Caffeinated Coffee Consumption and Mortality After Acute Myocardial Infarction

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Abstract and Introduction

Abstract

Background: Previous studies have generally suggested no effect of coffee consumption on the risk of acute myocardial infarction. The effect of coffee consumption on prognosis after acute myocardial infarction is uncertain.
Methods: In an inception cohort study, we observed 1935 patients who were hospitalized with a confirmed acute myocardial infarction between 1989 and 1994 at 45 community hospitals and tertiary care centers in the United States, as part of the Determinants of Myocardial Infarction Onset Study. Trained interviewers assessed self-reported caffeinated coffee consumption before infarction with a standardized questionnaire. We analyzed survival censored at December 31, 1995, using Cox proportional hazards regression.
Results: Of the 1902 patients for whom we had information on coffee intake, 315 (17%) died during a median follow-up period of 3.8 years. Coffee drinkers tended to be men, younger, and free of comorbidity, and they were more likely to be current smokers. Coffee consumption was not associated with an overall change in long-term post-infarction mortality rate. However, we did observe an unexpected and unexplained variation in the association between coffee consumption and mortality with time, with an apparent inverse association in the first 90 days after infarction.
Conclusions: Self-reported coffee consumption has no overall association with post-infarction mortality. The unexpected time variation in the effect of coffee intake requires evaluation in other studies.

Introduction

How coffee and caffeine consumption influence coronary and total mortality rates among healthy adults is controversial. Meta-analyses of studies on coffee consumption and incidence of coronary heart disease have generally suggested positive associations only in case-control studies,[1,2] although even prospective cohort studies have yielded heterogeneous results.[3] More recent studies have suggested that coffee has little, if any, independent association with coronary heart disease or total mortality rate.[4-9]

The effect of coffee and caffeine consumption on mortality among patients with established coronary heart disease is less well studied. A case-control study of sudden cardiac death in patients with established coronary heart disease found an increased risk only in patients who consumed >10 cups per day.[10] We know of no studies that have analyzed the relationship of caffeinated coffee or cola consumption with all-cause mortality rate specifically in patients with incident coronary heart disease.

To determine the effects of caffeinated coffee and cola consumption on mortality rate after acute myocardial infarction, we studied patients enrolled in the Determinants of Myocardial Infarction Onset Study (the Onset Study).[11,12] This prospective, multicenter, inception cohort study included chart reviews and face-to-face interviews with hospitalized patients who had confirmed acute myocardial infarction. We recently found that tea intake was associated with lower subsequent mortality rates in this population.[12] In this analyses, we hypothesized that neither coffee nor cola consumption would be associated with long-term mortality after acute myocardial infarction.

Methods

Onset Study Enrollment and Data Collection

The Onset Study was conducted in 45 US medical centers. Between August 1989 and September 1994, 1935 patients (601 women and 1334 men) were interviewed a median of 4 days after sustaining a myocardial infarction. Trained research interviewers identified eligible patients by reviewing coronary care unit admission logs and patient charts. For inclusion, patients were required to have a creatine kinase level higher than the upper limit of normal for each center, positive myocardial band isoenzymes, an identifiable onset of symptoms of infarction, and the ability to complete a structured interview. For these analyses, we excluded patients for whom information about coffee consumption was missing (n = 33), leaving 1902 eligible patients. The institutional review board of each center approved this protocol, and each patient gave informed consent.

Interviewers used a structured data abstraction and questionnaire form. Participants were asked their usual frequency of consumption of caffeinated coffee and cola during the last year individually. On the basis of their distributions within the Onset Study population, we categorized usual coffee consumption as none, </=7 cups/week, >7 to 14 cups/week, and >14 cups/week and usual cola consumption as none, </=2 cups/week, >2 to 7 cups/week, and >7 cups/week. We did not determine the consumption of decaffeinated beverages.

Other information collected from each interview and chart review included patient age, sex, medical history, and medication use (both prescription and nonprescription). We defined current aspirin use as the reported use of any aspirin or aspirin-containing product in the 4 days before the index myocardial infarction. We used 1990 US census data to derive median household income from US Postal Service zip codes.[13]

We searched the National Death Index for deaths of Onset Study subjects through December 31, 1995, and requested death certificates from state offices of vital records for all probable matches, using a previously validated algorithm.[14] Three physicians independently verified the determination of each death. Two physicians categorized the cause of each death as caused by cardiovascular disease or noncardiovascular disease, on the basis of information included on death certificates. Disagreements among raters were resolved by discussion.

Statistical Analysis

We analyzed continuous and binary variables using analysis of variance and exact tests, respectively. We used Cox proportional-hazards models to examine the association of coffee and cola intake with survival after adjustment for potentially confounding factors and tested the proportionality of hazards using time-varying covariates. When the proportional hazards assumption was violated, we created Cox models stratified by duration of follow-up and re-tested the proportional hazards assumption. The confounding factors we included were age, sex, previous myocardial infarction, previous angina, diabetes mellitus, hypertension, medication use (aspirin, β-adrenergic antagonists, calcium-channel blockers, digoxin, diuretics, lipid-lowering agents, and angiotensin-converting enzyme inhibitors), current smoking, previous smoking, body mass index, use of thrombolytic therapy, usual frequency of exertion (in 3 categories), usual alcohol consumption (in 3 categories), usual tea consumption (in 3 categories), household income, educational attainment (in 3 categories), and complications of congestive heart failure or ventricular tachycardia. Models that did not include use of lipid-lowering agents gave virtually identical results and are not shown here. We assigned indicator variables for subjects for whom information on education (n = 54) and income (n = 54) was missing. For all other covariates, subjects with information missing were deleted from multivariate models (n = 53). Models that assigned these subjects mean levels of continuous covariates and modal levels of binary covariates yielded nearly identical results and are not shown here. To ensure the robustness of our models, we performed stepwise Cox regression (with entry and stay *P* values of 0.20), forcing coffee or cola consumption into the models. These models yielded results essentially identical to those of the full models despite the smaller number of covariates included. For tests of linear trend, we treated the categories of coffee or cola consumption as continuous variable in the proportional hazards models. For all analyses, we present 95% CIs and probability values from 2-sided statistical tests.

Results

Patient Characteristics

Table I shows Onset Study patient characteristics according to coffee consumption. Coffee drinkers were generally younger, of higher socioeconomic status, less likely to have noncardiac comorbidity, less likely to be sedentary or alcohol abstainers, and more likely to be current smokers. On average, men were more likely to drink coffee than

were women. We found generally similar patient characteristics according to cola consumption (Table II), although coffee consumption was more closely related to prevalence of diabetes mellitus, whereas cola consumption was more clearly associated with higher body mass index.

Coffee Consumption and Mortality

Of the 1902 patients for whom information on coffee and cola intake was available, 315 (17%) died during a mean follow-up period of 3.8 years. A total of 235 (75%) of the deaths were caused by cardiovascular disease. Table III shows that there was an apparent inverse association between self-reported coffee consumption and long-term post infarction mortality rate in the crude analysis, with the mortality rate ranging from 6.27 deaths per 100 patient-years for the patients who abstained to 2.80 deaths per 100 patient-years for patients who reported consuming >14 cups per week. Controlling for the important demographic differences that correlated with coffee intake changed these results. As we hypothesized, we found no overall association of coffee intake and mortality in Cox regression models adjusted for confounding factors (Table III). The hazard ratios for all 3 categories of coffee consumers approached the null value, with no evidence of a substantive trend toward higher or lower mortality rate. Additional adjustment for tea intake or restriction to patients who abstained from tea did not change these results. The mortality rate was also similar between patients who abstained from coffee and the 309 patients who consumed >/=35 cups of coffee per week (adjusted hazard ratio, 0.88; 95% CI, 0.54-1.44).

Unexpectedly, the estimated effect of coffee consumption appeared to change with time in Cox models (P = .01). In the first 90 days of follow-up, during which 79 patients died, greater coffee consumption was associated with a lower adjusted mortality rate in a graded fashion (Table III). After 90 days, this pattern reversed, with a graded, positive relationship between coffee consumption and mortality rate. Exclusion of deaths during hospitalization (n = 15) did not change these results. We found a similar pattern of lower early mortality rate but greater late mortality rate among coffee drinkers in adjusted analyses stratified by median age or sex. Time-varying covariates for the 3 categories of coffee intake, which assess the interaction of exposure with time, were significant in analyses adjusted for age and sex (P = .14, .02, and .01), standard covariates (P = .08, .02, and .02), and standard covariates with additional measures of infarct severity and treatment (peak creatine kinase level, systolic blood pressure <90 mm Hg on admission, and angioplasty during hospitalization; P = .09, .02, and .02).

Caffeinated Cola Consumption and Mortality

After adjusting for covariates as in the analysis of coffee, we found no consistent relationship between caffeinated cola consumption and mortality rate. The hazard ratio for patients who consumed >/=7 servings per week compared with nondrinkers was 1.15 (95% CI, 0.76-1.73). There was no evidence of a dose-related positive or inverse association for total mortality rate (P_{trend} = .76) or cardiovascular mortality rate (P_{trend} = .28). Further adjustment for tea intake or coffee intake (with time variation) did not alter these findings. Using time-varying covariates, we found no evidence that the estimated effects of cola consumption varied with time (P = .48-.67).

Discussion

In this multicenter, prospective study of early survivors of acute myocardial infarction, we found no overall association of coffee consumption with post-infarction mortality, even among the heaviest coffee consumers. Unexpected time variation in the apparent effect of coffee was noted, although we could not define a plausible explanation for this finding. Cola consumption was not associated with post-infarction mortality.

We know of little data about the effect of coffee consumption on prognosis after acute myocardial infarction. In a case-control study of 168 patients with coronary heart disease, De Vreede et al found that sudden cardiac death was strongly associated with coffee consumption (odds ratio, 55.7; 95% CI, 6.4-482.8), but only at a rate of consumption >10 cups per day (which few of our or their patients reported).[10] In that study, lower amounts of coffee were associated with odds ratios of 1.8 to 2.8 that were not statistically significant. Because coffee consumption is not associated with the risk of a first acute myocardial infarction[1-9] and short-term trials of coffee consumption demonstrate no substantial risk in patients with known coronary heart disease,[15] we hypothesized that coffee consumption would be associated with no change in long-term prognosis after such an infarction. Our findings support this hypothesis, although we found unexpected time variation in the effect of coffee consumption. We know of no plausible explanation for this finding in the Onset Study, and it persisted in a variety of analyses. In the absence of a compelling explanation for this result, we suspect it to be the product of uncontrolled confounding or chance. We encourage other investigators to replicate our analysis before efforts to determine a possible mechanism are undertaken.

Study Limitations

Our study was limited to the assessment of caffeinated beverages, which represent the bulk of coffee and cola consumed in the United States. Although intake of decaffeinated coffee does not appear to confer a substantially different risk of coronary heart disease than caffeinated coffee,[9] we cannot necessarily extrapolate our results to consumption of decaffeinated coffee or cola. We also did not ascertain the use of chocolate, a minor source of caffeine, which contains approximately 7 mg of caffeine per serving of candy.

We asked participants to report their usual beverage consumption in the year before the infarction that resulted in their hospitalization. By measuring these variables prospectively, we minimized the possibility that infarction severity influenced the amount of coffee that patients consumed after their infarction; for example, if sicker patients disproportionately stop drinking caffeinated coffee after infarction, then study of post-infarction consumption will produce biased results.

Our results could also be influenced by inaccuracies in identification of deaths in Onset Study subjects. However, we used a validated method to search the National Death Index,[14] and 3 physicians who were blinded to beverage consumption confirmed each death.

It is unlikely that the absence of an association between coffee or cola consumption and prognosis is caused by our use of a baseline assessment of these (or other) variables. Cleophas et al found that coffee and tea consumption were essentially identical when considered 1 year before, during, or 1 year after an acute myocardial infarction,[16] which suggests that additional measurements are unlikely to have changed the rank-ordering of our participants. Furthermore, we have previously demonstrated strong inverse associations of tea[12] and alcohol[17] consumption with mortality in this cohort using identical methods, which demonstrates that our approach can yield significant findings between specific nutritional factors and post-infarction mortality.

Our findings only address the prognosis of early survivors of acute myocardial infarction. Because we excluded subjects with very early morbidity or mortality, we cannot address whether coffee or cola affect the case-fatality rate of acute myocardial infarction, although indirect evidence suggests that they do not.[15] We also cannot assess the prognosis of patients who sustain severe early instability after acute myocardial infarction, although our results can be generalized to most patients who survive hospitalization for acute myocardial infarction.

Conclusions

In summary, we found no overall association between coffee or cola consumption and survival after acute myocardial infarction. Our results generally support the hypothesis that coffee consumption poses little cardiovascular risk to patients with acute myocardial infarction and further extend this hypothesis to cola consumption. Further research is needed to explore the possibility of time variation in mortality risk among coffee drinkers, but our findings nonetheless are consistent with current American Heart Association dietary guidelines,[18] which do not specifically advise for or against consumption of coffee and other caffeinated beverages.

Tables

Table I. Characteristics of 1900 Onset Study participants according to usual weekly coffee consumption

	Usual weekly coffee consumption				
	0	>0-7 Cups	>7-14 Cups	>14 Cups	*P**
Number	494	517	290	601	
Age (y)†	65 ± 13	65 ± 12	62 ± 12	56 ± 11	<.001
Female (%)	41	36	33	18	<.001
White (%)	89	84	93	95	<.001
BMI (kg/m^2)†	27.3 ± 5.8	26.7 ± 4.9	27.9 ± 5.6	27.3 ± 4.6	.03
Current smoker (%)	18	24	30	56	<.001
Former smoker (%)	49	44	46	30	<.001
Hypertension (%)	48	51	46	35	<.001

Diabetes (%)	26	21	21	15	<.001
Previous MI (%)	35	30	29	22	<.001
Noncardiac comorbidity (%)	19	16	13	11	<.001
Regular use of (%)					
Aspirin	32	36	36	32	.44
β-Blockers	24	22	20	15	.001
Ca-blockers	29	27	27	17	<.001
ACE inhibitors	15	15	12	7	<.001
Digoxin	13	8	7	3	<.001
Diuretics	26	27	18	10	<.001
Lipid therapy	9	7	6	7	.48
Thrombolytic use (%)	28	31	41	45	<.001
CHF (%)	18	15	19	10	<.001
VT (%)	12	9	12	16	.02
Exertion >/=6 MET <1 weekly (%)	87	85	78	75	<.001
Income ($)[†,‡]	37248 ± 13702	38330 ± 13333	38459 ± 12655	39342 ± 12651	.08
Alcohol abstention (%)	71	58	54	49	<.001
Weekly tea intake (cups)[†]	6 ± 11	4 ± 10	4 ± 8	3 ± 8	<.001

Ca-blockers, Calcium-channel blockers; *CHF*, congestive heart failure during the index hospitalization, *VT*, ventricular tachycardia during the index hospitalization.
**P* values derive from exact tests for binary variables and from ANOVA for continuous variables.
[†]Mean values with standard deviations are shown for continuous variables.
[‡]Household income was derived from zip codes according to 1990 US Census Bureau data.

Table II. Characteristics of 1902 Onset Study participants according to usual weekly cola consumption

	Usual weekly cola consumption				
	0	**>0-2 Cups**	**>2-7 Cups**	**>7 Cups**	***P****
Number	1178	245	264	215	
Age (y)[†]	65 ± 12	59 ± 12	57 ± 12	53 ± 12	<.001
Female (%)	38	19	20	24	<.001
White (%)	92	86	87	86	<.001
BMI (kg/m^2)[†]	26.9 ± 5.8	27.3 ± 4.9	27.7 ± 5.6	28.4 ± 4.6	<.001
Current smoker (%)	28	38	37	52	<.001
Former smoker (%)	43	44	43	27	<.001
Hypertension (%)	47	42	38	37	.004
Diabetes (%)	22	17	16	22	.05

Previous MI (%)	31	28	21	25	.004
Noncardiac comorbidity (%)	15	13	13	15	.61
Regular use of (%)					
Aspirin	32	37	39	32	.06
β-blockers	23	16	15	14	<.001
Ca-blockers	27	18	23	17	<.001
ACE inhibitors	13	9	11	8	.06
Digoxin	9	7	4	7	.04
Diuretics	25	12	11	11	<.001
Lipid therapy	8	7	6	7	.70
Thrombolytic use (%)	33	44	38	40	.007
CHF (%)	17	16	11	8	.002
VT (%)	11	14	16	13	.27
Exertion >/=6 MET >1 weekly (%)	87	72	75	68	<.001
Income ($)[†,‡]	38776 ± 12734	38650 ± 13776	37756 ± 14101	36758 ± 13208	.18
Alcohol abstention (%)	64	43	46	58	<.001
Weekly tea intake (cups)[†]	4 ± 10	4 ± 8	3 ± 7	4 ± 10	.48

*P Values derive from exact tests for binary variables and from ANOVA for continuous variables.

[†]Mean values with standard deviations are shown for continuous variables.

[‡]Household income was derived from zip codes according to 1990 US Census Bureau data.

Table III. Hazard ratios and odds ratios for all-cause mortality after acute myocardial infarction according to usual weekly coffee consumption among Onset Study participants

	Usual weekly coffee consumption				
	0	**>0-7 Cups**	**8-14 Cups**	**>14 Cups**	***P* (trend)**
Number	494	517	290	601	
Deaths (%)	109 (22)	87 (17)	54 (19)	65 (11)	
Deaths within 90 days (%)	38 (8)	23 (4)	10 (3)	8 (1)	
Deaths beyond 90 days (%)	71 (14)	64 (12)	44 (15)	57 (9)	
Mortality rate per 100 person-years	6.27	4.71	4.91	2.80	
Age and sex-adjusted model	1.00	0.77	0.93	0.74	.13
95% CI[†]	Referent	(0.58-1.02)	(0.67-1.29)	(0.54-1.02)	
Full model*	1.00	0.90	1.14	1.13	.38
95% CI	Referent	(0.67-1.21)	(0.81-1.60)	(80-1.60)	
Hazard ratio for deaths within 90 days*	1.00	0.68	0.61	0.38	.01
95% CI	Referent	(0.39-1.18)	(0.30-1.27)	(0.17-0.86)	
Hazard ratio for deaths beyond 90 days*	1.00	1.03	1.39	1.52	.01

95% CI	Referent	(0.72-1.47)	(0.94-2.06)	(1.03-2.26)	

*The full model adjusted for age, sex, previous myocardial infarction, previous angina, hypertension, diabetes, body-mass index, current smoking, former smoking, educational attainment, race, household income, usual frequency of exertion, usual alcohol consumption, use of thrombolytic therapy, use of cardiac medications (aspirin, β-blockers, calcium-channel blockers, angiotensin-converting enzyme inhibitors, digoxin, diuretics, and lipid-lowering agents), and congestive heart failure or ventricular tachycardia during hospitalization.

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