Long-term alcohol and caffeine intake and risk of sudden cardiac death in women[1–3]

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ABSTRACT

Background: Alcohol and caffeine intakes may play a role in the development of sudden cardiac death (SCD) because of their effects on cholesterol, blood pressure, heart rate variability, and inflammation.

Objective: Our objective was to examine the association between long-term alcohol and caffeine intakes and risk of SCD in women.

Design: We examined 93,676 postmenopausal women who participated in the Women's Health Initiative Observational Study. Women were enrolled between 1993 and 1998 and were followed until August 2009. Women completed a food-frequency questionnaire at baseline and again at year 3. We modeled exposure to alcohol 3 ways: by using baseline intake only, a cumulative average of baseline and year 3 intake, and the most recent reported intake (a simple time-varying analysis).

Results: Intake of 5–15 g alcohol/d (about one drink) was associated with a nonsignificantly reduced risk of SCD compared with 0.1–5 g/d of baseline intake (HR: 0.64; 95% CI: 0.40, 1.02), of cumulative average intake (HR: 0.69; 95% CI: 0.43, 1.11), and of most recent intake (HR: 0.58; 95% CI: 0.35, 0.96), with adjustment for age, race, income, smoking, body mass index, physical activity, hormone use, and total energy. No association was found between SCD and total caffeine intake (mg/d) or cups of caffeinated coffee, decaffeinated coffee, and caffeinated tea.

Conclusions: Our results suggest that about one drink per day (or 5.1–15 g/d) may be associated with a reduced risk of SCD in this population; however, this association was only statistically significant for a model using the most recent alcohol intake. Total caffeine, regular coffee, decaffeinated coffee, and regular tea intake were not associated with the risk of SCD. This trial was registered at clinicaltrials.gov as NCT00000611. *Am J Clin Nutr* 2013;97:1356–63.

INTRODUCTION

Sudden cardiac death (SCD)[4] accounts for approximately one-half of all cardiac deaths (1), and, although coronary artery disease (CAD) underlies most SCD events, SCD may be the first manifestation of CAD in many individuals, especially women (2). Furthermore, women experience fewer SCD events than do men and are underrepresented in most studies of SCD, which makes the etiology of SCD in women less clear. Current efforts aimed at the primary prevention of SCD have focused on the placement of implantable defibrillators in patients with left ventricular dysfunction; however, only 30% of SCD events occur in this high-risk group (3), and prevention strategies applicable to the entire population are needed. Dietary habits, such as alcohol and caffeine intake, are associated with risk of CAD, are changeable, and therefore may provide a potential focus of preventative efforts.

Much previous research regarding alcohol and caffeine intakes and SCD has examined the acute effects of heavy consumption. For example, binge drinking can create a hyperadrenergic state that may induce arrhythmias (4). Long-term rather than acute intake of alcohol and caffeine may also influence the risk of SCD. For example, moderate alcohol intake has a beneficial effect on lipids, plaque rupture, and inflammation. Three large cohort studies confirm the adverse effect of heavy drinking and suggest a protective effect of moderate drinking on risk of SCD in men (5–7); however, other studies in men found no association (8–10) or an adverse association (11). To date, only one study has examined the effect of long-term alcohol intake in women; this study suggests that light-to-moderate drinking is associated with a reduced risk of SCD (12).

Like alcohol, coffee increases HDL cholesterol (13) which may protect against the development of atherosclerosis and SCD. On the other hand, coffee negatively effects subclinical inflammation (13) and plasma homocysteine concentrations (14).

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[2] The Women's Health Initiative program is funded by the National Heart, Lung, and Blood Institute, NIH, US Department of Health and Human Services (contracts N01WH22110, 24152, 32100-2, 32105-6, 32108-9, 32111-13, 32115, 32118-32119, 32122, 42107-26, 42129-32, and 44221).

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[4] Abbreviations used: CAD, coronary artery disease; FFQ, food-frequency questionnaire; MI, myocardial infarction; SCD, sudden cardiac death; WHI, Women's Health Initiative.

Received June 6, 2012. Accepted for publication March 14, 2013.

First published online April 24, 2013; doi: 10.3945/ajcn.112.044248.

The association between SCD and caffeine is less studied compared with alcohol (15, 16). Some studies show that large amounts of caffeine are associated with an increased risk of acute cardiac events (17–19). Case-control studies tend to show a negative effect of higher coffee intake, but cohort studies show either no effect or a protective effect on cardiovascular disease risk (16). Only one study has examined the association of long-term caffeine intake with risk of SCD; no relation between coffee and risk of SCD was found in men and women with recent nonfatal myocardial infarction (MI) (15).

Our objective was to investigate the relation between long-term alcohol and caffeine intakes and risk of SCD. Because heavy intake of alcohol and caffeine is associated with an increased risk of cardiovascular disease events, and because both may be linked to SCD through similar mechanisms, we chose to examine them simultaneously. We examined this association in postmenopausal women who now have the greatest population burden of cardiovascular disease, including SCD (20). We additionally analyzed the association of alcohol and caffeine with risk of non-SCD to explore potential differential associations.

SUBJECTS AND METHODS

Study participants

The Women's Health Initiative (WHI) Observational Study included 93,676 study participants at 40 study sites across the United States (21). All participants were female, postmenopausal, and aged 50–79 y at baseline (1993–1998). Women were excluded if they did not provide written informed consent, did not plan to reside in the study recruitment area for ≥3 y, had medical conditions predictive of a survival time of <3 y, had characteristics inconsistent with study compliance (alcoholism, drug dependency, mental illness, dementia), or were actively participating in another controlled trial. Other exclusion criteria were used for each of the trials, as described previously (22).

Exposure measurement

Dietary intake (total alcohol, wine, beer, liquor, and total caffeine) was measured in the WHI by using a validated (23) semiquantitative food-frequency questionnaire (FFQ) designed specifically for this postmenopausal population. Women completed the FFQ at baseline and year 3. The WHI FFQ asked participants to recall diet over the past 3 mo and included 122 items. Women reported their intake of beer, wine, and liquor using the following frequency categories for numbers of servings: never or <1/mo, 1–3/mo, 1/wk, 2–4/wk, 5–6/wk, 1/d, 2–3/d, 4–5/d, and ≥6/d. Medium servings were defined as a 12-oz (355-mL) can or bottle of beer, a 6-oz (177-mL) glass of wine, or 1 shot (1.5 oz, or 44 mL) of liquor. In a separate questionnaire, women reported whether they had ever consumed 12 drinks of any kind of alcohol over their lifetime and whether they still drank alcohol.

Total caffeine intake (in g/d) was calculated from the FFQ based on intake of the following beverages: soda (all types), coffee, and tea. Intake of these beverages was reported according to the same frequency categories as alcohol, and medium servings were defined as 12 oz (355 mL) or 1 can of soda and an 8-oz (237-mL) cup of coffee or tea. The FFQ did not differentiate between caffeinated and decaffeinated soda, coffee, or tea. The FFQ also did not ask about chocolate intake, so we could not consider this source of caffeine in the diet. The caffeine content of medications was not available in this data set; therefore, we were unable to consider this source of caffeine intake. The WHI FFQ nutrient database was derived from the Nutrition Data Systems for Research food and nutrient database (Nutrition Coordinating Center, University of Minnesota) (23).

Although the FFQ did not distinguish between caffeinated and decaffeinated coffee and tea, a separate questionnaire administered at baseline asked women about their usual consumption of regular (caffeinated) coffee, decaffeinated coffee, and regular tea. The exact questions were as follows: "How many cups of regular coffee (not decaf) do you usually drink each day? [count tall (12 oz. or more) cups and espresso drinks made with double shots as 2 cups]," "How many cups of decaf coffee do you usually drink each day? [count tall (12 oz. or more) cups and espresso drinks made with double shots of espresso as 2 cups]," and "How many cups of tea do you usually drink each day? (do not include decaf or herbal tea)."

Outcome measurement

Our primary endpoint, incident SCD, was defined as death from fatal MI, fatal definite CAD, or fatal possible CAD, and this cardiac death must have occurred within 1 h of symptom onset. Trained physician adjudicators reviewed medical records of potential CAD death cases, including death certificates, autopsy reports, circumstances of death recorded by next of kin, and all hospital records, including electrocardiograms, laboratory test results, and reports from all relevant cardiac procedures (hospitalized and nonhospitalized) (24). The medical record or interview of witnesses had to document that patient collapse was directly observed, as by hospital notes and cardiopulmonary resuscitation records or by a relative or observer clearly reporting that the patient was found unresponsive within <60 min from previous direct observation of stable clinical status. As a secondary analysis, we also examined non-SCD, defined as death >24 h after symptom onset. We excluded rapid deaths (1–24 h; n = 157) from all analyses (SCD and non-SCD) because of potential misclassification bias.

Covariates

Sociodemographic variables were measured by interview or by self-report at baseline with the use of standardized questionnaires (age, race, income, and education). Traditional CAD risk factors were also measured by self-report at baseline with the use of questionnaires [smoking status and physical activity (metabolic equivalents) per week from recreational activity] and by trained, certified staff at the baseline exam [height, weight, BMI (in kg/m^2), and waist-to-hip ratio]. Height was measured with a stadiometer, weight was measured while the participants were wearing light clothing, and BMI was calculated as weight (in kg) divided by height (in m) squared. Waist circumference was measured at the natural waist or narrowest part of the torso and hip circumference at the maximal circumference, both to the nearest 0.1 cm. Waist-to-hip ratio was calculated as the ratio of these 2 measures. Trained certified staff also measured pulse, and participants additionally reported their diet (with a validated FFQ) and comorbidities/disease history at baseline. We additionally

measured the following potential confounders (not included in **Table 1**): marital status, family history of MI, multivitamin use, medication use including drugs that prolong the QT-interval, and white blood cell count.

With the exception of hypertension, participants were considered to have a disease at baseline if they self-reported a physician diagnosis and were also using drugs for that disease. For example, high cholesterol was defined as self-report of physician diagnosis of

TABLE 1
Selected baseline characteristics stratified by sudden cardiac death status

	Sudden cardiac death (n = 239)	No cardiac death (n = 92,608)	P value[1]
Sociodemographic			
Age at screening (y)	69.0 ± 6.4[2]	63.5 ± 7.4	<0.01
Race [n (%)]			<0.01
American Indian/Alaska Native	3 (1.3)	410 (0.4)	
Asian/Pacific Islander	6 (2.5)	2653 (2.9)	
African American	31 (13)	7524 (8)	
Hispanic/Latino	2 (0.8)	3591 (3.9)	
White, non-Hispanic	195 (82)	77,122 (84)	
None of the above	2 (0.8)	1048 (1.1)	
Family income [n (%)]			<0.01
<$20,000	73 (32)	13,691 (16)	
$20,000–$74,999	129 (57)	54,565 (64)	
≥$75,000	23 (10)	17,529 (20)	
Smoking status [n (%)]			<0.01
Never-smoker	105 (45)	46,588 (51)	
Former smoker	104 (44)	39,018 (43)	
Current smoker	27 (11)	5675 (6)	
Completed high school [n (%)]	220 (92)	87,109 (95)	0.05
Physiologic			
BMI (kg/m^2)	28.5 ± 6.2	27.3 ± 5.9	<0.01
Waist-to-hip ratio [n (%)]			<0.01
Quartile 1: 0.28–0.76	37 (16)	25,860 (28)	
Quartile 2: 0.77–0.80	38 (16)	23,782 (26)	
Quartile 3: 0.81–0.86	55 (23)	22,221 (24)	
Quartile 4: 0.87–2.88	109 (46)	20,745 (22)	
Systolic blood pressure [n (%)]			<0.01
≤120 mm Hg	57 (24)	36,944 (40)	
>120 to 140 mm Hg	100 (42)	37,002 (40)	
>140 mm Hg	81 (34)	18,540 (20)	
Diastolic blood pressure [n (%)]			0.82
<90 mm Hg	222 (93)	86,573 (94)	
≥90 mm Hg	16 (7)	5896 (6)	
Behavioral			
Dietary total energy (kcal/d)	1650 ± 1586	1550 ± 692	0.33
Dietary total alcohol (g/d)	5.72 ± 15	5.47 ± 11	0.80
Dietary total caffeine (mg/d)	155 ± 133	158 ± 131	0.68
Physical activity (MET-h[3]/wk)	10.4 ± 12.7	13.7 ± 14.4	<0.01
Postmenopausal hormone use [n (%)]			<0.01
Never	105 (45)	27,683 (30)	
Past	59 (25)	19,226 (21)	
Current	71 (30)	44,040 (48)	
Comorbidity, history at baseline [n (%)]			
Diabetes	43 (18)	2891 (3)	<0.01
Hypertension	146 (61)	27,907 (30)	<0.01
Myocardial infarction	35 (15)	2144 (2)	<0.01
Prior coronary artery disease[4]	64 (27)	6685 (7)	<0.01
Congestive heart failure	16 (6.7)	814 (0.9)	<0.01
Coronary bypass surgery	17 (7.3)	788 (0.9)	<0.01
Angioplasty of coronary arteries	15 (6.4)	1070 (1.2)	<0.01
Carotid endarterectomy/angioplasty	10 (4.3)	311 (0.3)	<0.01
Atrial fibrillation	32 (14)	4270 (5)	<0.01
Angina	49 (21)	5322 (6)	<0.01

[1] Calculated by using t tests for continuous variables and chi-square tests for categorical variables.
[2] Mean ± SD (all such values).
[3] MET-h, metabolic equivalent task hours.
[4] Includes myocardial infarction.

high cholesterol and taking lipid-lowering medication. Hypertension was defined as high measured blood pressure or the use of antihypertensive medication. Prior CAD at baseline includes a history of the following: MI, cardiac arrest, coronary bypass surgery [angioplasty of coronary arteries, angina (doctor said you had angina "chest pains from a heart problem")], or revascularization.

Statistical analysis

Less than 6% of participants were missing data on the variables of interest and were excluded from our analysis, which resulted in a final sample size of 92,847. Person-years of follow up were calculated from the date of return of the baseline FFQ to the first of the following: SCD, death, or August 2009. HRs for SCD according to quintile or category of nutrient intake were computed with the use of Cox proportional hazards models, with control for confounders. Because alcohol and caffeine intakes did not remain constant between baseline and year 3, we used Cox proportional hazards regression with time-dependent exposure and covariates (diseases) using previously described methods (25). This approach uses information from both the FFQ completed at baseline and the FFQ completed at year 3.

Potential confounders were identified based on previous knowledge and existing literature. Potential confounders were included as covariates in multivariable models if the variable was *1*) associated with both SCD and the exposure of interest using a P value ≤ 0.20 and *2*) not on the causal pathway. Diseases such as diabetes and hypertension may be on the causal pathway because they can be caused in part by poor diet, and they are risk factors for SCD. To control for this, and to explore effect modification, we additionally ran our analysis stratified by CAD status at baseline. Furthermore, we present a fully adjusted model (model 2) and a model that includes the following potential mediators: atrial fibrillation, CAD, heart failure, diabetes, high cholesterol, and hypertension (model 3). We adjusted for energy intake by including total energy (kcal/d) in our multivariable models. We checked for multicollinearity among covariates, and none had a variance inflation factor >2.0.

To calculate tests for linear trend, the quintile median (ordinal variable) was assigned to each participant and modeled in separate proportional hazards models that included all other covariates. Because we used a priori hypotheses, we do not believe a correction for multiple comparisons was necessary (26, 27). We additionally ran our analyses using quartiles instead of quintiles, using the cumulative average method, and using baseline nutrient intake only to check the sensitivity of our results. The cumulative average method uses baseline diet information for all SCD events that happened before year 3 and the average of baseline and year 3 diet for all subsequent events. Models using most recent intake use baseline diet for all SCD events that happened before year 3 and diet reported at year 3 for all subsequent events. Baseline quantile categories were used to categorize year 3 and average total alcohol and total caffeine intake.

TABLE 2
Baseline characteristics according to quintile of total alcohol

	Total alcohol quintile (g/d)				
	1 (n = 20,466)	2 (n = 16,833)	3 (n = 18,119)	4 (n = 18,231)	5 (n = 19,666)
Mean alcohol (g/d)	0.00	0.02	0.87	4.52	21.9
Age (y)	64.1 ± 7[1]	63.8 ± 8	63.5 ± 7	63.1 ± 7	63.6 ± 7
Ethnicity (%)					
White	72	78	85	18	94
Black	16	10	7	5	3
Latino	6	5	4	3	2
Income (%)					
<$20,000	25	23	15	10	8
$20,000–$74,999	61	65	66	64	61
≥$75,000	14	12	19	26	31
Smoking status (%)					
Never-smoker	59	63	54	46	34
Past smoker	36	31	40	48	58
Current smoker	5	6	6	6	8
Waist-to-hip ratio (%)					
Quartile 1	25	23	28	32	30
Quartile 2	24	24	26	27	28
Quartile 3	24	25	24	23	23
Quartile 4	27	28	22	18	19
Pulse in 60 s (beats/min)	69.6 ± 12	70.1 ± 12	69.3 ± 12	68.8 ± 12	68.7 ± 12
Total physical activity (MET-h[2]/wk)	12.8 ± 15	10.3 ± 12	13.4 ± 14	15.3 ± 15	16.3 ± 15
Total energy (kcal/d)	1269 ± 585	1683 ± 687	1613 ± 849	1562 ± 631	1658 ± 632
Atrial fibrillation (%)	6	5	5	6	5
Congestive heart failure (%)	2	2	1	1	1
Diabetes (%)	7	5	2	1	1
Carotid artery disease (%)	0.5	0.4	0.3	0.3	0.3
Hypertension (%)	71	73	67	62	64

[1] Mean ± SD (all such values).
[2] MET-h, metabolic equivalent task hours.

Because we found no correlation between alcohol intake and caffeine intake ($r = 0.08$), we did not adjust for caffeine in our alcohol analyses and vice-versa and did not examine alcohol-caffeine interactions. All data analyses were conducted by using SAS version 9.2 (SAS Institute Inc). This study was approved by the institutional review boards of all collaborating institutions, and all participants gave informed consent.

RESULTS

A total of 239 women experienced SCD after an average of 11 y of follow-up in the observational study. We found that the following were independent risk factors for SCD in this cohort of postmenopausal women: older age, African American race, smoking, higher resting pulse, higher waist-to-hip ratio, and a history of heart failure, diabetes, MI, carotid artery disease, and hypertension (28). A history of atrial fibrillation was also associated with an increased risk of SCD; however, this association was not statistically significant (Table 1).

Women in higher quintiles of alcohol and caffeine intakes were more likely to be white, to be a current or former smoker, and to have a lower waist-to-hip ratio (**Tables 2** and **3**). Women in higher quintiles of alcohol and caffeine intakes were also less likely to have a history of atrial fibrillation, CAD, congestive heart failure, diabetes, and hypertension. Unlike women in higher quintiles of caffeine intake, women in higher quintiles of alcohol intake had higher incomes and were more active. Although alcohol and caffeine were associated with a similar set of risk factors, they were not correlated ($r = 0.08$).

Compared with very light alcohol intake (0.1–5 g/d), light alcohol intake (one drink or 5.1–15 g/d) was associated with a reduced risk of SCD by using baseline intake (HR: 0.64; 95% CI: 0.40, 1.02), the cumulative average intake (HR: 0.69; 95% CI: 0.43, 1.11), and a simple time-varying exposure analysis (HR: 0.58; 95% CI: 0.35, 0.96) (**Table 4**). This association was only statistically significant for the model using most recent alcohol intake. Compared with very light alcohol intake (0.1–5 g/d), no alcohol intake, moderate alcohol intake (15–30 g/d), and heavy alcohol intake (>30 g/d) were not associated with risk of SCD. Beer and liquor intake was low in this population; therefore, we had limited power to explore different types of alcohol, including wine, liquor, and beer. When we examined beer, wine, and liquor intake, none was individually associated with risk of SCD after adjustment for the others. Results for non-SCD were very similar (*see* Supplemental Tables 1 and 2 under "Supplemental data" in the online issue); however, the protective effect of alcohol appeared to extend to 30 g alcohol/d for non-SCD.

When we stratified our SCD analysis according to history of CAD at baseline, alcohol appeared to have a larger magnitude of association among women without a history of CAD, and HRs were attenuated among women with a history of CAD; however,

TABLE 3
Baseline characteristics according to quintile of total caffeine

	Total caffeine quintile (mg/d)				
	1 (n = 20,235)	2 (n = 19,405)	3 (n = 19,661)	4 (n = 17,128)	5 (n = 16,886)
Mean caffeine (mg/d)	19	75	148	182	368
Age (y)	63.8 ± 8[1]	64.4 ± 7	63.6 ± 7	63.4 ± 7	62.9 ± 7
Ethnicity (%)					
White	70	81	88	90	91
Black	17	9	5	4	4
Latino	6	5	3	3	2
Income (%)					
<$20,000	21	17	14	13	15
$20,000–$74,999	61	63	63	66	65
≥$75,000	18	20	22	21	20
Smoking status (%)					
Never-smoker	62	53	46	49	42
Past smoker	34	42	48	44	47
Current smoker	4	5	6	7	11
Waist-to-hip ratio (%)					
Quartile 1	26	27	29	28	29
Quartile 2	24	26	26	26	26
Quartile 3	25	24	23	24	23
Quartile 4	25	23	21	21	22
Pulse in 60 s (beats/min)	69 ± 12	69 ± 12	69 ± 12	70 ± 12	69 ± 12
Total physical activity (MET-h[2]/wk)	13.6 ± 15	13.8 ± 14	14.9 ± 15	12.7 ± 13	13.3 ± 14
Total energy (kcal/d)	1363 ± 661	1434 ± 610	1493 ± 619	1725 ± 666	1795 ± 829
Atrial fibrillation (%)	6	5	4	4	4
Coronary artery disease (%)	9	8	7	7	6
Congestive heart failure (%)	2	1	1	1	1
Diabetes (%)	5	4	3	2	3
Carotid artery disease (%)	0.4	0.4	0.4	0.4	0.4
Hypertension (%)	71	70	66	66	63

[1] Mean ± SD (all such values).
[2] MET-h, metabolic equivalent task hours.

TABLE 4
HRs (and 95% CIs) for sudden cardiac death according to alcohol intake by using 3 exposure models

Total alcohol (g/d)	No. of cases	Patient-years	HR (95% CI)[1]		
			Model 1[2]	Model 2[3]	Model 3[4]
Exposure model 1: baseline alcohol intake					
Never-drinker	7	12,371	1.84 (0.86, 3.93)	1.86 (0.86, 4.00)	1.54 (0.71, 3.33)
Former drinker[5]	9	29,764	1.09 (0.56, 2.15)	0.97 (0.49, 1.91)	0.84 (0.42, 1.65)
0.1–5 g/d	142	522,934	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)
5.1–15 g/d	21	147,098	0.54 (0.34, 0.85)	0.64 (0.40, 1.02)	0.72 (0.45, 1.15)
15.1–30 g/d	17	67,933	0.90 (0.54, 1.49)	1.11 (0.66, 1.86)	1.24 (0.74, 2.10)
>30 g/d	9	36,728	0.89 (0.45, 1.75)	0.91 (0.46, 1.81)	1.04 (0.52, 2.08)
Exposure model 2: cumulative average alcohol intake					
Never-drinker	3	4983	1.55 (0.49, 4.88)	1.59 (0.50, 5.05)	1.26 (0.39, 4.00)
Former drinker[5]	0	11,702	NA	NA	NA
0.1–5 g/d	137	509,954	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)
5.1–15 g/d	21	138,714	0.58 (0.37, 0.92)	0.69 (0.43, 1.11)	0.78 (0.49, 1.26)
15.1–30 g/d	12	64,271	0.69 (0.38, 1.24)	0.82 (0.45, 1.51)	0.94 (0.51, 1.74)
>30 g/d	9	30,495	1.09 (0.55, 2.13)	1.11 (0.55, 2.21)	1.29 (0.65, 2.59)
Exposure model 3: most recent alcohol intake					
Never-drinker	3	13,660	0.75 (0.24, 2.34)	0.72 (0.23, 2.27)	0.62 (0.20, 1.97)
Former drinker[5]	6	29,465	0.51 (0.19, 1.39)	0.44 (0.16, 1.20)	0.37 (0.14, 1.01)
0.1–5 g/d	152	530,476	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)
5.1–15 g/d	19	141,850	0.50 (0.31, 0.82)	0.58 (0.35, 0.96)	0.67 (0.40, 1.10)
15.1–30 g/d	15	64,791	0.81 (0.47, 1.41)	0.99 (0.56, 1.75)	1.12 (0.63, 1.97)
>30 g/d	10	36,586	0.87 (0.43, 1.77)	0.88 (0.42, 1.82)	1.02 (0.49, 2.11)

[1] HRs and 95% CIs were calculated by using multivariable Cox proportional hazard regression. NA, not applicable.
[2] Model 1 was adjusted for age and total energy intake.
[3] Model 2 was adjusted as for model 1 plus race, income, smoking status, pulse in 60 s, waist-to-hip ratio, BMI, physical activity, and hormone use.
[4] Model 3 was adjusted for model 2 plus potential mediators: atrial fibrillation, coronary artery disease, heart failure, diabetes, high cholesterol, and hypertension.
[5] There were no cases among the former drinkers for our cumulative average analysis.

the number of events among this population was small and our estimates were highly variable. We found no association between total caffeine, caffeinated (regular) coffee, decaffeinated coffee, or caffeinated tea and risk of SCD (**Table 5**).

DISCUSSION

In a large multiethnic cohort of postmenopausal women, we found that light alcohol intake (one drink a day or 5.1–15 g/d) was associated with a reduced risk of SCD compared with 0.1–5 g/d. This association was only statistically significant for a model using most recent alcohol intake. Three previous studies found an increased risk of SCD associated with heavy drinking and a protective effect of light-to-moderate drinking on risk of SCD in men (5–7); however, only one study has examined this association in women. This study (12), which used the Nurses' Health Study cohort, confirmed the potentially protective effects of light-to-moderate alcohol intake in women. They found a U-shaped relation between alcohol intake and SCD, with a nadir at 5–14.9 g/d. We found a similar U-shaped relation between alcohol intake and risk of SCD with an increased risk of never-drinkers and a protective effect of light drinking (one drink or 5.1–15 g/d) compared with very light drinking (0.1–5 g/d). We found no differential associations by type of alcohol, including wine, beer, or hard liquor.

Our results were similar when we used a simple time-varying exposure analysis (which uses most recent diet) and using the cumulative average method. Because we only had 2 measures of diet over time, at baseline and at year 3, both methods theoretically examined the effect of chronic, long-term alcohol intake, assuming that intake remains relatively constant after year 3.

We found that total caffeine, regular coffee, decaffeinated coffee, and regular tea intakes were not associated with risk of SCD in this population of postmenopausal women. Only one previous study has examined the association between coffee intake and SCD. This study, the Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico (GISSI-Prevenzione), found no relation between coffee and risk of SCD in men and women with recent nonfatal MI (15). Our study examined total caffeine intake, regular coffee, decaffeinated coffee, and regular tea and also found no association in women.

The strengths of our study included its prospective design, the inclusion of women from multiple ethnic groups, and geographic sites across the United States, physician adjudicated SCD, and comprehensive data on confounders. In addition, we used a validated FFQ designed specifically for postmenopausal women, which was administered twice during follow-up. The correlation coefficients between the FFQ and 8 d of dietary intake (four 24-h recalls and a 4-d food record) collected from 113 women participating in the WHI in 1995 was 0.89 for alcohol (23), which suggests good agreement.

Our study had several potential weaknesses, including residual confounding because of its observational nature, limited generalizability to men and premenopausal women, wide CIs, limited

TABLE 5
HRs (and 95% CIs) for sudden cardiac death according to intake of caffeine, coffee, and tea[1]

		Model 1[2]		Model 2[3]	
	No. of cases	HR (95% CI)[4]	*P*-trend	HR (95% CI)[4]	*P*-trend
Caffeine quintile					
1 (0–58 mg/d)	47	1.0 (Reference)		1.0 (Reference)	
2 (59–92 mg/d)	42	0.60 (0.40, 0.92)	0.17	0.65 (0.42, 0.99)	0.52
3 (93–178 mg/d)	34	0.71 (0.46, 1.09)		0.79 (0.51, 1.23)	
4 (179–266 mg/d)	35	0.66 (0.42, 1.04)		0.80 (0.50, 1.27)	
5 (267–855 mg/d)	47	0.81 (0.52, 1.28)		0.90 (0.56, 1.42)	
Regular coffee					
None	97	1.0 (Reference)		1.0 (Reference)	
1 cup/d	34	0.86 (0.58, 1.26)	0.51	0.90 (0.61, 1.33)	0.84
2–3 cups/d	55	0.86 (0.62, 1.20)		0.94 (0.67, 1.31)	
≥4 cups/d	19	0.97 (0.59, 1.59)		1.02 (0.61, 1.70)	
Decaffeinated coffee					
None	134	1.0 (Reference)		1.0 (Reference)	
1 cup/d	36	1.17 (0.81, 1.69)	0.52	1.23 (0.85, 1.78)	0.37
2–3 cups/d	26	0.97 (0.63, 1.47)		1.00 (0.66, 1.53)	
≥4 cups/d	9	1.43 (0.73, 2.81)		1.51 (0.76, 2.97)	
Regular tea					
None	144	1.0 (Reference)		1.0 (Reference)	
1 cup/d	32	1.23 (0.84, 1.80)	0.32	1.27 (0.86, 1.86)	0.30
2–3 cups/d	20	0.93 (0.58, 1.48)		0.93 (0.58, 1.49)	
≥4 cups/d	9	1.78 (0.91, 3.49)		1.77 (0.90, 3.48)	

[1] Total caffeine intake was measured at baseline and year 3; the most recent caffeine intake was used. Coffee and tea were measured at baseline only.
[2] Model 1 was adjusted for age and total energy intake.
[3] Model 2 was adjusted for age, total energy intake, race, income, smoking status, physical activity, waist-to-hip ratio, BMI, atrial fibrillation, coronary artery disease, heart failure, diabetes, high cholesterol, and hypertension.
[4] HRs (95% CIs) were calculated by using multivariable Cox proportional hazard regression.

power as a result of the small number of SCD events, and potential misclassification of both the exposure and outcome. Despite uniform data collection procedures and central adjudication, few of those who experienced SCDs were autopsied, and some sudden deaths because of cerebral hemorrhage, acute pulmonary embolism, or aortic rupture may have been incorrectly classified as SCDs. In addition, some SCDs may have been missed, for example if there was inadequate documentation of the timing of death. We believe that this potential bias, if present, would be nondifferential and would therefore bias our estimates toward the null. FFQs in general have several limitations, including the assumption that the FFQ represents average diet. Finally, it would be useful to have more information about pattern of alcohol intake, such as whether an individual with an average of 15 g alcohol/d drank 1 drink/d or 7 drinks in one day (1 drink is typically ~15 g alcohol).

In conclusion, light alcohol intake (5.1–15 g/d compared with 0.1–5 g/d) was associated with a reduced risk of SCD, whereas dietary caffeine intake was not associated with risk of SCD in this cohort of postmenopausal women. Previous research provides substantial evidence for the protective effect of light-to-moderate alcohol intake on cardiovascular health; however, alcohol may negatively influence other common chronic conditions such as cancer; therefore, caution should be taken before recommending light-to-moderate drinking as a public health message.

We acknowledge the WHI investigators (*see* Supplemental Appendix A under "Supplemental data" in the online issue).

The authors' responsibilities were as follows—CBE: conducted the research; MLB: performed the statistical analyses; MLB, EWT, DSM, AB, JWH, MLN, MSF, MAA, MMS, WL, YM-R, MCR, and CBE: wrote the manuscript; and MLB and CBE: had primary responsibility for the final content. All authors read and approved the final manuscript. No conflicts of interest were declared.

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