Letters to the Editor

Coffee consumption and plasma homocyst(e)ine: results from the Atherosclerosis Risk in Communities Study

Dear Sir:

Nygård et al (1) recently reported a direct association between coffee intake and plasma homocyst(e)ine concentrations in an adult population in Norway. This was described by the Norway investigators as an "unexpected finding during the analyses," and although slightly weakened, it persisted after smoking, dietary folate intake, and vitamin supplementation were controlled for. Nygård et al (1) speculated that increased plasma homocyst(e)ine could explain some of the alleged harmful health effects of excessive coffee intake (eg, coronary heart disease and adverse pregnancy outcomes), although they do not offer any biological or biochemical explanation for the finding.

Data from an ongoing ancillary study including participants of the Atherosclerosis Risk in Communities (ARIC) Study (2) offer an opportunity to attempt to replicate this finding in a population sample in the United States. The ARIC Study is a cohort study of the determinants and natural history of cardiovascular disease. As detailed elsewhere (2), a total of 15,792 adults (45–64-y old, 55% female) were initially recruited to participate in a baseline exam conducted between 1987 and 1989. This exam was conducted after participants fasted for ≥12 h and included the collection of plasma and serum samples, blood pressure measurements, anthropometry, electrocardiography, ultrasound examination of the carotid and popliteal arteries, as well as a detailed interview of personal and medical history. Usual dietary intake was assessed by using an interviewer-administered and slightly modified version of Willett’s semiquantitative food-frequency questionnaire (3, 4). Coffee intake was assessed by the question “In the past year, how often on average did you consume coffee, not decaffeinated?” Nine response categories were available ranging from “almost never” to “>6 times per day.” Average daily caffeine intake was estimated based on reported consumption of coffee, tea, and caffeinated soft drinks. Nutrient values of foods were computed by Willett et al (3) on the basis of data from the US Department of Agriculture and manufacturers. Keys score was estimated as a summary measure of dietary fat intake (4, 5). Total cholesterol was measured by enzymatic methods (6). Aliquots of plasma and serum samples were stored frozen at −70°C.

Every 3 y since the date of the baseline examination, participants have been invited for a follow-up examination; in addition, follow-up data from this cohort are obtained by annual telephone calls and review of hospital records and death certificates. Nested case-cohort studies are being conducted currently to investigate predictors of incident cardiovascular events. One such study included the measurement of plasma homocyst(e)ine in the stored frozen samples from a stratified random sample of the baseline cohort (n = 537). Analysis of covariance was used to calculate crude and adjusted means and proportions by categories of coffee intake after properly weighing for the stratified sampling design. Homocyst(e)ine values were skewed to the right; thus, mean homocyst(e)ine concentrations were calculated on a log scale and back exponentiated (geometric means).

Mean homocyst(e)ine concentrations and other characteristics according to categories of coffee intake are shown in Table 1. There was no evidence of a relation between coffee intake and homocyst(e)ine concentrations. The highest homocyst(e)ine concentrations were found among participants reporting an average of <1 cup of coffee/d. When stratified by sex, men had higher homocyst(e)ine concentrations than women but, again, no significant trend with reported usual coffee intake was evident in either sex (data not shown). Heavy coffee drinkers were thinner, had higher cholesterol concentrations, and were smokers more frequently (Table 1). Adjustment for all the other variables shown in Table 1 did not change the trends shown for homocyst(e)ine in a meaningful way (data not shown).

Alternatively, homocyst(e)ine concentrations were examined according to fifths of estimated average caffeine intake, with results that mirrored those shown in Table 1. There was a weak correlation between average caffeine intake and plasma homocyst(e)ine (Spearman r = 0.10).

These results are in contrast with the results from the Norwegian study (1). One reason for the discrepancy could be that coffee consumption in Norway is much higher than in the United States. The categories of coffee consumption in Nygård et al’s study went up to ≥9 cups/d. It could be argued that the coffee-homocyst(e)ine relation only occurs at higher intakes. However, a trend was already present for categories of coffee intake <5 cups of coffee/d in Nygård et al’s study. Moreover, when we calculated mean homocyst(e)ine concentrations in coffee drinkers reporting >6 cups/d (our highest response category, n = 27), the geometric mean of homocyst(e)ine concentration was 9.2 μmol/L, even lower than the mean for the highest category in Table 1.

Because of the relatively small sample size, limited power could also explain our negative results. These negative results, however, suggest that in a US population, the relation between coffee intake and plasma homocyst(e)ine, if present, is not a strong one. The consistency of trends across different subgroups in the Norwegian study make chance alone an unlikely explanation for the Norwegian results. Different methods of coffee preparation [eg, boiled coffee, which has stronger cho-
Lesterol-raising effects than filtered coffee (7, 8)] is also an unlikely explanation, given that only 2.4% of participants in Nygård et al’s study reported consuming boiled coffee (1).

It is possible that certain lifestyle characteristics (dietary or otherwise) associated with coffee intake in the average Norwegian but not in the average American could explain the discrepant results found in the studies. High consumption of cold breakfast cereal (fortified with folate) in the United States could attenuate the association between coffee intake and homocyst(e)ine. In the ARIC population, participants reporting never consuming breakfast cereal (n = 140) had higher homocyst(e)ine concentrations than the average; restricting the analysis in Table 1 to only these participants, however, did not show any significant trends with coffee consumption, although the numbers might be too small (results not shown). Alternatively, the results of the Norwegian study could stem from residual confounding by smoking or other unmeasured confounders.

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REFERENCES


Reply to FJ Nieto et al

Dear Sir:

We welcome the report of Nieto et al on the relation between plasma total homocysteine (tHcy) and coffee intake in 537 participants of the Atherosclerosis Risk in Communities (ARIC) Study. They were not able to reproduce our finding of an association between coffee consumption and plasma tHcy concentration in 16175 participants of the Hordaland Homocysteine Study (1). There are several possible explanations for the discrepant results between the two studies.

We found that the coffee-tHcy relation was particularly pronounced in subjects drinking ≥ 9 cups/d. The population...