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Letter to the Editor

Omega-3 Fatty Acid Supplementation for Endothelial Dysfunction in COPD: Another Fiasco? Or Maybe Not?

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Abbreviations: chronic obstructive pulmonary disease, COPD; flow-mediated dilatation, FMD

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To the Editor:

We read with great interest the report of Kim et al¹ on a 6-month randomized, double-blind, placebo-controlled trial investigating the effects of omega-3 fatty acid supplementation on endothelial function in patients with chronic obstructive pulmonary disease (COPD). COPD is a major source of morbidity and mortality for the contemporary world; cardiovascular disease contributes significantly to mortality and disease severity.² The relationship between COPD and cardiovascular disease is peculiar; smoking, chronic inflammation and hypoxia, oxidative stress, arterial stiffness, and endothelial dysfunction are

important determinants.³ Endothelial dysfunction is present in a significant subset of patients with COPD; through the years, several pharmacological and non-pharmacological interventions have been used in order to examine the effects of these on endothelial function in COPD individuals and the results are contradictory.⁴⁻⁶

The study from Kim et al¹ is an important addition to current literature, as, to our knowledge it is the first randomized trial examining the effects of omega-3 fatty acid on endothelial damage in COPD individuals, showing no differences for the primary outcome, i.e., change in brachial flow-mediated dilatation (FMD) from study baseline. However, it has several limitations that may limit its conclusions. First, the study population is rather small; from the 40 initially randomized patients, approximately 20%-30% of the patients did not undergo the study measurements for primary and secondary outcomes, limiting the study's power to detect changes in most of the studied parameters. Moreover, endothelial function via peripheral arterial tonometry was assessed only in the first 2 visits (0 and 4 months respectively), and not at study-end. Second, the participants were patients with moderate and severe COPD with the majority of them (79%) having emphysema on computed tomography. Thus, the results have limited generalizability to the general COPD population; to what extent they apply to individuals with mild or very severe COPD is unknown.

In addition, between-group comparisons and the

corresponding p -values for baseline characteristics are not reported, raising several questions about the comparability of the 2 study groups. In the same context, one could notice that there are significant mismatches regarding the medication of the 2 study groups; 60% and 35% of the participants in the placebo group were taking statins and calcium-channel-blockers, while the corresponding proportions in the active group were 30% and 5%, respectively. We believe that these significant mismatches have directly confounded the results of the primary outcome, as both drugs are known to affect the FMD measurements.^{7,8} Furthermore, while reading the manuscript, we were surprised with the reductions observed in lipid profile in the placebo group, whereas the corresponding changes in the active group were negligible. The higher statin intake

in the placebo group could be a potential explanation, but it would also be interesting to report if there were differences in other lifestyle habits (i.e., exercise programs, etc.), that may have confounded the study results. Finally, there are other FMD-derived indexes (i.e., hyperemia-induced shear stress and velocity changes) that have shown stronger correlations with cardiovascular risk factors compared with “classical” FMD⁷; hence, it would also be nice for authors to examine these metrics in post-hoc analyses. Proper designed clinical trials are needed in the future to examine these associations.

Declaration of Interest

The authors have nothing to declare related to this letter.

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