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ORIGINAL ARTICLE

# There is no Association Between the Omega-3 Index and Depressive Symptoms in Patients With Heart Disease who are Low Fish Consumers

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**Background** Long chain Omega-3 polyunsaturated fatty acids (LCn3PUFAs) may improve cardiovascular health and depression. This study investigated the relationships between erythrocyte membrane LCn3PUFA status, depression and angina symptoms in patients with heart disease.

**Methods** We recruited 91 patients (65 males and 26 females, mean age 59.2 ± 10.3 years) with heart disease and depressive symptoms (Center for Epidemiological Studies Depression Scale, CES-D ≥ 16) and low fish/fish oil intakes. The Omega-3 Index (EPA+DHA) of erythrocyte membranes (as a percentage of total fatty acids) was assessed by gas chromatography. Depression status was measured by both self-report and clinician-report scales; CES-D and the Hamilton depression scale (HAM-D). Angina symptoms were measured using the Seattle Angina Questionnaire and the Canadian Cardiovascular Society Classification for Angina Pectoris.

**Results** The mean Omega-3 Index was 4.8 ± 1.0% (±SD). Depression scores measured by CES-D and HAM-D were 29.2 ± 8.8 (moderate to severe) and 11.0 ± 5.7 (mild) (arbitrary units) respectively reflecting a different perception of depressive symptoms between patients and clinicians. Angina status was inversely associated with depression scores ($r > -0.26$, $P < 0.03$). There were no significant relationships between individual LCn3PUFA or the Omega-3 Index and either the depression scores or the angina symptoms.

**Conclusion** Worse angina status was associated with worse depression, but the Omega-3 Index was not associated with symptoms of depression or angina in patients with heart disease.

**Keywords** Omega-3 Index • Depression • Heart disease

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## Introduction

In patients with cardiovascular disease (CVD), depression is common and associated with high mortality rates [1]. Depression is also an independent risk factor for the development of coronary heart disease [2]. A number of pathophysiological factors including endothelial dysfunction, altered platelet activity and aggregation, inflammation and autonomic nervous system dysfunction have been suggested to link depression with adverse cardiac outcomes [3]. Also, as a major manifestation of coronary heart disease (CHD), angina may be one of the possible mediators in the relationship between CHD and depression. Depression can augment perceived pain [4] thus the sensation of angina may be increased in patients with depression [5].

The long chain Omega-3 polyunsaturated fatty acids (LCn3PUFAs) eicosapentaenoic acid (EPA) and docosahexaenoic acid) (DHA) may improve cardiovascular health and depression via a number of mechanisms. Cardiovascular benefits of LCn3PUFAs include lowering blood pressure and resting heart rate, improving heart rate variability and vascular endothelial function, decreasing serum triglycerides levels, inhibiting inflammation, platelet aggregation and new plaque development [6,7]. The exact mechanism by which LCn3PUFAs may influence depression remains unclear. However, DHA is highly concentrated in the retina, brain and nervous system [8], and plays important roles in the structure (neuronal membranes) and function (neurotransmission and receptor function) of neurons, the growth of neural cells, and the gene expression in the brain [9].

The role of LCn3PUFAs in improving endothelial function in the brain might optimise the auto-regulation of cerebral perfusion and blood brain barrier integrity, thus enhancing mental health by adequate oxygen and nutrition supply to brain regions [10]. LCn3PUFAs may also increase levels of monoaminergic neurotransmitters in the brain [11], and inhibit inflammation that is associated with depression [9]. The mechanisms underlying depression are complex and, while there is some evidence linking change to cerebrovascular structure and function with depression [12], other evidence suggests that inflammatory changes are central [13]. Changes in inflammatory markers following supplementation with LCn3PUFAs have been proposed to be central to improvements seen in vascular function in adults with metabolic syndrome [14]. Furthermore, low levels of Omega 3s have been associated with cerebral small vessel disease in acute ischaemic stroke patients [15]. In a meta-analysis of prospective cohort studies and randomised controlled trials (RCT), Chowdhury et al. [16] found moderate inverse associations between fish consumption and incidence of cerebrovascular disease. Interestingly, LCn3PUFAs measured as circulating biomarkers in observational studies or given as supplements in primary and secondary prevention trials were not associated with cerebrovascular disease, suggesting that the positive effects may be due to the wide variety of nutrients in fish or may reflect a healthier dietary pattern or higher socioeconomic status.

Despite evidence of mechanisms for how LCn3PUFAs may reduce the risk of developing CHD and depression, whether supplementation is beneficial for either condition remains controversial. Epidemiological studies have reported low LCn3PUFA status in patients with CHD compared with healthy age and gender matched controls [17]. Furthermore, The PREDIMED study reported [18] protection from cardiac mortality with LCn3PUFAs. Hazard ratios for meeting the recommended intake of LCn3PUAFS (500 mg/day) (n=5452, 75.7%) were, 0.61 (95% CI 0.39-0.96) for fatal cardiovascular disease, and 0.54 (95% CI 0.29-0.99) for fatal coronary heart disease. Evidence from large RCTs has shown beneficial effects of LCn3PUFAs on CHD mortality. Supplementation with LCn3PUFAs as part of cardiovascular disease management has been found to reduce the risk of non-fatal coronary events in Japanese hypercholesterolaemic patients (JELIS study), reduce the risk of death, non-fatal myocardial infarction and stroke in Italian patients with a history of myocardial infarctions (original GISSI-P) [19] and improve survival for patients with chronic heart failure (GISSI-HF) [20]. However, recent meta-analyses have generated conflicting results, with one concluding that supplementation with LCn3PUFA may not reduce the incidence of coronary events but may improve the odds of survival [21] while another concluded that there was no significant reduction in mortality from supplementation with LCn3PUFAs.[22]. Differences may be due to inclusion or exclusion of individual studies; however, it is currently suggested that there is neither a beneficial nor adverse effect of LCn3PUFA supplementation for primary or secondary prevention of coronary heart disease[23].

A major manifestation of CHD is the presence of angina symptoms. There is limited research investigating angina symptoms and LCn3PUFA and what few studies there are have provided mixed results. A small RCT of 20 patients with stable angina reported benefits associated with fish oil supplementation [24] but two other studies found no benefits [25,26]. Understanding relationships between angina symptoms, depression and Omega-3 status may help to explain these mixed findings.

Epidemiological studies have also reported low levels of LCn3PUFAs in people with depression [27]. Cross-sectional studies have also reported that depressed patients with heart disease have significantly lower blood levels of DHA compared with non-depressed patients [28–30]. There are mixed conclusions from meta-analyses as to whether Omega-3 supplements are beneficial for reducing the risk of depression [31,32]. A meta-analysis of clinical trials of treatment with LCn3PUFAs for depression concluded that the use of these supplements is effective in patients with a diagnosis of Major Depressive Disorders (MDD) and in depressive patients without a diagnosis of MDD.[33]

This study investigated associations of LCn3PUFA status, with (a) depression severity and (b) angina symptoms in patients with cardiac disease and depression who were low fish consumers. It was hypothesised that in patients with

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