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Reply to the letter "α-linolenic acid levels and risk of dementia; but which type of dementia"

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We thank comments from Dr. Ayçiçek et al. [1] on our previous manuscript [2] that provided an opportunity to discuss this interesting topic.

First of all, we would like to remind that we are focusing on 'disabling dementia', not clinical diagnosed dementia. The concept of disabling dementia aims to prevent any type of dementia that brings disabling. It is especially important to remember that, from public health point of view, preventing whichever subtypes of dementia should be remarked. We agree that clarifying etiology of each type of dementia is of interest, and showed the results for cases with history of stroke, and those without stroke as supplemental analysis. Our study, however, did not aim to clarify which type of dementia could be prevented by α-linolenic acid.

As for residual confounding, we do not have data on depression, head trauma, low vitamin B12 levels and thyroid functions. However, we do not believe these would impact the results materially, because the prevalence of these factors were likely to be very few in the general Japanese population, and these were unlikely to correlate with serum α-linolenic acid levels.

Dr. Ayçiçek et al. also concerned the reliability of disabling dementia diagnoses. We are sure that diagnoses based on NIA-AA or DSM-V criteria should be more precise to identify definite dementia cases in clinical settings, but to apply these

criteria to a number of participants in general settings is unrealistic due to time, cost and personnel. Using information from the National Long-term Care Insurance System, a compulsory insurance system of Japan, is one of the practical ways to keep completeness of surveillance, which should have higher priority from epidemiological point of view. We have compared our epidemiological diagnosis with diagnosis by psychiatrists and confirmed that the sensitivity and specificity of our diagnoses were 83% and 96%, respectively. (Noda H, et al. in submitting)

We agree that it is uncertain when dementia starts exactly in the life course. We used a strategy of constructing the baseline surveys at least 5 years before the dementia diagnosis to exclude overt dementia at baseline, but we agree that this strategy is not enough to exclude preclinical dementia.

True single measurement of α-linolenic acid levels could be a drawback of this study, but measuring serial measurements over 25 years for more than 7500 people is costly and not practical. This is why we chose the nested case-control design. We have confirmed a good repeatability of serum α-linolenic acid during 8 years as discussed in the paper [2], and thus we consider that single measurement did not largely dilute the association. As we concluded in the paper [2], the causality needs to be confirmed by randomized control trials.

Reference

[1] Ayçiçek GŞ, Kızılarslanoğlu MC, Ülger Z. α-linolenic acid levels and risk of dementia; but which type of dementia. Clin Nutr in press.

[2] Yamagishi K, Ikeda A, Chei CL, Noda H, Umesawa M, Cui R, Muraki I, Ohira T, Imano H, Sankai T, Okada T, Tanigawa T, Kitamura A, Kiyama M, Iso H; for the CIRCS Investigators. Serum α-linolenic and other ω-3 fatty acids, and risk of disabling dementia: community-based nested case control study. ***Clin Nutr*** in press

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