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COFFEE, ALCOHOL AND RISK OF CORONARY HEART DISEASE AMONG JAPANESE MEN LIVING IN HAWAII

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Abstract We examined the relation of coffee and alcohol consumption to the risk of coronary heart disease during a six-year period in a cohort of 7705 Japanese men living in Hawaii. The analysis was based on 294 new cases of coronary heart disease. There was a positive association between coffee intake and risk, but it became statistically insignificant when cigarette smoking was taken into account. There was a strong negative association between moderate alcohol consumption (up to 60 ml per

day), mainly from beer, and the risk of nonfatal myocardial infarction and death from coronary heart disease. This association remained significant in multivariate analysis, taking into account smoking and other risk factors. The correlation of alcohol consumption with the level of α cholesterol (positive) and β cholesterol (negative) may partly account for the observed negative association between alcohol and coronary heart disease. (N Engl J Med 297:405-409, 1977)

THE relation of coffee and alcohol consumption to the risk of coronary heart disease has long been of interest to health professionals and lay people. Recent epidemiologic studies in the United States and other Western countries have shown conflicting results. We have been following a large cohort of Japanese migrants and their descendants living in Hawaii for the development of cardiovascular disease since 1965. In this report the levels of coffee and alcohol consumption recorded at entry examination are related to the incidence of coronary heart disease during a six-year follow-up period.

METHODS

The Honolulu Heart Study is a prospective epidemiologic investigation of coronary heart disease and stroke in a cohort of men of Japanese ancestry, born in the years 1900-1919, and living on the island of Oahu in 1965. Of the 11,148 such men who were located by updating of World War II Selective Service files, 8006 underwent the base-line examination during the period 1965-1968.¹ Of these 8006 men, 301 were found to have definite evidence of coronary heart disease. For the remaining 7705 men, the risk of coronary heart disease during a six-year follow-up period was related to characteristics recorded at the base-line examination. New cases were found by re-examination near the second and sixth anniversary dates, and by comprehensive surveillance of morbidity and mortality based on hospital records, death certificates and autopsy records.² The criteria for diagnosis and classification of coronary heart disease have previously been described.³

Each participant in the base-line examination underwent an interview to obtain a detailed medical and social history, including diet and living habits, as well as a complete physical examination, a battery of laboratory tests and a 12-lead electrocardiogram with the subject resting. We obtained the information on coffee intake as

part of the 24-hour diet-recall interview⁴ by asking the number of 120-ml cups of coffee drunk during the 24 hours before the day of examination. We collected data on alcohol consumption both by the 24-hour diet-recall interview and by asking the "usual" amount of drinking of three kinds of alcoholic beverages (wine, beer and hard liquor) per day or per week (for nondaily drinkers). The latter data were used in this analysis. In calculating the amount of each alcoholic beverage we assumed, using an approximation of 1 oz as being equivalent to 30 ml, that 1 glass of wine contained 120 ml, 1 bottle of beer 360 ml, and 1 drink of hard liquor 45 ml. We calculated the total amount of absolute alcohol consumed per day using conversion rates of 10 per cent for wine, 3.7 per cent for beer, and 38 per cent for hard liquor according to the *United States Department of Agriculture Handbook No. 8*.⁵

Statistical Analysis

We estimated the risk for coronary heart disease in relation to coffee intake (cups per day) and alcohol consumption (milliliters per day) by computation of age-adjusted six-year incidence rates according to the amount of coffee and alcohol consumed. Age-adjustment was done in five-year groups by the direct method according to the age structure of the entire population at risk. We used the multivariate logistic regression computed by the method of Walker and Duncan⁶ both to test the significance of trends in age-adjusted incidence rates of coronary heart disease and to evaluate the independent significance of coffee and alcohol as predictors of risk, taking into account other relevant variables.

RESULTS

During the period from the initial examination to the sixth anniversary date of each study subject, definite coronary heart disease developed in a total of 294 men, including 43 cases of death attributed to coronary heart disease, 136 cases of nonfatal myocardial infarction, 27 cases of acute coronary insufficiency and 88 cases of angina pectoris. In the men who experienced more than one type of coronary heart disease, the first manifestation was used for classification.

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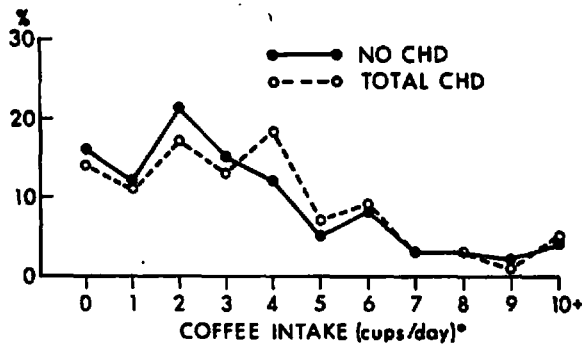


Figure 1. Frequency Distributions of Coffee Intake in Cases of Coronary Heart Disease (CHD) and Noncases.
*Number of 120-ml cups consumed during 24 hours.

Figure 1 shows the frequency distributions of coffee intake in the men in whom coronary heart disease developed and in those who remained free of it. The two distributions were generally similar except that the proportion of men consuming 4 cups per day was somewhat greater in the group with than in the group without coronary heart disease, whereas the reverse was true for the proportion of men consuming 2 cups per day. Table 1 shows the age-adjusted six-year incidence rate of coronary heart disease according to the amount of coffee intake reported at the base-line examination. A statistically significant increase in the rate was noted only for total coronary heart disease (all forms). However, this positive association between coffee and coronary disease was not significant in the multivariate analysis when cigarette smoking was taken into account.

Figure 2 shows the frequency distributions of total alcohol consumption in the groups with and without coronary heart disease. The proportion of nondrinkers was substantially greater in the former (59 per cent) than in the latter (47 per cent) whereas the reverse was true for the proportion of moderate drink-

ers who consumed 11 to 60 ml per day. Heavy drinkers consuming more than 60 ml per day were about equally distributed in the group with (4.5 per cent) and the group without coronary disease (5.5 per cent). Table 2 shows the age-adjusted six-year incidence rate of coronary heart disease according to the amount of total alcohol consumption. Drinkers were divided into quartile groups according to the amount of alcohol consumed per day. There was a definite and statistically significant trend of negative association between alcohol consumption and the total coronary heart disease and myocardial infarction. Similar trends were noted for death from coronary disease and angina pectoris, but they were not statistically

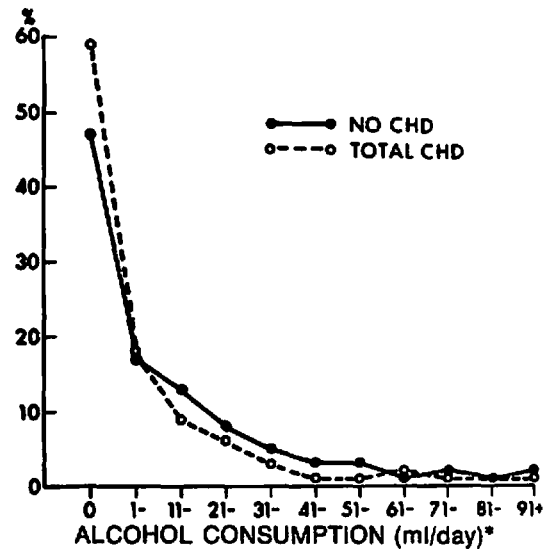


Figure 2. Frequency Distributions of Alcohol Consumption in Cases of Coronary Heart Disease (CHD) and Noncases.
*Sum of absolute alcohol contained in wine, beer and hard liquor consumed per day.

Table 1. Age-Adjusted Six-Year Incidence Rate of Coronary Heart Disease According to Coffee Intake.*

COFFEE INTAKE	MEN AT RISK	INCIDENCE RATE†				
		TOTAL CHD	CHD DEATH	MI	CI	AP
		per 1,000				
cup/day						
0	1,235	32.4	2.4	14.5	2.5	13.0
1-2	2,484	31.7	6.1	17.2	1.7	6.7
3-4	2,068	43.3	6.7	19.7	3.8	13.1
5+	1,918	43.5	6.2	16.9	5.6	14.8
Significance test for trend‡		P<0.05	NS¶	NS	NS	NS

*CHD denotes coronary heart disease, MI nonfatal myocardial infarction, CI acute coronary insufficiency, & AP angina pectoris.

†Age-adjusted in 5-yr groups by the direct method according to the age structure of the entire population at risk.

‡Based on the t values for logistic regression coefficients estimated by the Walker-Duncan method,* taking age into account.

¶Not significant.

significant. In contrast, the incidence of acute coronary insufficiency was appreciably greater in the group of men with the largest alcohol consumption (40 ml or more per day) than in those with smaller consumption or nondrinkers. However, this trend was not statistically significant. Figure 3 shows the trend of inverse relation between alcohol consumption and the risk of coronary heart disease, especially "hard" cases (death and myocardial infarction). As implied by the frequency distribution (Fig. 2), the declining trend of incidence of coronary heart disease was no longer seen beyond the level of alcohol consumption exceeding 60 ml per day. However, there were not enough heavy drinkers in this study cohort to assure the detection of a statistically significant increase or decrease in incidence at the higher levels of alcohol consumption.

To examine the relations of different alcoholic beverages to the risk of coronary heart disease, we com-

Table 2. Age-Adjusted Six-Year Incidence Rate of Coronary Heart Disease According to Alcohol Consumption.*

ALCOHOL CONSUMPTION†	MEN AT RISK	INCIDENCE RATE‡				
		TOTAL CHD	CHD DEATH	MI	CI	AP
ml/day		per 1,000				
0	3,565	46.0	6.8	21.2	2.8	15.2
1-6	1,034	41.2	6.3	22.0	3.2	9.7
7-15	962	30.7	4.2	14.0	3.1	9.4
16-39	1,024	26.7	4.0	15.6	3.0	4.1
40+	1,006	21.2	3.0	4.2	6.6	7.4
Significance test for trend		P<0.001	NS	P<0.001	NS	NS

*Abbreviations and statistical methods as in Table 1.
 †Sum of absolute alcohol contained in wine, beer & hard liquor usually consumed/day, with conversion rates of 0.10, 0.037 & 0.38, respectively.
 ‡Age-adjusted in 5-yr groups by the direct method according to the age structure of the entire population at risk.

puted age-adjusted six-year incidence rates of total coronary disease according to the amount of wine, beer and hard liquor consumed per day. Drinkers of each beverage were divided into two (below-median and above-median consumption) groups. As shown in Table 3, a trend of negative association was noted consistently between the consumption of each beverage and the risk of coronary disease though the trend was statistically significant only for beer. Beer was the most commonly consumed alcoholic beverage, accounting for about two thirds of the total alcohol consumption, whereas wine was the least popular beverage, mainly consumed by elderly men. Very low levels of both wine and hard-liquor consumption indicate that these beverages were drunk only occasionally.

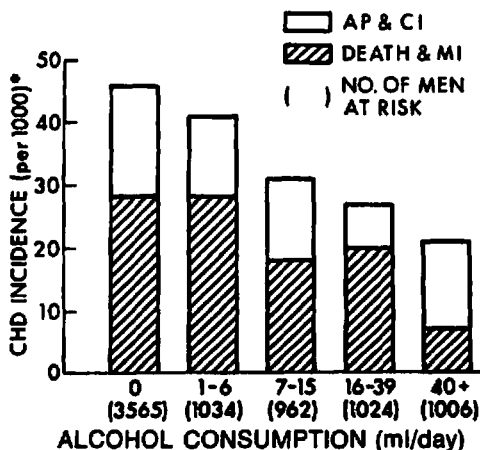


Figure 3. Six-Year Incidence of Coronary Heart Disease According to Alcohol Consumption.

*Age-adjusted in five-year groups by the direct method according to the age structure of the entire population at risk. CHD denotes coronary heart disease, AP angina pectoris, CI acute coronary insufficiency, and MI myocardial infarction.

It is possible that the higher incidence rate in non-drinkers was an artifact due to inclusion of the men who had stopped drinking before the base-line examination because of latent coronary heart disease or coronary-prone health conditions. To rule out this possibility, we computed the age-adjusted six-year incidence rate of total coronary heart disease separately for lifetime teetotalers, ex-drinkers and current drinkers. As shown in Table 4, the incidence was highest for ex-drinkers, lowest for current drinkers and intermediate for lifetime teetotalers. The differences between current drinkers and both ex-drinkers and lifetime teetotalers were statistically significant, whereas no significant difference was found between the latter two groups. Thus, the higher incidence of coronary heart disease in nondrinkers cannot be attributed to the possible existence of latent coronary disease in this group.

Table 3. Age-Adjusted Six-Year Incidence Rate of Total Coronary Heart Disease According to Consumption of Three Alcoholic Beverages.

BEVERAGE	USUAL CONSUMPTION*	MEN AT RISK	INCIDENCE RATE†
			per 1,000
	ml/day		
Wine	0	6,506	40.6
	1	588	27.1
	2+	576	28.9
	Significance test for trend		NS
Beer	0	3,386	45.6
	1-299	2,235	33.9
	300+	2,015	25.9
	Significance test for trend		P<0.001
Hard liquor	0	4,549	41.0
	1-2	1,538	38.1
	3+	1,501	29.1
	Significance test for trend		NS

*Consumption of each beverage without conversion to absolute alcohol.
 †Age-adjusted in 5-yr groups by the direct method according to the age structure of the entire population.

Another possibility is that the observed negative association of alcohol consumption with the risk of coronary heart disease resulted from confounding by other risk factors. Alcohol consumption correlated positively with cigarette smoking ($r = 0.24$), serum uric acid ($r = 0.18$), serum nonfasting triglyceride ($r = 0.09$) and systolic blood pressure ($r = 0.08$), and negatively with serum cholesterol ($r = -0.09$), subscapular skinfold ($r = -0.09$), age ($r = -0.05$) and relative weight ($r = -0.04$). The results of multivariate logistic analysis by the method of Walker and Duncan⁶ indicated that alcohol consumption had a significant negative association with the risk of "hard" cases (death from coronary disease and myocardial infarction), which became stronger when cigarette smoking and other major risk factors were taken into account.

Table 4. Age-Adjusted Six-Year Incidence Rate of Total Coronary Heart Disease According to Drinking Status.

STATUS	MEN AT RISK	CASES	INCIDENCE RATE ^a per 1,000	SIGNIFICANCE TEST FOR DIFFERENCE [†]
Never (A)	2,744	121	43.6	A vs B [‡]
Past (B)	821	47	55.7	B vs C [§]
Current (C)	4,026	119	30.0	C vs A [§]

^aAge-adjusted in 5-yr groups by the direct method according to the age structure of the entire population at risk.

[†]Based on the chi-square values with 1 degree of freedom.

[‡]Not significant.

[§]P<0.01.

DISCUSSION

Recent epidemiologic investigations of the relation between coffee intake and the risk of coronary heart disease have shown inconsistent results. The Boston Collaborative Drug Surveillance Program^{7,8} and Paul et al.⁹ reported a positive association of coffee intake with the disease, but other studies based on both case-control^{10,11} and prospective¹²⁻¹⁶ data failed to show a statistically significant association between coffee and coronary heart disease when cigarette smoking and other risk factors were taken into account. Our results are in accord with those in the latter reports. The positive association between coffee intake and the risk of total coronary heart disease can be accounted for by a significant correlation ($r = 0.25$) between coffee consumption and cigarette smoking, a strong risk factor in our study.³

The relation of alcohol consumption to coronary heart disease has also been a controversial matter. No statistically significant association was found between the two in several epidemiologic studies.^{9,17-20} On the other hand, a significant positive association between excessive drinking and an increased risk was reported by others.^{16,21-23} Three studies have shown a significant negative association between alcohol and coronary heart disease that could not be accounted for by smoking or other confounding variables.²⁴⁻²⁶

The present prospective study provides additional evidence for the negative association of alcohol consumption with the risk of coronary heart disease. This association was particularly strong with "hard" cases (death and myocardial infarction), it was observed in the range of moderate consumption rather than heavy drinking, and it was independent of confounding effects of the major risk factors. Although the conflicting reports in the literature have dealt with white populations, disagreement has also been noted in data from cross-sectional studies of Japanese men living in Hawaii (subsample of the present cohort) and in California. The mean alcohol consumption was significantly lower in cases of coronary heart disease than in the probability sample of those free of such disease among Japanese men living in Hawaii, whereas the reverse was true in those living in California (unpublished data). Although these inconsistent findings may suggest the possibility that the observed negative

association between alcohol and coronary heart disease is due not to the protective effect of alcohol per se but to some unmeasured characteristics (e.g., constitutional, psychologic or behavioral) of the men who drink, there is evidence against this explanation. In the first place not only was the incidence of coronary heart disease lower in drinkers than in nondrinkers, but also there was a decreasing gradient in the incidence with increasing consumption of alcohol. This finding is consistent with a possible direct beneficial effect of alcohol intake on the risk of coronary heart disease. Secondly, we observed this dose-response relation in the range of moderate consumption, so that physiologic and psychologic factors associated with heavy drinking habits are unlikely to have been involved. Thirdly, incidence of the disease was relatively high in ex-drinkers as well as in lifetime teetotalers. This finding also lends more support to the direct effect than to the selection-bias hypothesis.

The varying relations of alcohol consumption to different manifestations of coronary heart disease in the present study are not easy to explain. However, the weaker association of alcohol consumption with angina pectoris than with "hard" cases of coronary heart disease is consistent with the findings in an autopsy series of the Honolulu Heart Study cohort (unpublished data). Among the 226 autopsied cases, alcohol consumption reported at the base-line examination was distinctly lower in those with myocardial infarction than in those without it. On the other hand, the negative association between alcohol and the severity of coronary atherosclerosis, assessed independently of the evidence for myocardial infarction, was weaker and statistically not significant. The positive association, though not statistically significant, between alcohol and acute coronary insufficiency may have been due to sampling variation because of the small number of cases. It is interesting that out of the 11 patients with angina pectoris or coronary insufficiency as first manifestation who subsequently had myocardial infarction or sudden death from coronary heart disease, eight were lifetime teetotalers, and two consumed less than 5 ml of alcohol per day. This observation might suggest that alcohol has no relation to the process of atherosclerosis, but protects against the precipitation of myocardial infarction or coronary occlusion.

Regarding the mechanism of the negative association between alcohol and coronary heart disease, cirrhosis of the liver, rather than alcohol per se, was previously claimed to be primarily responsible for prevention or reduction of the process of atherosclerosis.²⁷ In the present study population, however, the level of alcohol drinking was rather modest in the light of the worldwide literature-survey data.²⁸ Nearly half the drinkers consumed less than 15 ml of absolute alcohol (roughly equivalent to 1 bottle of beer or 1 drink of whisky) daily, and only 3 per cent of them consumed 90 ml or more per day. Thus, it is unlikely that the lower risk of coronary heart disease among drink-

ers in this population can be attributed to gross hepatic dysfunction resulting from excessive intake of alcohol. This inference is substantiated by the fact that in the previously mentioned autopsy series from this study population, the negative association of alcohol consumption with myocardial infarction remained statistically significant even when all deaths from causes closely related to excessive alcohol consumption were excluded (unpublished data).

Alcohol intake has been known to have a substantial effect on lipid metabolism, especially triglyceride levels.²⁹⁻³¹ In the present study alcohol consumption was weakly correlated with levels of serum total cholesterol ($r = -0.09$) and nonfasting triglyceride ($r = 0.09$), but neither of these blood lipids could account for the negative association between alcohol and coronary heart disease. There are interesting data, however, to shed further light on the relation of alcohol and blood lipids to coronary heart disease. Thus, in a cross-sectional study of a probability sample taken from this study cohort, alcohol consumption was found to correlate more strongly with both α (high-density-lipoprotein) cholesterol ($r = 0.28$) and β (low-density-lipoprotein) cholesterol ($r = -0.24$) than with either total cholesterol ($r = -0.12$) or fasting triglyceride ($r = 0.11$). Strong associations of these two cholesterol fractions with the risk of coronary heart disease, operating independently and in opposite directions, have previously been reported from this study.³² It appears possible that the correlation of alcohol consumption with levels of α cholesterol (positive) and β cholesterol (negative) may partly account for the negative association between alcohol and coronary heart disease.

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