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Nutrition Noteworthy

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Reviewing the Evidence: Does Fish Consumption Reduce the Risk of Coronary Heart Disease and Myocardial Infarction?

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Introduction

According to the American Heart Association, cardiovascular disease has been the leading cause of death in the US every year since 1900, except for 1918. According to 1998 statistics, there are 949,000 cardiovascular deaths in the US per year. Approximately twelve million Americans currently have coronary heart disease and are at increased risk for myocardial infarction (1). These statistics provide a compelling reason for identifying substances that promote cardiovascular health.

The low rates of coronary heart disease among the Japanese and Greenland Eskimos, where fish is a large part of the diet, initially suggested that dietary fish intake may protect against cardiovascular disease and sparked a great interest in fish oil (2). Fish and other seafoods contain a special class of polyunsaturated fatty acids called long chain omega-3 fatty acids. The omega-3 acids present in fish and fish oils are called eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). While EPA and DHA can be obtained from the endogenous conversion of α -linolenic acid found in vegetable oils, the amount converted is believed to be small (3).

Proposed Mechanism of Action of Omega-3 Fatty Acids

There are many possible mechanisms for the beneficial effect of eating fish on cardiovascular disease. Fish oil fatty acids are incorporated into plasma membranes, where they affect the membrane characteristics. These fatty acids then decrease the production of some eicosanoids such as thromboxane A₂ (a clot-promoting substance which is inhibited by aspirin), while increasing the synthesis of others (prostaglandin I₃, an anticoagulant). The combined effect is a reduction in platelet aggregation and therefore increased bleeding times (4).

Omega-3 fatty acids have also been shown to reduce serum triglyceride levels (5). and, in some studies, LDL cholesterol as well (6). Large amounts of fish oil may lower blood pressure. Experimental data in primates (7). has shown that omega-3 fatty acids in fish have antiarrhythmic abilities.

Fish Intake and Risk of Myocardial Infarction: The Pro Side

Currently, the role of fish oil in the prevention of coronary artery disease and myocardial infarction is controversial. Despite the fact that numerous studies have been done to test the hypothesis, the verdict is still out. The following is a description of several prospective epidemiological studies that have shown decreased mortality due to heart attack for men who eat some fish compared to men who eat none.

In a 20-year follow-up study of 852 men in Zutphen, the Netherlands, men who ate as little as 30-44 g/day (approximately 1-2 fish meals a week) experienced more than 50% fewer deaths from coronary heart disease than men with no fish intake (8). Fish intake was determined by a dietician-conducted interview of participants and their wives. Of numerous variables including alcohol, energy, poly- and mono-unsaturated fat intake, only age, dietary cholesterol level and fish intake were significantly related to death from coronary heart disease during the 20 years. The risk ratios for death from coronary heart disease decreased with increasing fish consumption.

In the Diet and Reinfarction Trial (DART), a secondary prevention trial with 2,033 men, the risk of death from ischemic heart disease was significantly decreased in men who were advised to eat two fish meals per week compared to men who were advised to lower saturated fat or increase fiber in their diets. Despite this, the incidence of nonfatal myocardial infarction was the same for those who did and did not consume fish. The authors hypothesized that fish consumption may reduce the occurrence of fatal arrhythmias and therefore mortality, but have no effect on reinfarction (9).

An inverse trend was also observed among Western Electric workers in Chicago (10). In this sample of 1,822 men aged 40-55 years who were followed for 30 years, a 25% reduction in coronary disease mortality was seen in men with fish intake of 18-34 g/day compared to men who ate no fish. As in the Zutphen and DART studies, detailed dietary histories were used to determine fish intake. In particular, the study showed a reduced risk of non-sudden, but not sudden, death from myocardial infarction.

In contrast, the Physicians' Health Study showed that men who had low to moderate fish intake experienced a 52 % decrease in the risk of sudden death from myocardial infarction compared to men who ate no fish (11). Beginning in 1982, the study enrolled 22,071 US male physicians aged 40-84 years with no cardiovascular disease in order to test the efficacy of aspirin on cardiovascular disease and beta-carotene on cancer. The aspirin component of the study was terminated early and therefore allowed the investigators to examine dietary fish intake and cardiovascular risk. Follow-up was conducted for eleven years. Fish intake was determined by a dietary questionnaire and measurements of omega-3 fatty acids in adipose tissue showed that the questionnaire reliably reported their intake. While the differing results of the Physicians' Health Study and the Western Electric Study are concerning, there may be an explanation. The Western Electric study used death certificates alone to determine whether the deaths were sudden or non-sudden, while the Physicians' Health Study used next of kin reports, medical records and autopsy results to determine the timing of death.

Fish Intake and Risk of Myocardial Infarction: The Con Side

In contrast, several other prospective epidemiologic studies have not shown that eating fish confers a substantial cardiovascular benefit. In 1995, Ascherio, et al. (12). reported the results of the Health Professionals Follow-up Study, in which 44, 895 male health professionals aged 40 to 75 years were followed for six years. Fish intake was again determined by questionnaire and was corroborated by measurements of omega-3 fatty acids in adipose tissue. Unlike the previously mentioned studies, the investigators found no association between increased fish consumption and death caused by coronary artery disease. The study did demonstrate, however, that men who reported no fish consumption had the highest risk of fatal coronary disease, but the risk did not decrease with increasing fish intake as had been shown in the Zutphen, DART and Physicians' Health studies. The conclusion from the study was that while a little fish is good, more is not necessarily better.

The lack of evidence for a protective effect of fish oil was disconcerting to many researchers. While other investigators had previously reported similar findings to those of Ascherio, et al., the number of participants in the Health Professionals Follow-up Study was much larger than all of the other studies and the methods were more scientifically rigorous. For example, no relation had been previously reported in a study of 17,000 Norwegian men who were questioned about their

health and dietary habits by mail, but this form of data collection possesses many sources of potential error (13).

Some hypothesized that the men in the Health Professionals Follow-up Study with a high fish intake experienced no cardiovascular benefit because they had inadvertently also increased their consumption of methyl mercury, an environmental toxin present in some fish. Salonen, et al., demonstrated that both fish consumption and hair mercury levels had direct, approximately linear associations with the risk of acute myocardial infarction (14). Therefore, fish consumption could be either protective or harmful, depending on the dose.

Others have suggested that substances in fish other than omega-3 fatty acids may be responsible for the cardiovascular protective effect (15). The in vitro studies of omega-3 fatty acids described earlier showed that large quantities are required to produce beneficial effects such as reduced blood pressure and platelet aggregation. It is therefore unlikely that the reduction in cardiovascular risk can be explained by a relatively low intake of omega-3 fatty acids. Perhaps other beneficial substances that are not required in such a great amount are present in fish. This theory is further supported by the fact that the Health Professionals Follow-up Study showed even less of a benefit for omega-3 acids obtained from fish oil capsules rather than dietary sources.

Conclusion: What's the Verdict?

Epidemiologic data on the possible benefit of eating fish to reduce the risk of coronary artery disease have been inconsistent. More studies are needed to answer the many questions that have been raised by previous trials and to collect data that was previously overlooked. For example, evidence concerning the incidence of coronary artery disease is noticeably lacking because most of the studies focused only on the endpoint of fatal myocardial infarction.

While almost all of the trials studying the role of omega-3 fatty acids in cardiovascular health have been prospective epidemiological studies, this may not be the best method due to the large number of confounding variables which can impact cardiovascular health. Most of the authors exclude numerous variables in their analysis in order to obtain the best data possible. For example, Ascherio, et al. excluded men with diabetes, hypertension, hyperlipidemia and those who knew their baseline serum cholesterol levels. The question remains whether they were able to eliminate all of the confounding factors. While the authors' attempts to produce accurate data is commendable, perhaps controlled, randomized trials would provide better data and therefore the conclusions from different trials would be more consistent with each other.

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