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Coffee, Decaffeinated Coffee, Caffeine, and Tea Consumption in Young Adulthood and Atherosclerosis Later in Life: The CARDIA Study

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Abstract

Objective—Determine the association of coffee, decaffeinated coffee, caffeine, and tea consumption in young adulthood with the presence and progression of coronary artery calcified (CAC) plaque and carotid intima-media thickness (cIMT) later in life.

Methods and Results—CARDIA is a cohort of 5115 white and black adults who were 18–30 years when they completed a baseline clinic examination in 1985–1986. Subsequent examinations were conducted 2, 5, 7, 10, 15, and 20 years later. After multivariable adjustment, no association was observed between average coffee, decaffeinated coffee, or caffeine consumption (years 0 and 7) and presence of CAC [score >0 Agatston units (AU) at year 15 or 20], CAC progression (incident CAC at year 20 or an increase in CAC score ≥20 AU), or high cIMT (>80th percentile, year 20). Tea consumption, however, displayed a non-significant trend for an inverse association with CAC (p_{trend}0.08) and an inverse association with CAC progression (p_{trend}0.04), but no association with high cIMT (p_{trend}>0.2). Stratification of the coffee analyses by sex, race, or smoking yielded similar non-significant patterns.

Conclusion—We observed no substantial association between coffee or caffeine intake and coronary and carotid atherosclerosis. However, our results suggested an inverse association between tea and CAC, but not carotid atherosclerosis.

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Disclosures
None.

Keywords

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Coffee is one of the most widely consumed beverages in the world. More than half of all Americans drink coffee, with an average per capita intake of about 2 cups/day.1 Coffee is the primary source of caffeine in many populations, but also contains several other biologically active components that may have either harmful or beneficial cardiovascular effects. For instance, caffeine has been shown to lead acutely to an increase in blood pressure, though there is little evidence of an elevation in long-term studies.[2] Coffee contains the diterpene cafestol, which has been shown to increase serum low density lipoprotein (LDL)-cholesterol concentrations.[3] However, a higher coffee intake has also been associated with a substantially lower risk for type 2 diabetes, due at least in part, to a favorable influence on post-load glucose metabolism.[4, 5]

Despite the documented metabolic effects of coffee consumption from short-term intervention trials, results from studies of habitual coffee intake over long periods and coronary heart disease events have been equivocal. In the most recent meta-analysis conducted to date, summary measures of association from case-control studies suggest a direct association between coffee intake and coronary heart disease, compared to no consumption.[6] However, meta-analyses of cohort studies suggest no substantial association.[6–8] More recent analyses of US cohort studies suggest light-to-moderate consumption of coffee may modestly reduce risk of stroke,[9] all-cause, and cardiovascular disease mortality.[10, 11]

Tea is another widely consumed beverage purported to have beneficial cardiovascular effects. In carefully conducted meta-analyses of cohort and case-control studies of tea consumption, Peters et al.[12] estimated a summary 11% decrease in risk of myocardial infarction and Arab et al.[13] showed a 21% lower risk of fatal and non-fatal stroke with increases in tea consumption of 3 cups/d. Recent cohort studies have shown regular tea consumption may lower risk of hypertension[14] and death from cardiovascular disease.[15–17] Similar to coffee, the protective effects of tea on cardiovascular disease are believed to be largely attributed to the presence of high levels of polyphenols, primarily flavonoids.[18–21]

Although the relation of coffee consumption with metabolic risk factors for coronary heart disease and incident events has been a topic of frequent interest, few studies have determined whether coffee, caffeine, or tea may be associated with atherosclerosis.[22, 23] Even fewer have studied whether these factors may influence atherosclerotic disease progression. The Coronary Artery Risk Development in Young Adults (CARDIA) Study offered a unique opportunity to examine the shape of the dose-response association of habitual coffee, decaffeinated coffee, caffeine, and tea consumption during young adulthood with the subsequent development and progression of coronary and carotid atherosclerosis later in life.

Methods

Study population

CARDIA is a multicenter longitudinal study of the development and determinants of cardiovascular disease over time in 5115 young adults initially aged 18–30 years in 1985–1986. Black and white adults were recruited from 4 US cities (Birmingham, Alabama; Chicago, Illinois; Minneapolis, Minnesota; and Oakland, California) with population-based samples approximately balanced within center by sex, age (18–24 years and 25–30 years), race (white, black), and education (high school graduate or less, greater than high school graduate). To date, participants have been re-examined 2, 5, 7, 10, 15, and 20 years after baseline and retention

rates across examinations were 91%, 86%, 81%, 79%, 74%, and 72%, respectively. Further details of study recruitment and design are available.[24] All participants provided written informed consent at each examination, and institutional review boards from each field center and the coordinating center approved the study annually.

Clinical measurements

Participants were asked to fast for 12 hours and to avoid smoking and heavy physical activity 2 hours prior to their examination. Body weight was measured to the nearest 0.2 kg with a calibrated balance-beam scale. Height was measured with a vertical ruler to the nearest 0.5 cm. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Waist was measured with a tape in duplicate to the nearest 0.5 cm around the minimal abdominal girth. Blood pressure was measured on the right arm with a Hawksley random zero sphygmomanometer (WA Baum Company, Copaigue, NY) in seated participants following a 5-min rest. Three measurements were obtained at 1-min intervals. Systolic and diastolic blood pressure was recorded as the phase I and phase V Korotkov sounds, respectively. The average of the second and third measurements was used in analyses.

Blood was drawn by venipuncture according to a standard protocol.25 Plasma high-density lipoprotein (HDL) cholesterol and triglyceride concentrations were measured with an enzymatic assay by Northwest Lipids Research Laboratory (Seattle, WA). LDL-cholesterol was derived by the Friedewald equation.[26] Serum glucose and insulin measurements were performed at Linco Research (now Millipore, Inc., Billerica, MA). Glucose was measured at year 0 (i.e., baseline) using the hexokinase ultraviolet method by American Bio-Science Laboratories (Van Nuys, CA), and at year 7 using hexokinase coupled to glucose-6-phosphate dehydrogenase by Linco Research (St. Louis, MO). The insulin measurements were performed by using a radioimmunoassay with an overnight, equilibrium-incubation format.

Coffee, caffeine, tea, and other dietary information

The validated, interviewer-administered quantitative CARDIA dietary history has been previously described.[27, 28] Briefly, the CARDIA dietary history asked individuals to report foods eaten, including beverages, during the previous month using about 100 header questions, such as “Do you eat meat?” followed by open-ended responses. The CARDIA dietary history was administered at years 0, 7, and 20. Participants were asked to report their usual coffee consumption, including cappuccino and flavored coffee in fluid ounces or cups. Usual tea consumption either iced or hot was also queried. One cup of coffee or tea was considered approximately equal to 8 oz. (237 mL). We created categories of coffee and tea consumption (cups/d) based upon the overall distribution of intake prior to examining associations with atherosclerosis. Total daily caffeine intake (mg/d) was calculated from all caffeine containing beverages and foods reported. Nutrients were derived from the food and nutrient content databases developed by the Minnesota Nutrition Coordinating Center. We used the distribution of all participants to define quintiles of caffeine intake.

Other dietary measures from the CARDIA dietary history used in the current study included total energy (kcal/d), fruit and vegetable consumption (servings/d), and whole and refined grain intake (servings/d). The average of dietary information collected at years 0 and 7 was used in analyses, since the cumulative average consumption at two or more time points has been shown to more accurately reflect habitual intake than only a single assessment[29] and to reduce the possibility that the measurement of coronary calcified atherosclerosis at year 15 may have influenced coffee, caffeine, or tea consumption measured at year 20.

Computerized tomography

Coronary artery calcified (CAC) plaque was measured at years 15 and 20 by computerized tomography (CT) of the chest.30 Electron beam CT (Chicago and Oakland centers) and multidetector CT (Minneapolis and Birmingham centers) scanners were used to obtain 40 contiguous 2.5–3-mm-thick transverse images from the root of the aorta to the apex of the heart in 2 sequential scans. Participants were scanned over a hydroxyl-apatite phantom to allow monitoring of image brightness and noise and adjust for scanner differences. Data from both scans were transmitted electronically to the CARDIA CT Reading Center at Harbor-UCLA Medical Center (year 15) and Wake Forest University School of Medicine (year 20). A calcium score in Agatston units (AU)31 was calculated for each calcified lesion and the scores were summed across all lesions within a given artery and across all arteries (left anterior descending, left main, circumflex, and right coronary) to obtain the total calcium score. The presence of CAC was defined as a total calcified plaque score greater than 0 AU measured at years 15 or 20. For those with measures of CAC at both follow-up examinations (years 15 and 20), we also examined the association of coffee, caffeine, and tea consumption with 5-year progression of CAC, defined as incident CAC at year 20 or an increase in CAC score of ≥20 AU.32

Carotid ultrasound

High-resolution B-mode ultrasonography was used to capture images of the bilateral common carotid (CC) and carotid bulb/internal carotid (IC) arteries using a Logiq 700 ultrasound machine (General Electric Medical Systems) at the year 20 examination. One longitudinal image of the CC and three longitudinal images of the IC were acquired. Measurements of the maximal carotid intima-media thicknesses (cIMT) were made at a central reading center by readers blinded to all clinical information. The maximum cIMT of the CC and IC was defined as the mean of the cIMT of the near and far wall on both the left and right sides. The number of measurements that were available for averaging ranged from 1 to 4 for the CC and 1 to 16 for the IC.[33] A normalized composite cIMT measure was derived from combining the maximal cIMT of the CC and the IC (consisting of the arithmetic average of all IC and bulb measurements) by averaging these two measurements after standardization (subtraction of the mean and division by the standard deviation for the measurement). We used the distribution of all CARDIA participants examined (>80th percentile) to define high cIMT because a threshold to define a clinically significant cIMT has not yet been established.

Other measures

Standard questionnaires were used to maintain consistency in the assessment of demographic (age, sex, race, and education) and behavioral (physical activity, cigarette smoking, and alcohol use) information across CARDIA examination visits. The CARDIA Physical Activity History questionnaire queries the amount of time per week spent in 13 categories of leisure, occupational, and household physical activities over the past 12 mo.[34] Physical activity level was summarized as units of total activity incorporating moderate and high intensity activities. A score of 100 exercise units is roughly equivalent to participation in vigorous activity 2–3 hr/wk for 6 months of the year. Education was represented as years of schooling achieved by exam year 7. Cigarette smoking status at year 7 was classified as current, former, or never and was based upon information collected at baseline, year 2, 5, and 7. Total daily alcohol consumption was calculated from an interviewer-administered questionnaire.35

Sample for analysis

Of those who completed the year 15 (n=3672) or year 20 (n=3549) exam, 3042 and 3138 had data on CAC from each exam, respectively, and 3696 had data on CAC from at least one exam. A total of 3257 participants had data on cIMT at year 20. After excluding participants who were deemed unreliable because they reported an extreme energy intake (<800 or >8000 kcal/

d for men and <600 or >6000 kcal/d for women) at years 0 or 7, 3574 had data on CAC and 3175 had information on cIMT. In general, persons who were excluded, had missing data, or who were lost to follow-up were more likely to be black, younger, less educated, and smokers at baseline than were those included in the study sample, but there was little difference in their baseline coffee, caffeine, or tea consumption.

Statistical analysis

Participant characteristics were described according to average caffeinated coffee consumption using means and proportions. We used linear and logistic regression models to assess the significance level for linear trend across the categories of coffee for continuous and categorical characteristics, respectively, with adjustment for age, sex, and race. All continuous characteristics reflect the average of years 0 and 7, except age (year 0). Multivariable logistic regression models were used to estimate odds ratios and 95% confidence intervals for the presence of CAC, CAC progression, and high cIMT associated with each level of caffeinated and decaffeinated coffee, caffeine, and tea consumption compared with the lowest level. Initial models minimally adjusted for age (years), sex, race (white, black), smoking (current, former, never), and center (Birmingham, Chicago, Minneapolis, Oakland). Because coffee, caffeine, and tea intake may also be associated with other demographic, lifestyle, clinical, and dietary measures, fully adjusted models accounted additionally for educational attainment (less than high school, high school graduate, bachelor's degree, master's degree or higher), physical activity (exercise units), alcohol intake (mL/d), BMI (kg/m^2), total energy (kcal/d), fruit and vegetable intake (servings/d), and whole and refined grain intake (servings/d). Tests for a linear trend were performed by entering the categorical coffee, caffeine, and tea variables separately into the multivariable models as ordinal terms.

We also determined the association of coffee, caffeine, and tea consumption with the normalized composite cIMT expressed as a continuous variable in multivariable linear regression models. In addition, we examined associations with cIMT of the CC and IC separately as dichotomous outcome variables defined by the 80^{th} percentile and as continuous, natural logarithm-transformed variables.

Because coronary atherosclerosis is greater among men than women and among white than black adults[36] and coffee consumption varies across these subpopulations,[37] we also explored the association between coffee and atherosclerosis within models stratified by sex and race. In addition, we examined whether the coffee-atherosclerosis relation was present among current, former, or never smokers, since smoking is strongly associated with coffee intake and has been previously shown to modify this association.[23] We formally tested for the presence of effect modification by introducing a multiplicative interaction term into each multivariable model.

Like most reports of observational studies, ours did not apply multiplicity adjustments for the number of statistical tests conducted. However, the primary analyses were based on *a priori* hypotheses. Tests of statistical significance were 2-tailed, with an alpha level of 0.05. SAS version 9.1 (Cary, NC) was used to perform all analyses.

Results

The proportions of participants consuming none, <1, 1–2, 3–4, and >4 cups/d of caffeinated coffee were 37.2%, 31.0%, 15.7%, 10.7%, and 5.4%, respectively. Decaffeinated coffee consumption was low; 82.4% reported no consumption, 13.6% reported <1 cup/d, and 4.0% drank 1 cup/d or more. Approximately 31.1% reported no tea consumption, while 53.8%, 8.9%, and 6.2% reported <1, 1–2, and >2 cups/d, respectively. Table 1 displays the demographic, lifestyle, dietary, and clinical characteristics of the 3574 participants with information on CAC according to average caffeinated coffee consumption at years 0 and 7. Caffeinated coffee

consumption was positively associated with decaffeinated coffee, but not with tea. Higher coffee consumption, but not decaffeinated coffee consumption was strongly associated with smoking and a higher alcohol intake, while a higher tea consumption was associated with a lower prevalence of smoking and lower alcohol use (data not shown). Higher coffee consumption was also associated with older age, male gender, and white race (Table 1). Coffee was also associated with a higher total energy and caffeine intake, and inversely related to resting diastolic blood pressure and fasting insulin levels, although variability across categories of coffee was small.

Approximately 18.6% had CAC present defined as a score >0 AU at year 15 (prevalence=11.3%) or year 20 (prevalence=18.4%), and for those with measures of CAC at both exams (n=2415), 16.1% had CAC progression. Table 2 shows the adjusted associations of average caffeinated and decaffeinated coffee, caffeine, and tea consumption at years 0 and 7 with the presence of CAC at year 15 or 20 and CAC progression from year 15 to year 20. Caffeinated and decaffeinated coffee and caffeine intake greater than the lowest category of consumption did not increase or decrease odds for CAC or its progression. Tea consumption, however, displayed a non-significant trend for a lower presence of CAC (*p* for trend 0.08 in the fully adjusted model) and an inverse association with its progression (*p* for trend 0.04). Those who drank more than 2 cups/d of tea, compared to those who reported no tea consumption, had a 46% lower adjusted odds [OR=0.54 (95% CI: 0.30, 0.97)] of CAC progression.

The adjusted odds ratios and 95% confidence intervals for high cIMT at year 20 according to average coffee, caffeine, and tea consumption at years 0 and 7 are displayed in Table 3. No evidence for an association was observed between caffeinated or decaffeinated coffee, caffeine, or tea intake and cIMT. Similar non-significant results were observed when the standardized average maximum cIMT was treated as a continuous outcome variable and when cIMT of the CC and IC were considered separately as dichotomous and continuous outcome variables (data not shown).

Mean consumption of caffeinated coffee at years 0 and 7 was not significantly associated with the presence of CAC at years 15 or 20, progression of CAC from year 15 to 20, or cIMT at year 20 within multivariable models stratified by sex, race, and smoking status (*p* for trend >0.1, for all; *p* for interaction >0.2, for all; data not shown).

We also repeated all analyses combining information on caffeinated and decaffeinated coffee consumption (total coffee) at years 0 and 7; non-significant results were observed, including when analyses were stratified by sex, race, and smoking status (data not shown). In addition, a similar pattern of results was observed when we used an alternate definition of CAC progression defined as incident CAC at year 20 or an increase in CAC score of ≥1 AU between year 15 and 20 (data not shown).

Discussion

In this population-based cohort, we observed no evidence for a substantial association between the habitual consumption of coffee or caffeine during young adulthood and CAC measured 15–20 years later. Tea consumption, on the other hand, displayed an inverse association with 5-year progression of CAC. No association was observed between coffee, caffeine, or tea and cIMT of the CC or IC arteries. In addition, there was no association between coffee and the presence or progression of CAC or cIMT in subpopulations defined by sex, race, or smoking status.

In a comprehensive meta-analysis of epidemiologic data on tea and the primary prevention of cardiovascular disease published through 2000, participants who increased their tea

consumption by 3 cups/day had an 11% decrease in risk of myocardial infarction.[12] Several,[13, 16, 38] but not all[39] cohort studies and meta-analyses published since have identified protective associations between habitual tea intake and cardiovascular disease. Evidence for an association with atherosclerosis has been accumulating. Data from a subsample of 3454 Dutch adults aged 55 years and older from the population-based Rotterdam Study showed a significant inverse association between tea consumption and the presence of severe abdominal aortic calcified plaque reflected by the length of the calcified area.[40] In addition, a higher intake of green tea was associated with lower odds for significant stenosis of one or more coronary arteries among 117 Japanese[41] and 379 Chinese[42] men referred for angiography. Caution is needed in generalizing our results and the results of similar studies due to differences in the country of origin, sampling strategies, age of participants, measures of atherosclerosis, and the type and amount of tea consumed. However, in general, our results appear to be consistent with these studies and suggest additionally that tea consumption may beneficially influence the progression of CAC. Future studies are needed to confirm these findings.

All tea is derived from the same plant (Camellia sinensis), which is grown in over thirty countries. Black tea is primarily consumed in the US and Europe, while green tea is the main tea beverage consumed in East Asian countries, such as China and Japan. In the US, it has been estimated that approximately 21% of adults aged >20 years drink tea daily, generally similar to that observed in the current study (15%).[43] Black teas are produced by promoting the enzymatic oxidation of catechins, while green teas are generated by inactivating these enzymes. Although we did not collect information on the type of tea consumed by participants, it was likely to be predominately black tea. It should be noted that both green and black teas contain comparable total amounts of flavonoids, though their individual quantities may differ.44

The most widely mentioned mechanism linking regular tea consumption with reduced atherosclerosis includes the protective effects of flavonoids on the oxidation of low density lipoproteins[18] and the development of fatty streaks in animal models,[45] key events in early atherogenesis. Studies of apolipoprotein E deficient mice fed an atherogenic diet supplemented with tea catechins have shown reduced accumulation of femoral and aortic atherosclerosis compared to mice fed only an atherogenic diet.[20, 46] A second mechanism includes potential effects of flavonoids present in tea on the vascular endothelium, widely regarded to be involved in all stages of atherosclerotic plaque formation.[47–50] For example, Duffy et al.[48] showed tea consumption improved endothelium-dependent flow-mediated dilation two hours following the ingestion of tea and this effect was maintained after four weeks of daily tea consumption among patients with clinical cardiovascular disease. Additional mechanisms that may explain, at least in part, the association of tea with atherosclerosis include anti-thrombotic and anti-inflammatory effects of flavonoids present in tea.[51, 52]

We observed a non-significant trend for an inverse association between tea and the presence of CAC and a significant inverse association with CAC progression, but no evidence for an association with cIMT. In a cross-sectional, population-based study of 6597 French adults aged 65–85 years, Debette et al.[22] noted regular tea consumption was associated with a lower presence of carotid plaque in women; however, similar to our findings, there was no evidence of a relation with cIMT of the CC artery in either sex. These researchers speculated that tea consumption may be more strongly associated with advanced atherosclerosis as reflected by the presence of calcified carotid plaque as opposed to cIMT. Another explanation is that cIMT may not be a good indicator of the inflammatory process that is consistent with atherosclerotic disease, since age-related thickening has been shown to occur in the absence of overt atherosclerosis.[53]

We found no evidence to suggest that habitual coffee consumption may be associated with CAC or cIMT. Furthermore, there was no association among subgroups of men, women,

whites, blacks, smokers, and nonsmokers. To our knowledge, only a single report has been published to date examining whether coffee may be associated with atherosclerosis. In a subsequent analysis of 1570 older Dutch adults from the Rotterdam Study, van Woudenbergh et al.[23] showed a complex pattern of associations between coffee and CAC. A significant inverse association was observed among women, while among men, smoking appeared to modify this relation since a positive association was found among nonsmoking men, but not among men who were current smokers. These investigators were unable to explain why coffee appeared protective among women and subsequently harmful among nonsmoking men. Our null results suggest that the modest inverse association between coffee consumption, stroke, and cardiovascular mortality observed in recent studies may not be mediated by a beneficial influence of coffee on coronary or carotid atherosclerosis.[9–11]

Strengths of our study include a population-based sampling method; a biracial cohort; extensive data on potential confounders; a large sample size well balanced with respect to age, sex, race, and education that increased precision and permitted simultaneous adjustment for multiple variables; repeat assessments of coffee, caffeine, tea, and other potential confounding factors; the comprehensive CARDIA dietary history; and the standardized data collection protocols and rigorous quality control of the CARDIA study. Nevertheless, several limitations deserve mention. First, participants in the current study were followed from young adulthood into early middle age, a time when the prevalence of atherosclerotic plaque is still relatively low. In addition, although nearly two-thirds of participants reported drinking coffee, only about 16% reported consuming 3 cups/d or more. Thus, we cannot rule out a possible beneficial or hazardous association between habitual coffee consumption and CAC or cIMT among older adults and/or those with higher levels of intake. Second, although we have controlled for a number of potential confounders, the study is observational in nature and we could not exclude the possibility of residual confounding from unmeasured or inadequately measured confounders. Third, similar to most longitudinal studies, our results may be susceptible to non-response; however, retention of the cohort after 15 to 20 years was high and we noted no differences in baseline coffee, caffeine, or tea consumption between those who were included vs. those who were not included in the current study. Fourth, we could not differentiate the type of tea consumed by participants. Finally, as discussed earlier, the probability of committing a type I error may have increased with the number of statistical tests performed; however, our primary analyses were based upon predetermined hypotheses.

In conclusion, the present long-term, population-based study showed no substantial association between habitual coffee, decaffeinated coffee, or caffeine consumption assessed during young adulthood and well-documented markers of coronary and carotid atherosclerosis measured 15–20 years later. Tea consumption, however, displayed evidence for a protective association with coronary calcification. Our findings suggest that tea consumption may prevent the development and progression of coronary calcification, while coffee and caffeine intake at the levels reported in the current study do not appear to be beneficial or harmful.

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References

1. Lundsberg, LS. Caffeine consumption. In: GA, S., editor. Caffeine. Boca Raton, FL: CRC Pr; 1998.
2. Nurminen ML, Niittynen L, Korpela R, Vapaatalo H. Coffee, caffeine and blood pressure: a critical review. Eur J Clin Nutr 1999;53:831–839. [PubMed: 10556993]
3. Jee SH, He J, Appel LJ, Whelton PK, Suh I, Klag MJ. Coffee consumption and serum lipids: a meta-analysis of randomized controlled clinical trials. Am J Epidemiol 2001;153:353–362. [PubMed: 11207153]
4. van Dam RM, Dekker JM, Nijpels G, Stehouwer CD, Bouter LM, Heine RJ. Coffee consumption and incidence of impaired fasting glucose, impaired glucose tolerance, and type 2 diabetes: the Hoorn Study. Diabetologia 2004;47:2152–2159. [PubMed: 15662556]
5. van Dam RM, Hu FB. Coffee consumption and risk of type 2 diabetes: a systematic review. Jama 2005;294:97–104. [PubMed: 15998896]
6. Sofi F, Conti AA, Gori AM, Eliana Luisi ML, Casini A, Abbate R, Gensini GF. Coffee consumption and risk of coronary heart disease: a meta-analysis. Nutr Metab Cardiovasc Dis 2007;17:209–223. [PubMed: 17156982]
7. Greenland S. A meta-analysis of coffee, myocardial infarction, and coronary death. Epidemiology 1993;4:366–374. [PubMed: 8347748]
8. Kawachi I, Colditz GA, Stone CB. Does coffee drinking increase the risk of coronary heart disease? Results from a meta-analysis. Br Heart J 1994;72:269–275. [PubMed: 7946780]
9. Lopez-Garcia E, Rodriguez-Artalejo F, Rexrode KM, Logroscino G, Hu FB, van Dam RM. Coffee consumption and risk of stroke in women. Circulation 2009;119:1116–1123. [PubMed: 19221216]
10. Andersen LF, Jacobs DR Jr, Carlsen MH, Blomhoff R. Consumption of coffee is associated with reduced risk of death attributed to inflammatory and cardiovascular diseases in the Iowa Women's Health Study. Am J Clin Nutr 2006;83:1039–1046. [PubMed: 16685044]
11. Lopez-Garcia E, van Dam RM, Li TY, Rodriguez-Artalejo F, Hu FB. The relationship of coffee consumption with mortality. Ann Intern Med 2008;148:904–914. [PubMed: 18559841]
12. Peters U, Poole C, Arab L. Does tea affect cardiovascular disease? A meta-analysis. Am J Epidemiol 2001;154:495–503. [PubMed: 11549554]
13. Arab L, Liu W, Elashoff D. Green and black tea consumption and risk of stroke: a meta-analysis. Stroke 2009;40:1786–1792. [PubMed: 19228856]
14. Yang YC, Lu FH, Wu JS, Wu CH, Chang CJ. The protective effect of habitual tea consumption on hypertension. Arch Intern Med 2004;164:1534–1540. [PubMed: 15277285]
15. Mineharu Y, Koizumi A, Wada Y, Iso H, Watanabe Y, Date C, Yamamoto A, Kikuchi S, Inaba Y, Toyoshima H, Kondo T, Tamakoshi A. Coffee, green tea, black tea and oolong tea consumption and risk of mortality from cardiovascular disease in Japanese men and women. J Epidemiol Community Health. 2009
16. Kuriyama S, Shimazu T, Ohmori K, Kikuchi N, Nakaya N, Nishino Y, Tsubono Y, Tsuji I. Green tea consumption and mortality due to cardiovascular disease, cancer, and all causes in Japan: the Ohsaki study. Jama 2006;296:1255–1265. [PubMed: 16968850]
17. Mukamal KJ, Maclure M, Muller JE, Sherwood JB, Mittleman MA. Tea consumption and mortality after acute myocardial infarction. Circulation 2002;105:2476–2481. [PubMed: 12034652]
18. de Whalley CV, Rankin SM, Hoult JR, Jessup W, Leake DS. Flavonoids inhibit the oxidative modification of low density lipoproteins by macrophages. Biochem Pharmacol 1990;39:1743–1750. [PubMed: 2344371]
19. Yoshida H, Ishikawa T, Hosoai H, Suzukawa M, Ayaori M, Hisada T, Sawada S, Yonemura A, Higashi K, Ito T, Nakajima K, Yamashita T, Tomiyasu K, Nishiwaki M, Ohsuzu F, Nakamura H. Inhibitory effect of tea flavonoids on the ability of cells to oxidize low density lipoprotein. Biochem Pharmacol 1999;58:1695–1703. [PubMed: 10571243]
20. Miura Y, Chiba T, Tomita I, Koizumi H, Miura S, Umegaki K, Hara Y, Ikeda M, Tomita T. Tea catechins prevent the development of atherosclerosis in apoprotein E-deficient mice. J Nutr 2001;131:27–32. [PubMed: 11208934]
21. Vinson JA, Teufel K, Wu N. Green and black teas inhibit atherosclerosis by lipid, antioxidant, and fibrinolytic mechanisms. J Agric Food Chem 2004;52:3661–3665. [PubMed: 15161246]

22. Debette S, Courbon D, Leone N, Gariepy J, Tzourio C, Dartigues JF, Barberger-Gateau P, Ritchie K, Alperovitch A, Amouyel P, Ducimetiere P, Zureik M. Tea consumption is inversely associated with carotid plaques in women. Arterioscler Thromb Vasc Biol 2008;28:353–359. [PubMed: 18063810]
23. van Woudenbergh GJ, Vliegenthart R, van Rooij FJ, Hofman A, Oudkerk M, Witteman JC, Geleijnse JM. Coffee consumption and coronary calcification: the Rotterdam Coronary Calcification Study. Arterioscler Thromb Vasc Biol 2008;28:1018–1023. [PubMed: 18323515]
24. Hughes GH, Cutter G, Donahue R, Friedman GD, Hulley S, Hunkeler E, Jacobs DR Jr, Liu K, Orden S, Pirie P, et al. Recruitment in the Coronary Artery Disease Risk Development in Young Adults (Cardia) Study. Control Clin Trials 1987;8:68S–73S. [PubMed: 3440391]
25. Friedman GD, Cutter GR, Donahue RP, Hughes GH, Hulley SB, Jacobs DR Jr, Liu K, Savage PJ. CARDIA: study design, recruitment, and some characteristics of the examined subjects. J Clin Epidemiol 1988;41:1105–1116. [PubMed: 3204420]
26. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972;18:499–502. [PubMed: 4337382]
27. McDonald A, Van Horn L, Slattery M, Hilner J, Bragg C, Caan B, Jacobs D Jr, Liu K, Hubert H, Gernhofer N, et al. The CARDIA dietary history: development, implementation, and evaluation. J Am Diet Assoc 1991;91:1104–1112. [PubMed: 1918764]
28. Liu K, Slattery M, Jacobs D Jr, Cutter G, McDonald A, Van Horn L, Hilner JE, Caan B, Bragg C, Dyer A, et al. A study of the reliability and comparative validity of the cardia dietary history. Ethn Dis 1994;4:15–27. [PubMed: 7742729]
29. Hu FB, Stampfer MJ, Rimm E, Ascherio A, Rosner BA, Spiegelman D, Willett WC. Dietary fat and coronary heart disease: a comparison of approaches for adjusting for total energy intake and modeling repeated dietary measurements. Am J Epidemiol 1999;149:531–540. [PubMed: 10084242]
30. Carr JJ, Nelson JC, Wong ND, McNitt-Gray M, Arad Y, Jacobs DR Jr, Sidney S, Bild DE, Williams OD, Detrano RC. Calcified coronary artery plaque measurement with cardiac CT in population-based studies: standardized protocol of Multi-Ethnic Study of Atherosclerosis (MESA) and Coronary Artery Risk Development in Young Adults (CARDIA) study. Radiology 2005;234:35–43. [PubMed: 15618373]
31. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M Jr, Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. J Am Coll Cardiol 1990;15:827–832. [PubMed: 2407762]
32. Greenlund KJ, Kiefe CI, Giles WH, Liu K. Associations of job strain and occupation with subclinical atherosclerosis: The CARDIA Study. Ann Epidemiol 2010;20:323–331. [PubMed: 20382332]
33. O'Leary DH, Polak JF, Kronmal RA, Manolio TA, Burke GL, Wolfson SK Jr. Cardiovascular Health Study Collaborative Research Group. Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. N Engl J Med 1999;340:14–22. [PubMed: 9878640]
34. Jacobs DR Jr, Hahn LP, Haskell WL, Pirie P, Sidney S. Validity and reliability of short physical activity history: CARDIA and Minnesota Heart Health Program. J Cardiopulm Rehabil 1989;9:448–459.
35. Dyer AR, Cutter GR, Liu KQ, Armstrong MA, Friedman GD, Hughes GH, Dolce JJ, Raczynski J, Burke G, Manolio T. Alcohol intake and blood pressure in young adults: the CARDIA Study. J Clin Epidemiol 1990;43:1–13. [PubMed: 1969463]
36. Loria CM, Liu K, Lewis CE, Hulley SB, Sidney S, Schreiner PJ, Williams OD, Bild DE, Detrano R. Early adult risk factor levels and subsequent coronary artery calcification: the CARDIA Study. J Am Coll Cardiol 2007;49:2013–2020. [PubMed: 17512357]
37. Paynter NP, Yeh HC, Voutilainen S, Schmidt MI, Heiss G, Folsom AR, Brancati FL, Kao WH. Coffee and sweetened beverage consumption and the risk of type 2 diabetes mellitus: the atherosclerosis risk in communities study. Am J Epidemiol 2006;164:1075–1084. [PubMed: 16982672]
38. Suzuki E, Yorifuji T, Takao S, Komatsu H, Sugiyama M, Ohta T, Ishikawa-Takata K, Doi H. Green tea consumption and mortality among Japanese elderly people: the prospective Shizuoka elderly cohort. Ann Epidemiol 2009;19:732–739. [PubMed: 19628408]

39. Sesso HD, Paffenbarger RS Jr, Oguma Y, Lee IM. Lack of association between tea and cardiovascular disease in college alumni. Int J Epidemiol 2003;32:527–533. [PubMed: 12913023]
40. Geleijnse JM, Launer LJ, Hofman A, Pols HA, Witteman JC. Tea flavonoids may protect against atherosclerosis: the Rotterdam Study. Arch Intern Med 1999;159:2170–2174. [PubMed: 10527294]
41. Sasazuki S, Kodama H, Yoshimasu K, Liu Y, Washio M, Tanaka K, Tokunaga S, Kono S, Arai H, Doi Y, Kawano T, Nakagaki O, Takada K, Koyanagi S, Hiyamuta K, Nii T, Shirai K, Ideishi M, Arakawa K, Mohri M, Takeshita A. Relation between green tea consumption and the severity of coronary atherosclerosis among Japanese men and women. Ann Epidemiol 2000;10:401–408. [PubMed: 10964006]
42. Wang QM, Gong QY, Yan JJ, Zhu J, Tang JJ, Wang MW, Yang ZJ, Wang LS. Association between green tea intake and coronary artery disease in a Chinese population. Circ J 2010;74:294–300. [PubMed: 20019411]
43. Song WO, Chun OK. Tea is the major source of flavan-3-ol and flavonol in the U.S. diet. J Nutr 2008;138:1543S–1547S. [PubMed: 18641204]
44. Hodgson JM. Tea flavonoids and cardiovascular disease. Asia Pac J Clin Nutr 2008;17 Suppl 1:288–290. [PubMed: 18296358]
45. Laughton MJ, Evans PJ, Moroney MA, Hoult JR, Halliwell B. Inhibition of mammalian 5-lipoxygenase and cyclo-oxygenase by flavonoids and phenolic dietary additives. Relationship to antioxidant activity and to iron ion-reducing ability. Biochem Pharmacol 1991;42:1673–1681. [PubMed: 1656994]
46. Hayek T, Fuhrman B, Vaya J, Rosenblat M, Belinky P, Coleman R, Elis A, Aviram M. Reduced progression of atherosclerosis in apolipoprotein E-deficient mice following consumption of red wine, or its polyphenols quercetin or catechin, is associated with reduced susceptibility of LDL to oxidation and aggregation. Arterioscler Thromb Vasc Biol 1997;17:2744–2752. [PubMed: 9409251]
47. Shenouda SM, Vita JA. Effects of flavonoid-containing beverages and EGCG on endothelial function. J Am Coll Nutr 2007;26:366S–372S. [PubMed: 17906190]
48. Duffy SJ, Keaney JF Jr, Holbrook M, Gokce N, Swerdloff PL, Frei B, Vita JA. Short- and long-term black tea consumption reverses endothelial dysfunction in patients with coronary artery disease. Circulation 2001;104:151–156. [PubMed: 11447078]
49. Hodgson JM, Burke V, Puddey IB. Acute effects of tea on fasting and postprandial vascular function and blood pressure in humans. J Hypertens 2005;23:47–54. [PubMed: 15643124]
50. Nagaya N, Yamamoto H, Uematsu M, Itoh T, Nakagawa K, Miyazawa T, Kangawa K, Miyatake K. Green tea reverses endothelial dysfunction in healthy smokers. Heart 2004;90:1485–1486. [PubMed: 15547040]
51. Erdman JW Jr, Balentine D, Arab L, Beecher G, Dwyer JT, Folts J, Harnly J, Hollman P, Keen CL, Mazza G, Messina M, Scalbert A, Vita J, Williamson G, Burrowes J. Flavonoids and heart health: proceedings of the ILSI North America Flavonoids Workshop, May 31–June 1, 2005, Washington, DC. J Nutr 2007;137:718S–737S. [PubMed: 17311968]
52. Kang WS, Lim IH, Yuk DY, Chung KH, Park JB, Yoo HS, Yun YP. Antithrombotic activities of green tea catechins and (−)-epigallocatechin gallate. Thromb Res 1999;96:229–237. [PubMed: 10588466]
53. Finn AV, Kolodgie FD, Virmani R. Correlation between carotid intimal/medial thickness and atherosclerosis: a point of view from pathology. Arterioscler Thromb Vasc Biol 2010;30:177–181. [PubMed: 19679833]

Table 1

Participant demographics, lifestyle characteristics, dietary intakes, and clinical factors according to average caffeinated coffee consumption at years 0 and 7: The CARDIA Study.[a]

	Caffeinated coffee (cups/d)					
	0	**< 1**	**1–2**	**3–4**	**> 4**	***p* for trend[b]**
n (%)	1328 (37.2)	1108 (31.0)	562 (15.7)	383 (10.7)	193 (5.4)	
Caffeinated coffee (cups/day)	0	0.39	1.46	2.84	6.69	
Selected characteristics						
Age, year 0 (yrs)	24.4	25.1	25.9	26.3	26.6	<0.001
Sex, (% women)	57.8	57.3	57.5	47.0	49.2	0.008
Race, (% black)	60.0	50.2	31.1	18.8	16.6	<0.001
Education > HS, year 7 (%)	34.7	43.5	50.0	53.3	35.2	0.04
Alcohol (ml/day)	8.2	9.9	12.7	15.4	17.2	<0.001
Physical activity (exercise units)	369.2	363.2	408.8	400.0	392.3	>0.2
Smoking, year 7 (% smokers)	19.7	21.1	25.4	34.7	51.3	<0.001
Daily dietary data						
Total energy (kcal)	2758.3	2669.1	2640.8	2765.9	2891.9	0.01
Fruits and vegetables (servings/day)	6.6	6.7	6.7	6.9	6.7	>0.2
Red meat (servings/day)	2.8	2.6	2.5	2.6	2.8	>0.2
Whole grains (servings/day)	1.7	1.7	1.9	1.9	1.8	0.07
Refined grains (servings/day)	6.0	5.9	5.6	5.8	5.8	>0.2
Decaffeinated coffee (cups/day)	0.06	0.11	0.21	0.16	0.19	0.004
Total caffeine (mg/d)	58.5	116.2	290.2	542.3	1244.0	<0.001
Tea (cups/day)	0.55	0.53	0.46	0.56	1.08	>0.2
Clinical and physical characteristics						
BMI (kg/m^2)	25.8	25.2	24.8	25.0	25.6	>0.2
Waist circumference (cm)	80.6	79.6	79.0	80.9	81.9	>0.2
Systolic blood pressure (mmHg)	109.8	109.2	108.4	109.0	109.3	>0.2
Diastolic blood pressure (mmHg)	69.1	68.9	68.1	68.5	68.5	0.003
Fasting blood concentration						
Insulin (μU/mL)	13.7	12.7	11.8	11.3	11.4	0.006
Glucose (mg/dL)	85.1	85.4	85.4	86.7	87.2	>0.2

	Caffeinated coffee (cups/d)					
	0	**< 1**	**1–2**	**3–4**	**> 4**	***p* for trend[b]**
HDL cholesterol (mg/dL)	52.6	52.8	53.2	52.5	51.1	0.08
LDL cholesterol (mg/dL)	109.2	109.0	109.3	111.4	111.3	>0.2
Triglycerides (mg/dL)	76.2	79.0	75.4	87.3	91.5	>0.2

[a] Except where noted, all values are the average of year 0 and year 7 measurements.

[b] *p* for trend is based upon age-, sex-, and race-adjusted analyses.

Table 2

Adjusted odds ratios (OR) and 95% confidence intervals (CI) for presence of coronary artery calcified plaque (CAC) at years 15 or 20 and progression of CAC from year 15 to 20 according to average coffee, caffeine, and tea consumption at years 0 and 7.

	Presence of CAC (n=3574)[a]				Progression of CAC (n=2415)[b]			
	No of cases/noncases	Unadjusted percent	Model 1[c] OR (95% CI)	Model 2[d] OR (95% CI)	No of cases/noncases	Unadjusted percent	Model 1[c] OR (95% CI)	Model 2[d] OR (95% CI
Caffeinated coffee (cups/d)								
0	220/1108	16.6	1.00 (referent)	1.00 (referent)	120/725	14.2	1.00 (referent)	1.00 (referent)
< 1	187/921	16.9	0.90 (0.71, 1.13)	0.94 (0.74, 1.18)	106/645	14.1	0.92 (0.68, 1.23)	0.95 (0.70, 1.28)
1–2	107/455	19.0	0.90 (0.68, 1.19)	0.96 (0.72, 1.28)	69/338	17.0	0.98 (0.69, 1.40)	1.07 (0.75, 1.53)
3–4	92/291	24.0	0.90 (0.68, 1.19)	0.91 (0.66, 1.25)	62/212	22.6	1.03 (0.70, 1.51)	1.06 (0.72, 1.57)
> 4	57/136	29.5	1.11 (0.75, 1.64)	1.07 (0.72, 1.59)	32/106	23.2	1.04 (0.63, 1.71)	1.01 (0.61, 1.68)
p for trend			>0.2	>0.2			>0.2	>0.2
Decaffeinated coffee (cups/d)								
0	547/2397	18.6	1.00 (referent)	1.00 (referent)	316/1659	16.0	1.00 (referent)	1.00 (referent)
< 1	85/396	17.7	0.99 (0.75, 1.29)	1.05 (0.80, 1.38)	53/286	15.6	1.04 (0.74, 1.45)	1.10 (0.78, 1.54)
≥ 1	31/118	20.8	0.99 (0.64, 1.55)	1.07 (0.68, 1.68)	20/81	19.8	1.29 (0.74, 2.23)	1.39 (0.79, 2.43)
p for trend			>0.2	>0.2			>0.2	>0.2
Total caffeine (mg/d)								
< 26.6	117/596	16.4	1.00 (referent)	1.00 (referent)	58/387	13.0	1.00 (referent)	1.00 (referent)
26.6–75.9	107/604	15.1	0.82 (0.61, 1.12)	0.78 (0.57, 1.07)	58/399	12.7	0.94 (0.62, 1.42)	0.89 (0.58, 1.35)
76.0–169.0	131/574	18.6	0.89 (0.66, 1.20)	0.85 (0.63, 1.16)	77/401	16.1	1.10 (0.74, 1.63)	1.03 (0.68, 1.54)
169.1–342.7	133/589	18.4	0.80 (0.59, 1.09)	0.77 (0.56, 1.06)	80/432	15.6	0.94 (0.63, 1.41)	0.92 (0.61, 1.39)
> 342.7	175/548	24.2	0.85 (0.62, 1.16)	0.80 (0.58, 1.10)	116/407	22.2	1.13 (0.76, 1.69)	1.06 (0.70, 1.60)
p for trend			>0.2	>0.2			>0.2	>0.2
Tea (cups/d)								
0	237/875	21.3	1.00 (referent)	1.00 (referent)	128/568	18.4	1.00 (referent)	1.00 (referent)
< 1	333/1588	17.3	0.81 (0.66, 1.00)	0.85 (0.69, 1.04)	209/1131	15.6	0.85 (0.65, 1.10)	0.86 (0.66, 1.12)
1–2	57/261	17.9	0.83 (0.58, 1.18)	0.84 (0.59, 1.21)	35/196	15.2	0.81 (0.52, 1.26)	0.79 (0.50, 1.25)
> 2	36/186	16.2	0.74 (0.48, 1.13)	0.72 (0.47, 1.11)	17/131	11.5	0.59 (0.33, 1.06)	0.54 (0.30, 0.97)
p for trend			0.07	0.08			0.06	0.04

[a] Presence is defined as a CAC score >0 Agatston units at year 15 or 20.

[b] Progression of CAC is defined as incident CAC at year 20 or an increase in CAC score by ≥20 Agatston units between years 15 and 20.

[c] Model 1 adjusts for baseline age (years), sex, race (white, black), smoking (smoker, former, never), and center (Birmingham, Chicago, Minneapolis, Oakland).

[d] Model 2 adjusts for variables in model 1 and for educational attainment (less than high school, high school graduate, bachelor's degree, master's degree or higher), physical activity (exercise units), BMI (kg/m^2), alcohol intake (ml/d), total energy (kcal/d), fruit and vegetable intake (servings/d), and whole and refined grain intake (servings/d).

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Table 3

Adjusted odds ratios (OR) and 95% confidence intervals (CI) for high carotid intima-media thickness (cIMT) at year 20 according to average coffee, caffeine, and tea consumption at years 0 and 7.

	High cIMT (n=3175)[a]			
	Cases/noncases	Unadjusted percent	Model 1[b] OR (95% CI)	Model 2[b] OR (95% CI)
Caffeinated coffee (cups/d)				
0	217/939	18.8	1.00 (referent)	1.00 (referent)
< 1	205/798	20.4	1.10 (0.87, 1.38)	1.22 (0.96, 1.54)
1–2	97/404	19.4	1.05 (0.78, 1.40)	1.16 (0.86, 1.58)
3–4	75/274	21.5	1.12 (0.80, 1.57)	1.20 (0.85, 1.70)
> 4	44/122	26.5	1.30 (0.84, 1.99)	1.31 (0.84, 2.03)
p for trend			>0.2	0.17
Decaffeinated coffee (cups/d)				
0	533/2073	20.5	1.00 (referent)	1.00 (referent)
< 1	85/353	19.4	1.01 (0.77, 1.33)	1.03 (0.78, 1.37)
≥ 1	20/111	15.3	0.76 (0.46, 1.28)	0.75 (0.44, 1.29)
p for trend			>0.2	>0.2
Total caffeine (mg/d)				
< 26.6	106/517	17.0	1.00 (referent)	1.00 (referent)
26.6–75.9	126/485	20.6	1.29 (0.95, 1.76)	1.28 (0.93, 1.76)
76.0–169.0	137/507	21.3	1.30 (0.95, 1.76)	1.32 (0.96, 1.81)
169.1–342.7	128/524	19.6	1.29 (0.94, 1.76)	1.31 (0.94, 1.82)
> 342.7	141/504	21.9	1.32 (0.95, 1.83)	1.30 (0.93, 1.84)
p for trend			0.16	0.18
Tea (cups/d)				
0	205/748	21.5	1.00 (referent)	1.00 (referent)
< 1	336/1387	19.5	0.96 (0.78, 1.18)	0.99 (0.80, 1.24)
1–2	61/237	20.5	1.21 (0.85, 1.72)	1.22 (0.85, 1.76)
> 2	35/165	17.5	1.02 (0.66, 1.56)	0.95 (0.61, 1.47)
p for trend			>0.2	>0.2

[a] High cIMT is defined as >80th percentile of the normalized composite cIMT of the common and internal carotid arteries.

[b] Models 1 and 2 adjust for variables listed in the footnote of Table 2.