Reviewer's report

Title: Intake ratio of n-3/n-6 PUFAs and risk of breast cancer: a meta-analysis of 274135 adult females from 11 independent prospective studies

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Reviewer: Michel de Lorgeril

Reviewer's report:

As I said in my previous review, I think it is an important article to be published. However I am still not happy with the “Intake ratio of n-3/n-6 PUFAs” which is not meaningful, in my opinion.

It is clear now that only serum phospholipids were used to determine the n-3/n-6 ratio; and it is also clear that this is not (by far) a good indicator of dietary intakes, in particular for the non-essential n-6 and n-3 fatty acids. Thus the combination with data obtained from questionnaire is debatable.

Well, why not?

If they persist in that presentation, it cannot be said that they are studying an “intake ratio”. Definitely, this is a combination of dietary and metabolic (endogenous) factors.

Thus, even the title should be changed.

It is better to say: “Ratio of n-3/n-6 PUFAs and the risk of breast cancer: …” which better reflects what is studied: data from dietary questionnaire in one side and data from blood samples in the other side.

The combination of the data should be presented as a “predictive factor” or as a “risk factor” and not as an evaluation of the diet by two different techniques.

Once the authors have understood that serum phospholipids do not provide the same information as the dietary questionnaire, the lack of significant relationship between serum PL ratio and BC risk is easier to explain. Thus part of the discussion (in particular, about heterogeneity) should be rewritten.

They are right, for instance, when they write that “lower n-3/n-6 ratio in the diet will lead to lower ratio of n-3/n-6 PUFAs in serum PL”. However, because of endogenous confounders (hormonal factors for instance), the strength of the relation between the ratio in phospholipids and the risk might be lower compared with the relation between the ratio in diet and the risk.

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
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