## α-Linolenic Acid and Nonfatal Acute Myocardial Infarction

*To the Editor:*

Baylin et al[1] found an inverse relation between α-linolenic acid in adipose tissue and nonfatal acute myocardial infarction (AMI). This relation is controversial mainly for nonfatal AMI,[2–4] given that α-linolenic acid may be largely antiarrhythmic, but this issue has not been adequately studied in European populations. In America and northern Europe, the major dietary sources of α-linolenic acid are rapeseed and canola oils. In Italy, these oils are scarcely consumed, and major dietary sources of α-linolenic acid include olive and mixed-seed oils, butter, cheese, and rabbit meat. Thus, although average intake of α-linolenic acid in Italy is comparatively high, data in this population with different dietary sources would be interesting.

We analyzed the relation between α-linolenic acid and nonfatal AMI in a case-control study conducted between 1995 and 1999 in Milan, Italy.[5] Cases consisted of 507 patients in hospital with a first episode of nonfatal AMI and 478 control patients admitted to the same hospitals for acute conditions unrelated to AMI risk factors (34% traumas, 30% nontraumatic orthopedic disorders, 14% surgical conditions, and 22% miscellaneous other diseases). Interviews, which were conducted in the hospital using a structured questionnaire, included information on sociodemographic factors, anthropometric variables, tobacco, alcohol, other lifestyle habits, medical history, physical activity, and family history of AMI. Information on diet was based on a validated food frequency section, including intake frequency and portion size of 78 foods and additional questions on the type and amount of fats for seasoning and cooking; the intake of α-linolenic acid was computed using an Italian food composition database.[5] The odds ratios (OR) were derived using unconditional multiple logistic regression, including terms for age, sex, and selected AMI confounding factors.[5]

Compared with the lowest quintile of intake (<1.03 g/day) the age- and sex-adjusted OR for the subsequent quintiles of α-linolenic acid were 0.70, 0.69, 0.83, and 0.93, and the multivariate OR were 0.71, 0.70, 0.86, and 1.03 (95% CI, 0.55 to 1.92); the upper cut points for the 2nd, 3rd, and 4th quintiles were 1.24, 1.49, and 1.89 (g/day), respectively. In our study, the food frequency questionnaire was satisfactorily valid and reproducible,[5] cases and controls were interviewed in the same hospitals and came from the same geographical area, participation was >95%, and a different recall of major sources of α-linolenic acid intake on the basis of the disease status is unlikely.

Thus, these data do not support a relation between α-linolenic acid intake and risk of nonfatal AMI in this Italian population.


## Acknowledgments

This work was partly supported by "Ministero della Salute" (contract no. 177, RF 2001).



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### *Response*

Tavani et al discussed interesting data on dietary α-linolenic acid and nonfatal acute myocardial infarction (MI) in an Italian population, where, in contrast to Costa Rica, α-linolenic acid was not associated with MI. We see several possible explanations for the inconsistent results between these studies. First, it is likely that some of the differences depend on the methods used to assess α-linolenic acid. Our study assessed α-linolenic acid in adipose tissue, an excellent biomarker of intake.[1] Data presented by Tavani et al used a dietary questionnaire, a method that may be prone to differential information bias in case-control studies. Compared with direct measurements of α-linolenic acid in adipose, the content of α-linolenic in foods is difficult to assess and may be more prone to error.

In Costa Rica and many other countries, α-linolenic acid usually shares food sources with *trans* and saturated fat because of partial hydrogenation of vegetable oils or their presence in dairy products and meat. In one study, a marginally significant protective trend for α-linolenic acid was found only after adjusting for *trans* and saturated fat.[2] Other studies that did not find a protective effect for α-linolenic acid and MI have been strongly confounded by *trans* fatty acid intake.[3,4] The antagonistic effects of these nutrients were not considered in the multivariate analysis of the Italian study.

Differences between these studies could also be due to the fact that low α-linolenic levels may be harmful only when they are very low and that all of the protective effects could occur in the range below the Italian levels. For instance, in the European Community Multicenter Study on Antioxidants, Myocardial Infarction, and Breast Cancer (EURAMIC), centers with lower mean adipose tissue α-linolenic acid tended to show a stronger protective effect than those with higher levels.[5] Consistent with these data, the lowest quintile for intake of α-linolenic acid is substantially lower in Costa Rica (<0.71 g/d)[1] than in Italy (<1.03 g/d). Finally, it is possible that α-linolenic acid plays a more prominent role in MI among populations with low intake of marine n-3 fatty acids since fish intake in Costa Rica is lower (<1/wk) than that in Italy (1 to 2/wk).

In sum, data suggest that negative studies of α-linolenic and MI are largely confounded by other nutrients, particularly *trans* and saturated fatty acids. It is also possible that the lack of association in some studies is due to a potential threshold effect of α-linolenic acid. In the Costa Rican population, α-linolenic acid is strongly protective against the risk of MI.

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