Alcohol intake, drinking patterns, and risk of nonfatal acute myocardial infarction in Costa Rica[1–3]

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ABSTRACT

Background: Moderate alcohol consumption is associated with a lower risk of myocardial infarction (MI). Whether alcohol is truly protective or whether the amount, type, or pattern of intake is the most important is still under debate.

Objective: The purpose of this study was to determine whether alcohol intake and drinking patterns are associated with plasma lipids and the risk of MI in Costa Ricans, a population with a low intake of wine.

Design: We conducted a study of 2090 cases of a first nonfatal acute MI and 2090 population-based controls matched by age, sex, and residence in Costa Rica, a country with diet and lifestyles different from those of Western countries. Alcohol and dietary intakes were assessed by using validated questionnaires.

Results: In a multivariate conditional regression model that controlled for other cardiovascular disease risk factors, the lowest risk of MI [odds ratio (OR) = 0.44; 95% CI: 0.31, 0.61] was observed for those who drank on average 3 drinks/wk (compared with lifelong abstainers). When we looked at the frequency of consumption, we found that the risk of MI among daily drinkers (OR = 0.64; 95% CI: 0.41, 1.01) was not significantly different ($P = 0.23$) from that of weekend drinkers (OR = 0.76; 95% CI: 0.59, 0.98) regardless of the amount consumed. HDL cholesterol increased with the amount and frequency of alcohol intake. Similar to a few other populations, apparent protection was observed at very low alcohol intakes.

Conclusion: Low to moderate consumption of alcohol 1–2 d/wk is independently associated with a reduced risk of MI. *Am J Clin Nutr* 2005;82:1336–45.

KEY WORDS Myocardial infarction, coronary heart disease, CHD, alcohol, patterns, HDL, cholesterol, Costa Rica

INTRODUCTION

Moderate consumption of alcohol in developed countries has been associated with a reduced risk of myocardial infarction (MI) (1–3). This evident protection is thought to be due to improved plasma lipid profiles, particularly an increase in HDL cholesterol (4–6), increased adiponectin (7), reduced plasma fibrinogen (8), viscosity (9), platelet activity (10, 11), C-reactive protein (8, 12), and improved insulin sensitivity (13). However, the protective effect of alcohol is not uniform across sex and populations or socioeconomic classes (14, 15), which raises doubts as to whether alcohol per se is truly protective or instead is a marker for another protective factor associated with alcohol consumption (4). Others have suggested that certain types of alcohol, eg, wine, may be more protective than others (16–18).

Growing evidence (2, 6, 14) suggests that the amount and pattern of intake, rather than the type of alcohol (19, 20), are more important in explaining the effects of alcohol in populations. Other studies suggest that sex (14) and genetic diversity of alcohol users (6, 21) may also play an important role in explaining the observed protection and differences across studies. For instance, in a recent prospective study, alcohol was inversely related to MI in white Americans but was hazardous for hypertension and MI in African Americans (14, 22). These disparities could be due to differences in alcohol intake patterns or the prevalence of functional genetic polymorphisms in genes encoding alcohol-metabolizing enzymes that have been reported across races (23–26). Polymorphisms in the alcohol dehydrogenase gene have been associated with changes in both HDL cholesterol and risk of MI in moderate drinkers (6). Apart from one multicountry study (3) in which consumption of alcohol was marginally associated with a reduced risk of MI, to date, no large case-control studies have investigated the association between alcohol intake, patterns, and risk of MI in developing countries where diet and lifestyles differ from those in Western cultures.

We conducted a large ($n = 4548$), matched, incident case-control study of residents of the Central Valley of Costa Rica, a country with low wine intake, to determine whether alcohol users, compared with self-reported lifelong abstainers, are less likely to have an MI. We also determined whether the pattern of alcohol drinking is associated with the risk of MI or intermediate phenotypes such as plasma lipid concentrations.

SUBJECTS AND METHODS

Study population

All subjects were Hispanic Americans who lived in the Central Valley of Costa Rica between 1994 and 2004. The details of the study design are published elsewhere (27–29). Briefly, eligible cases were men and women who were determined to be survivors

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of a first acute MI by 2 independent cardiologists at any of the 6 recruiting hospitals in the catchment area. To achieve 100% ascertainment, fieldworkers visited the 6 hospitals daily. All cases met the World Health Organization criteria for MI, which require typical symptoms plus either elevations in cardiac enzyme concentrations or diagnostic changes on an electrocardiogram (30). Cases were ineligible if they *1*) died during hospitalization, *2*) were 75 y or older on the day of their first MI, or *3*) were physically or mentally unable to answer the questionnaire. Enrollment was carried out while the cases were in the hospital's step-down unit. Cases were matched by age (±5 y), sex, and area of residence to population control subjects who were randomly identified with the aid of data from the National Census and Statistics Bureau of Costa Rica. Because of the comprehensive social services provided in Costa Rica, all persons living in the catchment area had access to medical care without regard to income. Therefore, the control subjects came from the source population that gave rise to the cases and were not likely to have had undiagnosed cardiovascular disease because of poor access to medical care. Control subjects were ineligible if they had ever had an MI or if they were physically or mentally unable to complete the questionnaires. After enrollment of cases at the hospital step-down unit, all cases and controls were visited at their homes for the collection of dietary and health information, anthropometric measurements, and biological specimens. Participation was 98% for cases and 88% for controls. All subjects gave informed consent on documents approved by the Human Subjects Committee of the Harvard School of Public Health and the University of Costa Rica. To avoid the potential for recall bias among the cases, data were collected as close to the diagnosis of MI as possible. Data collection was completed within 2 wk of discharge from the hospital for 73% of the cases.

Data collection

Sociodemographic characteristics, smoking status, socioeconomic status, physical activity, and medical history data were collected during the in-home interview. Each subject provided a fasting blood sample for assessment of plasma lipids (28, 29). Blood was collected from cases after the MI. We collected dietary data by using a semi-quantitative food-frequency questionnaire (FFQ) that was developed and validated specifically to assess nutrient intake in the Costa Rican population (28, 31). In addition to foods, the FFQ assessed the frequency of intake of the 5 commonly consumed alcoholic beverages: beer, rum, whiskey, vodka, and wine. We estimated the amount of alcohol consumed per day by multiplying the number of servings per day by the amount of alcohol per serving, which was 12.8 g for beer, 14 g for liquor, and 11 g for wine. We estimated the number of drinks per day by dividing the total amount of alcohol consumed per day by 14, the amount of absolute alcohol in a standard drink (32). In addition to the FFQ, alcohol intake and patterns were assessed with the use of another questionnaire that also assessed potential confounders.

Statistical analysis

SAS software version 8.00 (SAS Institute Inc, Cary, NC) was used for all statistical analyses, and all *P* values presented are two-tailed. Individuals who had missing values for major confounders ($n = 308$, or 6.8% of the total study population) and those whose alcohol intake on the FFQ was not consistent with alcohol intake status on the general questionnaire ($n = 60$, or 1.3%) were excluded. This left 2090 cases and 2090 matched controls for the final analysis of alcohol intake. Analyses on amount and type of alcohol consumed had a total of 4180 matched cases and controls, but because of missing data, analyses on patterns of alcohol intake had 3864 subjects and analyses that used the number of drinking days had 3298 subjects.

Individual nutrients were correlated with total energy intake and were thus adjusted for total energy from sources other than alcohol as described elsewhere (28, 33). We also estimated the amount of energy consumed as fat and expressed this as a percentage of daily energy intakes from sources other than alcohol. The distribution of potential confounders by case-control status and alcohol intake was assessed with the use of the paired *t* test, Wilcoxon's signed-rank test, or analysis of variance for continuous variables or with the use of the chi-square test or Cochran-Armitage test for trend for categorical variables.

Lifelong abstainers were those subjects who reported zero alcohol consumption on the FFQ and no alcohol use in their lifetime on the general questionnaire. We assessed the possibility of an association between alcohol intake and MI by sequentially adding potential confounders to the model and then assessing their effect on point estimates and model fit. Because missing data on the pattern of alcohol intake caused case-control pairs to be broken, we used unconditional logistic regression that included matching variables and potential confounders in the models to investigate the association between patterns of alcohol intake and MI. In these analyses, we compared weekend drinkers (1–2 d/wk), daily drinkers, and those with no regular drinking pattern with lifelong abstainers. We also examined drinking patterns in terms of the number of drinking days per week by comparing past drinkers and current drinkers (drinking 1–2 d/wk, 3–5 d/wk, and 6–7 d/wk) with lifelong abstainers. We explored whether drinking patterns were independent of alcohol intake by further adjusting the odds ratios for alcohol patterns by the amount of alcohol consumed per day.

We performed subgroup analyses to explore further the effects of potential confounders such as smoking, sex, area of residence, and folate intake. Folate was included because it has a known biological interaction with alcohol intake and may protect against MI (34, 35). In these analyses, we used unconditional logistic regression with matching variables and potential confounders in the model. In all unconditional analyses, we computed the Hosmer-Lemeshow statistic to test for the goodness-of-fit of the models. We also investigated the relation between alcohol intake and MI after stratifying the drinkers into those drinking ≤ 3 or >3 d/wk or those drinking on weekends only versus daily drinkers.

To test whether the observed effects of alcohol were mediated by changes in plasma lipids, we performed multivariate linear regression analyses with lipids as outcomes and categories of alcohol intake or pattern as the independent variable. These analyses were restricted to the controls because blood from cases was obtained after the MI. The lipids assessed were triacylglycerol, LDL cholesterol, HDL cholesterol, and total cholesterol. Because of their potential effects on plasma lipids, we adjusted the lipid means for the following covariates: smoking, physical activity, abdominal obesity, sex, age, income, history of diabetes, history of hypertension, and intakes of saturated fat, polyunsaturated fats, *trans* fat, and dietary cholesterol.

TABLE 1
Characteristics of myocardial infarction cases and population-based controls in Costa Rica[1]

Variable	Controls ($n = 2090$)	Cases ($n = 2090$)	P
Age (y)[2]	58.2 ± 11.3[3]	58.5 ± 11.0	N/A
Women (%)[2]	27	27	N/A
Living in rural area (%)[2]	26	26	N/A
History of diabetes (%)	14	25	< 0.0001
History of hypertension (%)	29	38	< 0.0001
Current smoker (%)	21	40	< 0.0001
Smoking intensity (cigarettes/d)	4.6 ± 9.1	11.9 ± 15.3	< 0.0001
Current drinker (%)	53	49	0.01
BMI (kg/m^2)	26.4 ± 4.2	25.9 ± 4.0	0.0001
Abdominal obesity[4]	0.95 ± 0.07	0.97 ± 0.07	< 0.0001
Physical activity (MET)	1.56 ± 0.69	1.51 ± 0.69	0.001
Formal education (y)	7.6 ± 5.3	7.1 ± 5.4	0.001
Household income (US$)	570 ± 428	497 ± 391	< 0.0001
Total cholesterol (mmol/L)	4.86 ± 1.01	4.37 ± 1.03	< 0.0001
LDL cholesterol (mmol/L)	2.82 ± 0.88	2.41 ± 0.88	< 0.0001
HDL cholesterol (mmol/L)	1.32 ± 0.31	1.16 ± 0.28	< 0.0001
Triacylglycerol (mmol/L)	1.69 ± 1.10	1.80 ± 1.04	< 0.0001
Daily dietary intake			
Energy (kcal)	2447 ± 767	2700 ± 943	< 0.0001
Animal fat (% of energy)	13.0 ± 4.7	14.4 ± 5.4	< 0.0001
Vegetable fat (% of energy)	19.4 ± 5.1	18.5 ± 4.7	< 0.0001
Saturated fat (% of energy)	11.7 ± 2.9	12.4 ± 3.1	< 0.0001
Polyunsaturated fat (% of energy)	7.1 ± 2.3	6.8 ± 2.3	< 0.0001
trans Fat (% of energy)	1.33 ± 0.65	1.36 ± 0.65	0.13
Cholesterol (mg/1000 kcal)	120 ± 53	129 ± 60	< 0.0001
Carbohydrate (% of energy)	56 ± 7	55 ± 7	< 0.0001
Protein (% of energy)	13.2 ± 2.1	13.4 ± 2.2	0.0003
Fiber (g/d)[5]	24.6 ± 6.0	23.7 ± 6.1	< 0.0001
Folate (μg/d)[5]	431 ± 112	422 ± 117	0.004

[1] MET, metabolic equivalents. P obtained from paired t test or Wilcoxon signed-rank test for continuous variables or McNemars test for categorical variables.
[2] Matching variable.
[3] $\bar{x}$ ± SD (all such values).
[4] Same as waist-to-hip ratio.
[5] Energy-adjusted by using the residual method.

RESULTS

Characteristics of the study population

The characteristics of the cases and controls are shown in **Table 1**. The proportion of current drinkers was significantly higher ($P = 0.01$) for the controls (53%) than the cases (49%). Cases were more likely to smoke, to have abdominal obesity, to have a history of diabetes or hypertension, and to consume a diet high in total energy and animal fat but low in dietary fiber. The body mass index of the cases was lower than that of the controls, possibly because the cases lost weight after their MI. However, body mass index in older populations is difficult to interpret because the conversion of muscle mass to fat mass can lead to an apparent loss in body weight but a gain in fat mass or central adiposity (36). Abdominal obesity was higher in the cases. The general characteristics of the control and MI case populations by alcohol intake status are shown in **Table 2**. Persons in the higher categories of alcohol intake were younger, were mainly male, lived in urban areas, were more likely to smoke, were more educated and physically active, and were less likely to have a history of diabetes or hypertension.

Beer was the most preferred beverage (data not shown). In cases and controls, respectively, 26% and 30% consumed beer, whereas 5.1% and 7.5% consumed wine. The proportion consuming liquor was similar for the cases (13%) and controls (13%). The median (minimum–maximum) alcohol intake in current drinkers was 6.0 (0–246) g/d for cases and 5.5 (0–174) g/d for controls. Most current drinkers consumed <14 g/d (71% of cases and 76% of controls). The proportion of current drinkers consuming up to 28 g/d was 85% in cases and 89% in controls, and 91% and 94%, respectively, for those consuming up to 42 g/d.

The distribution of potential dietary confounders by category of alcohol use is shown in **Table 3**. Except for total energy intake, which increased with increased alcohol intake, no distinct confounding patterns were detected.

Alcohol intake from various beverages according to drinking pattern is shown in **Table 4**. Except for individuals consuming ≥15 g alcohol/d, where most alcohol was consumed as liquor, the mean amount of alcohol from beer was similar to that from liquor. In controls who were current drinkers, 25% reported binge drinking (>5 drinks on a typical drinking day) and 12%

TABLE 2
Characteristics of population-based controls ($n = 2090$) and myocardial infarction cases ($n = 2090$) by categories of alcohol intake in Costa Rica[1]

	Alcohol intake category[2]							
Variable	Never drinker	Past drinker	<4.9 g/d	5.0–9.9 g/d	10.0–14.9 g/d	15.0–29.9 g/d	>30 g/d	P^3
n								
Controls	426	559	523	200	147	114	121	
Cases	445	625	475	125	148	118	154	
Women (%)								
Controls	67	14	28	10	7	6	0	< 0.0001
Cases	67	15	24	15	9	5	4	< 0.0001
Living in urban area (%)								
Controls	71	72	75	76	75	80	77	0.003
Cases	73	73	76	71	73	68	78	0.17
History of diabetes (%)								
Controls	19	14	13	11	10	10	10	< 0.0001
Cases	35	23	25	14	19	13	15	< 0.0001
History of hypertension (%)								
Controls	40	25	27	27	21	25	24	< 0.0001
Cases	52	32	38	33	39	33	28	< 0.0001
Secondary education (%)								
Controls	33	31	43	50	51	55	42	< 0.0001
Cases	28	33	45	46	49	45	28	< 0.0001
Current smoker (%)								
Controls	7	21	18	27	34	30	43	< 0.0001
Cases	21	45	32	46	60	45	59	< 0.0001
Smoking intensity (cigarettes/d)								
Controls	3.3 ± 6.7[4]	1.5 ± 7.4	1.0 ± 11	0.9 ± 8.1	3.6 ± 11	1.8 ± 8.2	7.1 ± 9.7	0.001
Cases	12 ± 14	12 ± 17	8 ± 13	13 ± 16	13 ± 15	10 ± 15	14 ± 16	< 0.0001
Age (y)								
Controls	61 ± 12	60 ± 10	57 ± 11	56 ± 11	55 ± 11	55 ± 10	53 ± 11	< 0.0001
Cases	62 ± 11	60 ± 10	59 ± 11	56 ± 11	54 ± 12	54 ± 10	52 ± 11	< 0.0001
BMI (kg/m^2)								
Controls	27 ± 4.7	26 ± 4.0	26 ± 4.3	27 ± 4.1	26 ± 3.8	26 ± 4.1	26 ± 4.2	0.01
Cases	27 ± 4.7	26 ± 3.9	26 ± 3.9	25 ± 3.7	26 ± 3.7	26 ± 3.2	25 ± 3.8	0.001
Abdominal obesity[5]								
Controls	0.91 ± 0.08	0.96 ± 0.07	0.95 ± 0.08	0.97 ± 0.07	0.98 ± 0.06	0.97 ± 0.06	0.99 ± 0.05	< 0.0001
Cases	0.93 ± 0.08	0.98 ± 0.07	0.97 ± 0.07	0.97 ± 0.07	0.98 ± 0.06	1.00 ± 0.06	0.99 ± 0.05	< 0.0001
Physical activity (MET)								
Controls	1.52 ± 0.66	1.60 ± 0.72	1.52 ± 0.61	1.50 ± 0.65	1.60 ± 0.72	1.65 ± 0.76	1.71 ± 0.93	0.001
Cases	1.44 ± 0.59	1.52 ± 0.68	1.47 ± 0.61	1.56 ± 0.75	1.53 ± 0.73	1.65 ± 0.82	1.60 ± 0.99	0.0001
Monthly household income (US$)								
Controls	519 ± 383	456 ± 338	577 ± 426	685 ± 458	642 ± 501	709 ± 505	672 ± 488	< 0.0001
Cases	445 ± 362	443 ± 362	542 ± 400	588 ± 433	559 ± 388	542 ± 414	541 ± 432	< 0.0001

[1] Means and proportions are age-adjusted. MET, metabolic equivalents.
[2] A standard drink is defined as 14 g alcohol.
[3] For categorical variables, Cochran-Armitage test for trend; for continuous variables, one-way ANOVA.
[4] $\bar{x} \pm$ SD (all such values).
[5] Same as waist-to-hip ratio.

drank >10 drinks on a typical drinking day in the previous year (data not shown). Most controls who were alcohol users reported no significant changes in their alcohol intake in the past 10 y. Except for heavy drinkers (≥30 g/d), most people reported drinking on 1–2 d/wk and these days were mainly on weekends.

Alcohol intake and myocardial infarction

Although the overall chi-square test for association was significant for all models, the *P* for trend was not significant for multivariate models 1 and 2 (**Table 5**). After adjustment for dietary and nondietary confounders, a significant trend in odds ratios was detected (*P* for linear trend = 0.02). In the analyses adjusted for smoking (Table 5), consumption of ≤14.9 g alcohol/d was significantly ($P < 0.05$) inversely associated with the risk of MI. A nonsignificant ($P > 0.05$) inverse association with MI was still evident at higher levels of consumption. In multivariate-adjusted analyses, individuals who consumed as little as one half a drink per week were less likely to have an MI than were lifelong abstainers. However, the strongest inverse association was observed in those who consumed 3 drinks weekly. For instance, in a multiple comparison of odds ratios (multivariate model 4) with the Bonferroni correction, the risk of MI in those who consumed 3 drinks/wk was significantly ($P <$ 0.0001) less than that of those who consumed 0.5 drinks/wk.

TABLE 3
Potential dietary confounders in population-based controls ($n = 2090$) and myocardial infarction cases ($n = 2090$) by categories of alcohol intake in Costa Rica[1]

	Alcohol intake category							
Daily intakes	Never drinker	Past drinker	<4.9 g/d	5.0–9.9 g/d	10.0–14.9 g/d	15.0–29.9 g/d	>30 g/d	P^2
n								
Controls	426	559	523	200	147	114	121	—
Cases	445	625	475	125	148	118	154	—
Total energy (kcal)								
Controls	1993 ± 747[3]	2244 ± 744	2351 ± 680	2526 ± 689	2589 ± 722	2596 ± 742	2855 ± 990	< 0.0001
Cases	2236 ± 818	2432 ± 890	2517 ± 830	2788 ± 766	2530 ± 932	2581 ± 914	2764 ± 1233	< 0.0001
Energy, nonalcohol sources (kcal)								
Controls	2226 ± 747	2418 ± 744	2435 ± 679	2440 ± 688	2515 ± 721	2455 ± 737	2650 ± 942	< 0.0001
Cases	2385 ± 818	2714 ± 890	2596 ± 830	2733 ± 766	2722 ± 932	2842 ± 914	2836 ± 1233	< 0.0001
Total fat (% of energy)								
Controls	32 ± 6	32 ± 6	32 ± 6	33 ± 6	34 ± 6	34 ± 6	33 ± 6	< 0.0001
Cases	32 ± 5	33 ± 6	33 ± 6	35 ± 6	34 ± 6	35 ± 6	34 ± 7	< 0.0001
Saturated fat (% of energy)								
Controls	11 ± 3	10 ± 3	10 ± 3	11 ± 3	11 ± 3	11 ± 2	10 ± 3	< 0.0001
Cases	11 ± 3	11 ± 3	11 ± 3	12 ± 3	11 ± 3	12 ± 3	11 ± 3	< 0.0001
Monounsaturated fat (% of energy)								
Controls	12 ± 4	11 ± 4	12 ± 5	13 ± 4	13 ± 4	13 ± 4	12 ± 4	0.0004
Cases	11 ± 3	12 ± 3	12 ± 4	14 ± 5	13 ± 4	13 ± 4	13 ± 4	< 0.0001
Polyunsaturated fat (% of energy)								
Controls	6 ± 2	6 ± 2	6 ± 2	6 ± 2	7 ± 2	7 ± 2	6 ± 2	< 0.0001
Cases	6 ± 2	6 ± 2	6 ± 2	6 ± 2	6 ± 2	6 ± 2	6 ± 3	0.01
trans Fat (% of energy)								
Controls	1.30 ± 0.63	1.35 ± 0.70	1.30 ± 0.62	1.38 ± 0.65	1.41 ± 0.63	1.38 ± 0.64	1.37 ± 0.62	0.24
Cases	1.38 ± 0.67	1.31 ± 0.61	1.40 ± 0.65	1.32 ± 0.65	1.42 ± 0.70	1.33 ± 0.58	1.32 ± 0.69	0.31
Cholesterol (mg/1000 kcal)								
Controls	113 ± 50	117 ± 54	117 ± 51	126 ± 51	132 ± 52	129 ± 59	126 ± 52	< 0.0001
Cases	118 ± 51	133 ± 64	128 ± 64	123 ± 46	133 ± 53	132 ± 53	146 ± 66	< 0.0001
Carbohydrate (% of energy)								
Controls	57 ± 7	57 ± 7	57 ± 7	55 ± 7	54 ± 6	54 ± 6	56 ± 8	< 0.0001
Cases	56 ± 7	56 ± 7	55 ± 7	54 ± 7	54 ± 7	53 ± 7	54 ± 8	< 0.0001
Protein (% of energy)								
Controls	13 ± 2	13 ± 2	13 ± 2	13 ± 2	14 ± 2	14 ± 2	13 ± 2	< 0.0001
Cases	14 ± 2	13 ± 2	13 ± 2	13 ± 2	14 ± 2	14 ± 2	13 ± 2	0.09
Fiber (g)[4]								
Controls	25 ± 6	25 ± 6	25 ± 6	24 ± 5	24 ± 6	24 ± 6	25 ± 6	0.001
Cases	25 ± 6	23 ± 6	24 ± 6	24 ± 6	24 ± 6	24 ± 6	23 ± 6	0.002
Folate (μg)[4]								
Controls	432 ± 113	429 ± 118	436 ± 108	419 ± 102	427 ± 109	434 ± 118	436 ± 102	0.33
Cases	432 ± 117	416 ± 118	412 ± 110	417 ± 118	418 ± 112	460 ± 120	437 ± 125	0.004
Thiamine (mg)[4]								
Controls	1.81 ± 0.30	1.81 ± 0.30	1.82 ± 0.28	1.81 ± 0.24	1.82 ± 0.31	1.82 ± 0.30	1.78 ± 0.28	0.94
Cases	1.82 ± 0.30	1.80 ± 0.29	1.79 ± 0.30	1.79 ± 0.27	1.79 ± 0.29	1.87 ± 0.29	1.77 ± 0.30	0.27
Vitamin B-6 (mg)[4]								
Controls	2.33 ± 0.56	2.27 ± 0.89	2.35 ± 0.60	2.28 ± 0.49	2.31 ± 0.47	2.38 ± 0.56	2.44 ± 0.60	0.38
Cases	2.35 ± 0.60	2.21 ± 0.56	2.25 ± 0.54	2.21 ± 0.54	2.29 ± 0.57	2.28 ± 0.45	2.31 ± 0.57	0.001
Vitamin B-12 (μg)[4]								
Controls	5.4 ± 3.6	5.5 ± 3.9	5.4 ± 3.5	5.6 ± 3.3	6.0 ± 3.5	6.7 ± 3.8	6.2 ± 4.1	0.001
Cases	6.2 ± 4.3	5.9 ± 3.9	5.6 ± 3.5	6.2 ± 4.4	6.4 ± 3.8	6.5 ± 4.3	6.5 ± 4.5	0.004
Vitamin E (mg)[4]								
Controls	9.1 ± 3.6	8.9 ± 3.7	9.8 ± 3.9	9.8 ± 3.8	9.7 ± 3.6	9.9 ± 3.6	9.6 ± 3.9	0.001
Cases	8.9 ± 3.3	8.6 ± 3.3	9.3 ± 3.5	9.6 ± 4.0	9.2 ± 3.4	9.2 ± 3.6	8.7 ± 3.2	0.001

[1] Means and proportions are age-adjusted.
[2] One-way ANOVA.
[3] $\bar{x} \pm$ SD (all such values).
[4] Nutrients are adjusted for intake of total energy from nonalcohol sources and do not include supplements.

TABLE 4
Alcohol intake patterns among population-based controls and myocardial infarction cases who are current drinkers in Costa Rica[1]

	Alcohol intake (g/d)[2]				
	<4.9	5.0–9.9	10.0–14.9	15.0–29.9	≥30.0
n					
Controls	523	200	147	114	121
Cases	475	125	148	118	154
Mean maximum no. of drinks/d					
Controls	1.4 ± 4.8[3]	3.3 ± 4.2	6.1 ± 6.6	3.6 ± 5.8	8.6 ± 8.7
Cases	2.5 ± 5.5	3.0 ± 4.8	2.6 ± 5.8	3.7 ± 5.3	12 ± 9.3
Alcohol from beer (g/d)					
Controls	0.5 ± 0.7	3.0 ± 2.5	5.3 ± 4.9	6.9 ± 4.5	15 ± 22
Cases	0.4 ± 0.7	2.9 ± 2.6	5.3 ± 5.0	7.0 ± 4.2	20 ± 25
Alcohol from liquor (rum, whiskey, or vodka) (g/d)					
Controls	0.4 ± 0.8	3.2 ± 2.8	6.4 ± 5.2	12 ± 5.0	36 ± 31
Cases	0.5 ± 0.8	3.4 ± 2.8	6.2 ± 5.1	13 ± 5.3	41 ± 31
Alcohol from wine (g/d)					
Controls	0.2 ± 0.6	0.3 ± 0.9	0.7 ± 2.2	1.2 ± 2.8	1.3 ± 5.4
Cases	0.1 ± 0.4	0.3 ± 0.9	0.7 ± 2.4	0.6 ± 1.6	0.9 ± 5.9
Duration of alcohol use (y)					
Controls	53 ± 13	52 ± 12	59 ± 12	49 ± 11	52 ± 12
Cases	53 ± 13	50 ± 12	52 ± 13	52 ± 11	43 ± 12
Drinks on 1–2 d/wk (%)					
Controls	85	86	62	47	23
Cases	94	83	71	62	22
Drinks on 3–5 d/wk (%)					
Controls	5	12	23	29	14
Cases	4	14	17	19	19
Drinks on 6–7 d/wk (%)					
Controls	10	2	14	24	63
Cases	2	4	12	19	59
Daily drinker (%)					
Controls	1	1	17	25	61
Cases	0.4	0.9	14	20	59
Weekend drinker (%)					
Controls	33	71	61	52	28
Cases	34	69	66	61	25
No regular drinking pattern (%)					
Controls	66	28	22	23	11
Cases	65	30	20	19	16
Alcohol intake increased in the past 10 y (%)					
Controls	9	9	13	18	23
Cases	6	12	16	25	37

[1] Means and proportions are age-adjusted.
[2] A standard drink is defined as 14 g alcohol.
[3] $\bar{x}$ ± SD (all such values).

Although an inverse association was still evident for individuals in the categories above 10 g/d, the magnitude of the association was not as strong as that observed for those consuming 5.0–9.9 g/d.

The association between alcohol drinking patterns and the risk of MI in analyses adjusted for cardiovascular disease risk factors and alcohol intake is shown in **Table 6**. The risk of MI in daily drinkers was 0.64 (95% CI: 0.41, 1.01), whereas it was 0.76 (95% CI: 0.59, 0.98) for weekend drinkers. In a direct comparison with weekend drinkers as the reference group, the risk of MI in daily drinkers was 0.84 (95% CI: 0.56, 1.26; $P = 0.23$), which suggests that the 2 groups did not differ significantly with regard to their risk of MI.

We performed stratified analyses to determine whether the association between alcohol and MI was independent of selected confounders such as smoking and intake of folate. The results of these analyses were similar to those of the conditional analyses in Table 5 (data not shown).

We explored whether the observed inverse association of alcohol was through its effect on plasma lipids as suggested by others (5, 6). Mean HDL-cholesterol concentrations in controls across alcohol intake amounts and patterns are shown **Figure 1** and **Figure 2**, respectively. Plasma HDL-cholesterol concentrations increased significantly ($P = 0.01$) with increasing alcohol intake. Triacylglycerol also increased with an increase in alcohol intake and pattern but the differences were not as remarkable as

TABLE 5
Alcohol intake and risk of nonfatal acute myocardial infarction in Costa Rica[1]

Variable	Never drinkers (n = 871)	Past drinkers (n = 1184)	<4.9 g/d (n = 998)	5.0–9.9 g/d (n = 325)	10.0–14.9 g/d (n = 295)	15.0–29.9 g/d (n = 332)	≥30 g/d (n = 275)	P for trend	Chi-square test P
Alcohol intake (g/wk)	0	0	7	46	87	140	413	—	—
Alcohol intake (drinks/wk)	0	0	0.5	3.3	6.2	10	30	—	—
Multivariate 1[2]	1.00	0.86 (0.69, 1.07)	0.77 (0.62, 0.95)	0.46 (0.34, 0.62)	0.68 (0.49, 0.93)	0.78 (0.56, 1.10)	0.75 (0.53, 1.04)	0.32	< 0.0001
Multivariate 2[3]	1.00	0.90 (0.71, 1.13)	0.83 (0.66, 1.05)	0.49 (0.36, 0.69)	0.73 (0.52, 1.01)	0.84 (0.59, 1.20)	0.76 (0.54, 1.08)	0.29	< 0.0001
Multivariate 3[4]	1.00	0.82 (0.65, 1.04)	0.77 (0.61, 0.98)	0.43 (0.31, 0.61)	0.61 (0.43, 0.86)	0.71 (0.49, 1.04)	0.58 (0.41, 0.84)	0.02	< 0.0001
Multivariate 4[5]	1.00	0.81 (0.64, 1.03)	0.77 (0.61, 0.97)	0.44 (0.31, 0.61)	0.61 (0.43, 0.86)	0.70 (0.48, 1.02)	0.58 (0.40, 0.84)	0.02	< 0.0001

[1] Odds ratios (95% CIs) by categories of alcohol intake. A standard drink is defined as 14 g alcohol.
[2] Conditional odds ratios adjusted for smoking.
[3] Adjusted for history of diabetes, history of hypertension, abdominal obesity, physical activity, and income.
[4] Additionally adjusted for intake of total energy, dietary fiber, saturated fat, *trans* fat, and polyunsaturated fat.
[5] Further adjusted for intake of folate.

for HDL cholesterol (data not shown). We did not detect significant differences in total or LDL-cholesterol concentrations across categories of alcohol intake or patterns, even after we adjusted the analysis for variables that could influence plasma lipids (data not shown).

DISCUSSION

We have shown that moderate consumption of alcohol is independently associated with a reduced risk of MI and that low to moderate daily drinking is comparable with drinking on only 1–2 d/wk, as in the context of non-Western lifestyles. Beer was the most preferred beverage (30% of the population), followed by liquor (13%) and wine (7.5%). Alcohol intake was also significantly associated with HDL-cholesterol concentrations, which indicates that HDL cholesterol, a lipoprotein with well-known protection against MI, may mediate the observed protection.

The observed associations are not likely to have been confounded by age, sex, area of residence, income, dietary intake, or the presence of "sick-quitters" in the reference group because of the study's matched design, the restriction of recruitment to survivors of a first nonfatal acute MI, the use of randomly selected population controls, the use of lifelong alcohol abstainers as the reference group, and the various statistical adjustments made for both lifestyle and dietary variables. The inverse associations observed in the main analyses persisted even in analyses stratified by smoking status or other potential confounders, which further suggests that the observed association between alcohol consumption and MI is not spurious.

The proportion of alcohol users (43% of men and 16% of women) in our study is lower than that in the Atherosclerosis Risk in Communities Study (55% of men and 34% of women) (14) and the Health Professionals Follow-up Study (88%) (2) but is higher than that in the INTERHEART study (25%) (3). The median intake of alcohol by current alcohol users in Costa Rica (5.5 g/d) was lower than that in the Health Professionals Follow-up Study (6 g/d) (37), and the range of alcohol intake in the United States may be wider than that in Costa Rica (2, 14). The absence of a wide range of intake, together with a low number of daily drinkers in our study population, precluded analyses that would further investigate the risk of MI at higher intakes or an interaction with frequency of alcohol consumption.

Our data support results from earlier prospective (1, 6, 14, 21, 38–41) and case-control (3, 42) studies which suggest that moderate alcohol intake protects against MI and that it may do so by raising HDL cholesterol (5, 6). Our data show that drinking as little as one-half a drink per week (or <4.9 g/d) is inversely associated with nonfatal MI. This observation is consistent with previous studies showing an inverse association between very low alcohol intake and cardiovascular disease mortality (43, 44). The reasons for the apparent protection in light drinkers are not clear. HDL-cholesterol concentrations in the light drinkers were not significantly different from those of the lifelong abstainers. One possible explanation could be that light drinkers have a

TABLE 6
Alcohol intake patterns (weekend compared with daily drinkers) and risk of nonfatal acute myocardial infarction in Costa Rica[1]

	Never drinkers (n = 871)	Past drinkers (n = 1184)	Weekend drinkers (n = 825)	Daily drinkers (n = 218)	No regular pattern (n = 766)	Chi-square test P
Alcohol intake (g/d)	0	0	11	48	5	—
Alcohol intake (drinks/d)	0	0	0.8	3.4	0.4	—
Multivariate 1[2]	1.00	0.90 (0.72, 1.11)	0.78 (0.62, 0.98)	0.78 (0.56, 1.08)	0.76 (0.61, 0.95)	0.09
Multivariate 2[3]	1.00	0.88 (0.70, 1.11)	0.83 (0.65, 1.07)	0.81 (0.57, 1.16)	0.76 (0.60, 0.97)	0.24
Multivariate 3[4]	1.00	0.85 (0.67, 1.07)	0.77 (0.60, 0.98)	0.66 (0.46, 0.95)	0.71 (0.56, 0.91)	0.05
Multivariate 4[5]	1.00	0.85 (0.67, 1.07)	0.76 (0.59, 0.98)	0.64 (0.41, 1.01)	0.71 (0.56, 0.91)	0.06

[1] Odds ratios (95% CIs) by alcohol intake pattern. A standard drink is defined as 14 g alcohol.
[2] Conditional odds ratios adjusted for smoking.
[3] Adjusted for history of diabetes, history of hypertension, abdominal obesity, physical activity, and income.
[4] Additionally adjusted for intake of total energy, dietary fiber, saturated fat, *trans* fat, polyunsaturated fat, and folate.
[5] Further adjusted for total intake of alcohol as a continuous covariate.

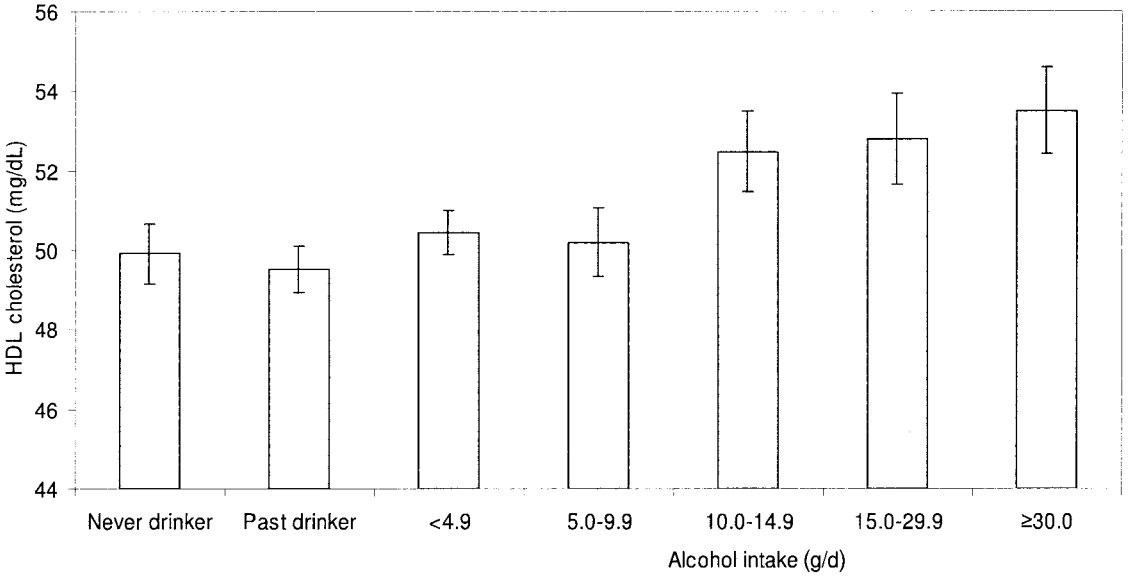

FIGURE 1. Mean (±SEM) plasma HDL-cholesterol concentration in controls by alcohol intake ($n = 2090$). Means are adjusted for smoking status, physical activity, abdominal obesity, sex, age, income, history of diabetes, history of hypertension, and intakes of saturated fat, polyunsaturated fat, *trans* fat, and dietary cholesterol. There was a significant main effect for alcohol intake, $P = 0.01$ (ANOVA).

healthier lifestyle than do abstainers. It is therefore possible that the observed protection in this group may be partly attributed to residual confounding, underreporting of alcohol intake, or healthy lifestyle as reported in the study by Gronbaek et al (44). The other potential explanation is the benefit of light drinking on hemostasis. Alcohol, in vitro or even when consumed in modest amounts, has been shown to have an immediate and sustainable effect on clotting mechanisms within a few hours of consumption (45–48). Thus, the potential protection of alcohol in very light drinkers could occur via the coagulation pathway. Unfortunately, we do not have data in the present study on markers of hemostasis to test this potential association. Another potential reason for benefit at modest levels may be the higher prevalence of the polymorphism in alcohol dehydrogenase that is associated with slower alcohol oxidation (25). If the alcohol dehydrogenase *ADH1C*2* allele is prevalent among Costa Ricans, then alcohol, even in minimal amounts, would be expected to remain unoxidized longer and confer a protective effect on MI through various mechanisms (6, 8, 9, 12, 13, 21). Future studies in this population that will investigate the potential interaction between alcohol intake and variation in genes for alcohol-metabolizing enzymes are warranted.

Our data agree with those of others (2) in that the amount and pattern of alcohol intake are associated with a reduced risk of MI. In this study, we found that the risk of MI in daily drinkers was comparable with that in weekend drinkers. Unlike in countries with high wine intakes, as reviewed elsewhere (10, 49), wine intake is very low in Costa Rica. Thus, our results suggest that the

FIGURE 2. Mean (±SEM) plasma HDL-cholesterol concentration in controls by alcohol intake pattern ($n = 2090$). Means are adjusted for smoking status, physical activity, abdominal obesity, sex, age, income, history of diabetes, history of hypertension, and intakes of saturated fat, polyunsaturated fats, *trans* fat, dietary cholesterol, and alcohol. There was a significant main effect for alcohol pattern, $P < 0.0001$ (ANOVA).

observed inverse association between alcohol and MI is not due to components of wine (20, 50) but to alcohol per se as shown in some studies of beer drinkers (41).

In summary, these data show that low to moderate consumption of alcohol on 1–2 d/wk is independently associated with a reduced risk of MI. Furthermore, these data support earlier studies suggesting that the apparent protective effect of alcohol is partly mediated through increases in plasma HDL cholesterol, especially at higher intakes. The finding of an inverse association at minimal levels of alcohol intake may indicate residual confounding or the presence of other protective mechanisms such as anticoagulation and warrants further investigation that should probably involve exploration of an interaction with genetic effects.

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EKK performed the analyses and wrote the manuscript, AB prepared the food-frequency questionnaire data, ER-N contributed to data preparation, EBR contributed to the analysis of the data, and HC designed and supervised the execution of the study. All authors participated in the interpretation of the results and the editing of the manuscript. None of the authors had a conflict of interest.

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