Fish consumption and cardiovascular diseases

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Population studies indicate that a high intake of fish, such as reported in the early Eskimo and Japanese studies, is associated with a low mortality of coronary heart disease (CHD). This has been associated with measurable effects on a series of established and possible risk factors. A much lower daily intake of fish was recorded in most of the later population studies and had only small or unmeasurable effects on established risk factors. However, the association of fish intake with reduced CHD mortality, particularly sudden cardiac death, seems to be reasonably well established. Beneficial effects are found at a level of consumption of about 30 g per day, or one fish meal per week compared with populations rarely or never consuming fish. Such findings are also reflected in studies that include analysis of fatty acid composition in adipose tissue and cell membranes. Furthermore, there seem to be indications that fish consumption has a significant association with a low mortality in population groups with a high risk for CHD, whereas in low-risk populations this association is less impressive. Not all observational studies, however, observed a significant association between fish intake and CHD mortality. Population studies on fish consumption and consumption of omega-3 fatty acids have several limitations which may explain these discrepant results. Not all observational studies have included confounding factors in their statistical analysis and residual confounding is likely in nearly all studies. Fish consumption may be a marker for a healthier lifestyle or, alternatively, fish consumers may be at higher self-perceived risk for CHD and are therefore eating fish to reduce their high baseline risk. Other dietary factors may be associated with fish consumption and many studies include only a single measure of fish consumption and, thus, have no ability to account for changes in intake over time.

Introduction

Thrombosis and atherosclerosis are the main occlusive vascular lesions causing cardiovascular diseases and death in humans. Both processes have been associated with the intake of dietary lipids. Early studies mainly connected dietary saturated fatty acids with high serum cholesterol levels and in this way explained the association between diet and increased morbidity and mortality of coronary heart disease (CHD). This association was strengthened by observations in many European countries during The Second World War showing a reduction in mortality from CHD related to a drastic reduction in the consumption of dietary fats due to war time food shortage[1,2]. Of particular interest was the observation in Norway during this war period that reductions in surgical thrombosis and mortality from CHD occurred simultaneously[3]. The shape of the mortality curve related to CHD clearly indicated that these changes followed the change in diets within a short period of time. This may suggest that thrombosis as well as atherosclerosis were affected by the dietary changes.

In addition it should be emphasized that Norwegians also had a marked increase in the consumption of fish during this period with a low mortality of CHD[2].

The Eskimo studies

A new dimension in the relationship between dietary fats and mortality from CHD was suggested by Dyerberg et al. who noted that Greenland Inuits had an age-adjusted mortality of myocardial infarction that was approximately one-tenth that of Danes in spite of a high fat, high cholesterol, low carbohydrate diet (Table 1). Their diet was also rich in monounsaturated fatty acids and polyunsaturated fatty acids (PUFAs) of the omega-3 family from marine sources and low in saturated fatty acids (FAs) and omega-6 PUFAs[4–6]. Later X-ray studies of the abdominal aorta and ultrasonographic examinations of the carotid and femoral arteries have indicated a similar occurrence and severity of atherosclerosis in Greenlanders and Danes[7,8]. The observations suggested that the risk for thrombotic events was more pronounced in the Greenland Inuits. However, recent autopsy studies have shown that the degree of atherosclerosis in the abdominal aorta and

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coronary arteries of the Alaskan Eskimos is far less than that observed in Alaska non-natives[9]. Inuits from Canada and Alaska have shown an epidemiology related to cardiovascular risk factors similar to the Inuits of Greenland[10].

A series of risk factors associated with increased tendency to CHD have been evaluated in the Eskimos and comparable non-native population groups. This include both accepted risk factors, such as serum lipids, haemostatic variables, smoking and hypertension, and possible risk factors mainly related to vascular compliance and inflammatory mediators. The original studies considered the most important effects of omega-3 FA to be related to effects on haemostasis (platelets) and serum lipids (triglycerides, HDL cholesterol).

**Further relationships between dietary omega-3 fatty acids and CHD**

The low mortality rate from CHD among Japanese fishermen has also been related to their high consumption of fish and fish products[11]. However, as with the Eskimos, the Japanese diet differed from Western diets in more than simply the omega-3 fatty acid content. Thus, it was of great significance when Kromhout et al., in a dietary study from Holland, showed that subjects with a low fish consumption e.g. 30 g of fish per day over many years, had a CHD mortality about 50% lower than subjects who ate no fish at all[13]. A similar conclusion was based on observations from the multiple risk factor intervention trial (MRFIT) reported in 1990[14].

A follow-up of the mortality data from the Seven Countries Study[14] indicated a weak, non-significant correlation coefficient between fish consumption at baseline and 15-year mortality of CHD. One of the remarkable features of this study was that the six cohorts with a low mortality from CHD had very variable fish consumption patterns. In eastern Finland where mortality was high, the consumption of fish was also high. These results suggested that a high intake of fish does not protect against CHD in cultures with concomitant high consumption of saturated fats. This pattern confirmed a population study carried out in northern Norway[15].

A recent systematic review of prospective cohort studies[16] further investigated the relationship between consumption of fish and CHD mortality. These cohorts formed a total of 116,764 individuals. The studies were of varying quality and were graded along a scientific quality score (0–6). Of the 11 studies identified, four were judged to be of high quality, of which two were performed in populations at low risk for CHD and two in individuals at a higher risk. The two studies performed in populations at low risk showed no protective effect of fish consumption whereas the two high-quality studies that included individuals at higher risk suggested that 40–60 g fish per day was optimal and associated with a risk reduction of 40–60%.

Results of the four studies of intermediate quality supported the view that fish consumption was inversely associated with CHD mortality in high-risk populations only (Table 2). In another recent study, mortality from all causes, ischaemic heart disease and stroke in 36 countries was related to fish consumption when adjusted for other sources of animal fat, animal protein alcohol and cigarette consumption[17]. The influence of observation time of this relationship over a period over 30 years was carried out. The logarithm of fish consumption was independently, significantly and inversely associated with the logarithm of all-cause ischaemic heart disease and stroke mortality in all three time periods from 1961 to 1991 in both sexes, after adjusting for confounding factors. It is interesting that these associations remained significant even after exclusion of Iceland and Japan, countries with the highest amount of fish consumption and the lowest all-cause mortality rate.

**Table 1 Dietary fats in Greenland Eskimo and Danish diets**

<table>
<thead>
<tr>
<th></th>
<th>Eskimos</th>
<th>Danes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage of total calories from fat</td>
<td>39</td>
<td>42</td>
</tr>
<tr>
<td>Percentage of total fatty acids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saturated</td>
<td>23</td>
<td>53</td>
</tr>
<tr>
<td>Monounsaturated</td>
<td>58</td>
<td>43</td>
</tr>
<tr>
<td>Polyunsaturated</td>
<td>19</td>
<td>13</td>
</tr>
<tr>
<td>PS ratio</td>
<td>0.84</td>
<td>0.24</td>
</tr>
<tr>
<td>Intake per day (g)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n-3 PUFAs</td>
<td>14</td>
<td>3</td>
</tr>
<tr>
<td>n-6 PUFAs</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>0.70</td>
<td>0.42</td>
</tr>
</tbody>
</table>

Data from Bang et al[19].

Fish consumption and sudden death

It has been estimated that at least half of the deaths caused by CHD result from electrical instability of the heart culminating in ventricular fibrillation. Studies of cardiac myocytes and in animals with experimental occlusion of coronary arteries have indicated that saturated fatty acids might promote ventricular arrhythmia, whereas omega-3 and omega-6 PUFAs had antiarrhythmic effects, with the omega-3 PUFAs seeming more potent[18,19]. A population-based case-control study that included 334 patients with primary cardiac arrest and 493 control subjects seems to confirm the experimental studies[20]. When compared with no intake of omega-3 PUFAs, an intake of 0.45 g of omega-3 FA per day or one fatty fish meal per week was associated with a relative risk of primary cardiac arrest of 0.4. Compared with a red blood cell membrane n-3 PUFA level of 3.3% of total fatty acids, a level of 5-6% was associated with a 70% reduction in the risk of primary cardiac arrest.

The observation from the U.S. physicians’ health study, which included 20,551 U.S. male physicians 40–85

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years of age and free of myocardial infarction and cerebral vascular disease at baseline, and who had completed a semi-quantitative food frequency questionnaire on fish consumption and were then followed up to 11 years, confirmed these observations. There were 133 deaths over the course of the study and these prospective data suggested, after adjustment for coronary risk factors and prior cardiovascular disease, that consumption of fish at least once per week was associated with a 52% lower risk of sudden death in men.121

Recent studies evaluating the relationship between consumption of omega-3 fatty acids and pulse rate variability have added a new dimension to the possible cardioprotective effects of omega-3 fatty acids.221 Consumption of one fish meal per week compared with no fish has been associated with an increase in heart rate variability, which has been associated with a lower risk of arrhythmic death after myocardial infarction.222

Conclusions

Population studies on fish consumption and consumption of omega-3 fatty acids have several limitations. Many observational studies have included confounding factors in their statistical analysis, although residual confounding exists in nearly all studies. Fish consumption may be a marker for a healthier lifestyle; alternatively, fish consumers may be at higher self-perceived risk for CHD and are therefore eating fish to reduce their high baseline risk. Other dietary factors may be associated with fish consumption and many studies include only a single measure of fish consumption and, thus, have no ability to account for changes in intake over time. This also is reflected in studies including analysis of fatty acid composition in adipose tissue, red blood cells, etc.

Despite all these limitations, the population studies seem to indicate that a high fish intake, such as reported in the early Eskimo and Japanese studies, is associated with a low mortality of CHD. These effects have been associated with measurable effects on a series of established and possible risk factors. A much lower daily intake of fish has been observed in most of the later population studies. This intake has only small or unmeasurable effects on established risk factors. However, their association with reduced CHD mortality, particularly sudden cardiac death, seem to be reasonably well established. Beneficial effects are found at a level of consumption of about 30 g per day, or one fish meal per week, compared with populations rarely or never consuming fish. Finally, there seem to be some indications that, in population groups with a high risk for CHD, fish consumption has a significant association with a low mortality whereas in low-risk populations this association disappears. There are also exceptions to this general statement and many unanswered questions remain.

References


