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EDITORIAL

Potential usefulness of fish oil in the primary prevention of acute coronary syndrome

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This editorial refers to 'Fish intake and acute coronary syndrome*†, by L.J. Bjerregaard *et al.* on page 29

Acute coronary syndrome (ACS) is a major health problem and leads to a large number of hospitalizations annually in Europe.[1] ACS refers to a group of clinical conditions caused by myocardial ischaemia, including unstable angina pectoris, non-ST-segment elevation myocardial infarction (NSTEMI), ST-segment elevation myocardial infarction (STEMI), and sudden cardiac death. ACS results from a common underlying pathophysiological mechanism, i.e. plaques vulnerable to rupture or erosion, with different degrees of superimposed thrombosis and distal embolization. Vulnerable plaques that are likely to rupture or erode have evidence of inflammation, together with thin fibrous caps and large lipid cores. The platelet-rich thrombus, developed in association with pro-coagulant-vulnerable blood, can release vasoconstrictor substances such as serotonin and thromboxane A_2 that may induce vasoconstriction at the site of plaque rupture or in the microcirculation.

Bjerregaard *et al.* followed-up 25 573 men and 28 653 women in the large cohort of the Danish health system for 7.6 years.[2] During that period, ACS developed in a total of 1122 cases, among which the number of 'non-fatal' events was much higher than that of 'fatal' events ($n = 175$). A significant association was found between the intake of fatty fish and the incidence of ACS in men, whereas in women only a trend was seen in the highest quintile. A high consumption of fish or long-chain omega (*n*)-3 polyunsaturated fatty acids (*n*-3 PUFAs) rich in fish oil is thought to be associated with a reduction in deaths from coronary artery diseases, i.e. fatal myocardial infarction and sudden cardiac death.[3] Although there has been debate as to whether *n*-3 PUFAs may reduce 'non-fatal' cardiovascular events, the study by Bjerregaard *et al.* may provide a clue to this important issue.

n-3 PUFAs possess several beneficial effects on the pathological processes of ACS, including reduction in blood pressure and plasma levels of triglyceride, inhibition of thrombus formation and inflammation, and stimulation of endothelial production of nitric oxide.[4,5] These pleiotropic effects of *n*-3 PUFAs beyond their lipid-lowering effect (*Figure 1*) may not only prevent the development of atherosclerotic plaques but also stabilize them, as reported in an experimental study using Apo-E deficient mice[6] and in a clinical study using samples obtained at carotid endarterectomy.[7] A recent study using multidetector row computed tomography demonstrated a significant correlation between serum *n*-3 PUFA levels and the extent of coronary soft plaques and calcification in Japanese patients with ACS.[8] Even after partial or complete occlusion of the coronary artery, *n*-3 PUFAs could attenuate myocardial ischaemia/reperfusion injury, through mechanisms mediated in part by the opening of K(Ca) channels and nitric oxide in rabbits.[9] Importantly, fish oil or *n*-3 PUFAs have unique feature of suppression of arrhythmias

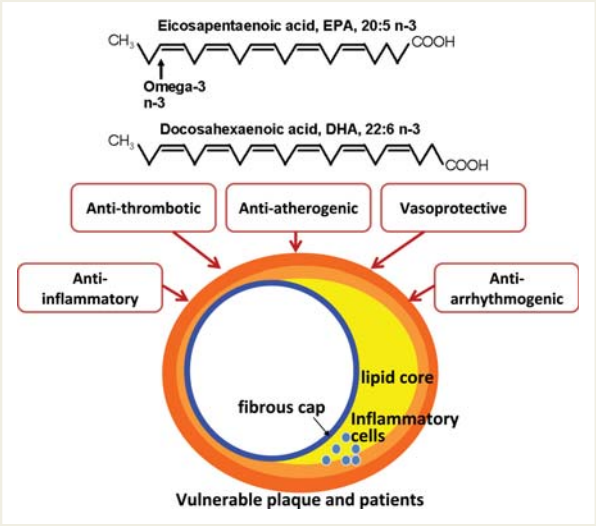

Figure 1 Pleiotropic effects of (*n*)-3 polyunsaturated fatty acids (*n*-3 PUFAs), which are beneficial for vulnerable plaque and patients who develop acute coronary syndrome (ACS).

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through several actions on the ionic channels that regulate transmembrane action potentials.[10,11]

The study of Bjerregaard *et al.* indicates the potential role of fish oil in the primary prevention of 'non-fatal' cardiovascular events such as ACS.[2] However, several issues remain to be elucidated. First, baseline intake of *n*-3 PUFAs from the sources (fish), which would be associated with the frequency of consumption and the serving sizes of the specific fish, was not precisely assessed. Secondly, no evidence has been found for the effective dosage and combination of fish oil components such as eicosapentaenoic acid and docosahexaenoic acid. Thirdly, males and females appear to differ in their ability to synthesize *n*-3 PUFA with a resultant difference in their plasma concentrations. These issues remain to be clarified in future studies.

Conflict of interest: none declared.

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