life.[2]

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