Correspondence

Letter by Alter and Rupp Regarding Article, “OMEGA, A Randomized, Placebo-Controlled Trial to Test the Effect of Highly Purified Omega-3 Fatty Acids on Top of Modern Guideline-Adjusted Therapy After Myocardial Infarction”

To the Editor:

In the OMEGA study on patients after myocardial infarction,1 the anticipated statistical power of 80% was not reached, which was attributed to the low incidence of sudden cardiac death in patients receiving current guideline-adjusted medical treatment. To detect an improvement of clinical outcome by omega-3 fatty acids, it is considered important to focus on patients with poor heart function. In OMEGA, only 3.9% patients exhibited severe myocardial infarction with a consecutively impaired left ventricular ejection fraction (LVEF) <35%, which was in accordance with the large proportion (41%) of patients with non–ST-elevation myocardial infarction. Because there was a significant increase in sudden death risk with worsening LVEF, and the benefit of omega-3-acid ethyl esters-90 (1 g/day) on sudden death was 4-fold higher in patients with a LVEF of ≤40% than in those with an EF of >50%,2 further information is required in OMEGA for patients with low LVEF or geometric remodeling. Because serum levels of highly unsaturated fatty acids were depressed in patients with left ventricular dilatation and low LVEF,3 it appears that such a deficiency of omega-3 fatty acids had not occurred in most of the patients of OMEGA. Thus, in addition, a reduced abundance of omega-3 fatty acids in terms of the omega-3 fatty acid receptor GPR120 with antiinflammatory and insulin-sensitizing action4 is expected to be absent in many patients of OMEGA.

Although treatment with angiotensin-converting enzyme inhibitors interferes with ventricular remodeling involving fibrosis and dilatation, an adverse increase in wall stress,5 which is related to decreased heart rate variability, often cannot be prevented. Increased wall stress can lead to the opening of stretch-activated cation channels, increasing the risk of sudden cardiac death. Because echocardiography-based volumetric and mass data are probably available for many patients of OMEGA, wall stress calculations should be performed. It is recommended to reanalyze the clinical data and to examine the hypothesis that omega-3 fatty acids improve clinical outcome in patients with dilated ventricles and increased wall stress. Any progress in this respect would provide important mechanistic insight into omega-3 fatty acids after myocardial infarction.

To achieve and maintain increased omega-3 fatty acid levels, a controlled continuous intake is required because of the short half-life of omega-3 fatty acids in the blood. OMEGA followed the intention-to-treat principle, and adherence to medication was only checked during visit 2 and by pill counts at the final visit. It is, therefore, also considered essential to present the blood levels of fatty acids, and clinical outcomes should be related to the levels of highly unsaturated fatty acids. It would be of particular interest to examine whether any depression of omega-3 levels in patients with LVEF <35% was prevented by administration of omega-3-acid ethyl esters-90.

Disclosures

None.

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References


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