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Drinking patterns are associated with variations in atherosclerotic risk factors in French men

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Summary *Background* While a relationship between alcohol and cardiovascular risk factors is well established, data suggest that the type of alcoholic beverage could modulate this relationship. *Aim of the study* To determine whether drinking patterns modulate the relationship between alcohol and cardiovascular risk factors. *Methods* We tested the relationship between preference of alcoholic beverages and atherosclerotic risk factors in a cross-sectional study of 2,126 men. A hierarchical clustering method determined six drinking patterns, 'low drinkers', 'high quality wines', 'beer and cider', 'digestives', 'local wines', and 'table wines', according to the preferential intake of alcoholic beverages. Logistic models estimated the relative risk of abnormal markers in the drinking patterns compared with low drinkers. Unadjusted estimates investigated the relationship with the cluster as a group, while adjustment on alcohol, nutritional and socio-demographic factors investigated the relationship with the preference of alcoholic beverage in itself. *Results* Abstainers had high total plasma homocysteine (tHcy), even after full adjustment (odds ratio (OR) = 1.6, 95 % confidence interval (CI): 1.0, 2.8). Drinkers of high quality wine had low lipoprotein(a), high tHcy and high body mass index; beer and cider drinkers had high tHcy and waist circumference. Drinkers of digestives had high triacylglycerol; after adjustment they were at risk of low apolipoprotein A-I (OR = 3.1, 95 % CI: 1.2, 7.3), and high tHcy (OR = 4.9, 95 % CI: 1.2, 33.3). Local wines drinkers were similar to low drinkers. Table wine drinkers had high apolipoprotein B, high triacylglycerol, and high waist-to-hip ratio. *Conclusions* Our data suggest that preference of alcoholic beverage could indicate groups at specific risks of atherosclerotic disease.

Key words alcoholic beverages – cardiovascular disease – cluster analysis – lipids – risk factors

Introduction

Alcohol intake is a strong determinant of many biological and anthropometric cardiovascular risk factors [1–3]. Its influence has been demonstrated to be modulated by drinking patterns, considering either the type of alcoholic beverage consumed [4], drinking with or outside meals [5], or week-end versus daily drinking [6]. Several studies have observed a specific reduction in risk of atherosclerotic vascular disease associated with wine intake, as compared with other alcoholic beverages. However, this beneficial effect of wine may be due to confounding by factors associated with wine drinking

in countries where wine is not the traditional alcoholic drink, especially socio-economic factors. France is a country with a traditional habit of high and regular wine drinking, especially in men, across all social classes, but the type and quality of the wine consumed differ according to the socio-economic level. Statistical techniques are being more and more often used to summarize the relationship between various conditions and diet by establishing clusters of subjects with homogeneous dietary habits [7]. These techniques have rarely been used to establish patterns of alcohol drinking in the general population [8], while they have been used to establish clusters of alcoholics [9, 10]. In a previous paper, we described how we determined drinking patterns among men included in a cohort study, the SU.VI.MAX dietary intervention study [11], taking advantage of the wide range of alcohol drinking and the large variety of alcoholic beverages consumed in France [12]. In the present study, we investigated the relationship between these drinking patterns and the major risk factors for atherosclerotic vascular disease, in a cross sectional study. We attempted to test the hypothesis that the type of alcoholic beverage modulates the association between risk factors for atherosclerotic vascular disease and alcohol intake.

Materials and methods

Subjects

Subjects were participants in the SU.VI.MAX study, an ongoing randomized double-blind placebo-controlled primary-prevention trial designed to evaluate the effect of daily antioxidant supplementation (vitamin C, vitamin E, β-carotene, selenium and zinc) at near-nutritional doses on the incidence of cancer and ischemic heart disease. The design of the study has been described elsewhere [11]. Briefly, a total of 12,735 eligible subjects (women aged 35–60 years and men aged 45–60 years) were enrolled in 1994, and followed up for eight years. All subjects were encouraged to provide dietary data in the form of 24-hour dietary recalls every two months. For the present study, we included only the 2,150 men who had completed at least twelve 24-hour dietary recalls over the first two years of the study and had had no major health event during the first twelve dietary recalls (cancer or cardiovascular disease). We further excluded eight subjects with reported dietary intakes of less than 800 kcal/day, and 16 men with a very high alcoholic intake of over 100 grams per day, because they represented too small a sample to be studied as a specific pattern. A total of 2,126 men were included in the assessment of alcohol consumption.

The SU.VI.MAX study has been approved by the Ethical Committee for Studies with Human Subjects of Paris-Cochin (CCPPRB number 706), and by the "Commission Nationale Informatique et Liberté", CNIL number 334641.

Dietary assessment

The 24-hour dietary recalls were provided in a random assessment of four weekdays and two weekend days per year [13]. Subjects transmitted the corresponding data via the Minitel Telematic Network or Internet, which connected them to the main SU.VI.MAX computer server. They were helped by conversational facilities of the software and by an instruction manual for the codification of foods, which included photographs for estimating portion sizes [14]. Data on alcohol intake included 37 different alcoholic beverages. They were grouped into eight large categories of alcoholic drinks, as presented in the appendix. For wines, two ways of grouping drinks were investigated, either by wine color, or by quality of wine. The latter gave a better discrimination between groups and was subsequently used. It described three groups of wines. High quality wines included guaranteed vintage wines, and high quality wines, as defined by the French legislation. Local wines were non-vintage wines from a single origin, whereas table wines, the cheapest wines, had a non-specified origin, as they are usually composed of a mixture of several wines. Champagne was considered separately, as it is usually consumed in a different setting than other wines, festive occasions and outside meals. We used the first 12 recalls in order to include potential seasonal and weekly variations. Daily intakes of nutrients were calculated from food consumption using the French computerized food composition table CIQUAL [15].

Classification of drinking habits

In a previous study, we described how we determined drinking patterns in our studied population [12]. We first defined a group of abstainers, whose alcohol intake was less than 5 g per day (n = 329; mean (SD) alcohol intake = 1.9 (1.6) g/day). Among the remaining 1,797 men, we used the hierarchical agglomerative clustering method, with Ward's minimum variance method and squared Euclidean distance, to establish drinking patterns. These patterns described intake of eight types of alcoholic beverages, namely beer and cider, table wines (red, rosé or white), local wines (red, rosé or white), high quality wines (red, rosé or white), champagne, low-alcohol aperitifs (fruit punch, fortified wine, sangria, kir/royal kir, amer picon/Americano, picon-beer, cocktails), high-alcohol aperitifs (aniseed aperitifs, Whisky – Bourbon, vodka, gin, tequila, rum, Marie-Brisard), and digestives (brandy, liquor). Cluster analysis allowed us

to identify six patterns established on the basis of mean alcohol intake of specific beverages: 'low drinkers' (n = 670; 15.7 (8.9) g alcohol/day), 'high quality wines' (n = 584; 31.6 (17.1) g alcohol/day, characterized by a high intake of champagne, high quality wines, and high-alcohol aperitifs), 'beer and cider' (n = 190; 33.2 (17.0) g alcohol/day), 'digestives' (n = 54; 33.5 (20.6) g alcohol/day, behavior close to that of 'high quality wines', except for a specifically high consumption of digestive beverages), 'local wines' (n = 238; 36.2 (18.6) g alcohol/day, characterized by a high intake of local wines and of low-alcohol aperitifs), and 'table wines' (n = 61; 46.2 (14.7) g alcohol/day, characterized by a high intake of table wines as well as of high-alcohol aperitifs). Lifestyle characteristics of the groups have been described in a previous paper [12]. Briefly, low drinkers and abstainers were rather similar, except for a few specific characteristics. Abstainers spent more time at leisure physical activity than low-drinkers. They were more often non-smokers, but when smoking, they tended to smoke more heavily than low drinkers do. A low level of leisure time physical activity characterized drinkers of high quality wine. Drinkers of beer and cider had a rather high level of education, with a high proportion of white-collar workers. Drinkers of digestives spent little time having leisure physical activity, and had a high level of education. Drinkers of local wines were often retired, and rarely unemployed or handworkers. They had a rather high level of leisure physical activity, had often stopped smoking, and had rarely been heavy smokers. Table wine drinkers were the highest alcohol consumers. They were the oldest subjects, had the lowest level of education, included the lowest proportions of white-collar workers, and the highest proportions of farmers/workers and of inactive/unemployed men. They had the lowest level of leisure physical activity, but the highest level of overall physical activity. They also included the lowest proportion of non-smokers, and they tended to smoke heavily.

Anthropometric, clinical and biological data

Blood samples were obtained during the first year of follow-up, in vacutainer tubes (Becton Dickinson), after a 12-hour fasting period. Fasting glucose, total cholesterol, and triacylglycerol were measured by enzymatic methods (Technicon DAX). Serum concentrations of apolipoprotein A-I and apolipoprotein B lipoproteins were determined with a precipitation method in liquid phase (nephelometry) using a specific anti-serum, with a Behring BNA automate. Serum concentrations of lipoprotein(a) were determined with an immuno-enzymatic method (ELISA). Total plasma homocysteine (tHcy) was determined in a randomly selected sub-sample of 851 men, by the HPLC procedure and fluorometric detection using a BioRad kit (Hercule SA). Laboratory quality insurance included analysis of serum from standard pools with each run, and international standards when available.

All biological data were studied as normal versus abnormal. For tHcy, we chose a 10 µmol/l limit [16], which provided a sufficient proportion of abnormal values for a high study power. The apolipoprotein B to apolipoprotein A-I ratio was considered as abnormal over 1.0 [17]. Subjects treated for diabetes n = 44, or high cholesterol, n = 220 were classified as abnormal for fasting glucose or total cholesterol respectively. Mixed hyperlipidemia was defined as total cholesterol over 240 mg/dl, or treated high cholesterol, and triacylglycerol over 150 mg/dl.

Anthropometric and clinical data were recorded during the second year of follow-up, when about half of the dietary recalls were obtained. Height, weight, and waist and hip circumferences were measured on subjects in their underwear, using standardized procedures. Overweight corresponded to a body mass index value of 25 kg/m^2 or over. Waist circumference was considered as abnormal if equal or over 94 cm [18]. Diastolic and systolic blood pressure was measured once on each arm using a standard mercury sphygmomanometer in subjects who had been lying down for 10 minutes, and the mean value was recorded. High blood pressure was defined as systolic blood pressure over 140 mmHg and/or diastolic blood pressure over 90 mmHg, or in case of treated hypertension (n = 350).

Statistical analysis

Statistical analyses were carried out using the SAS (version 8, 1999, SAS Institute Inc., Cary, NC) statistical software package.

In order to take into account the potential association between alcohol consumption and risk of abnormal cardiovascular risk markers, several analyses were carried out. We first investigated the raw relationship between patterns and risk factors in logistic regression models only adjusted on age, and taking the low drinkers pattern as the reference. Then, we investigated the relationship between risk factors and patterns, independently of the quantity of alcohol intake in logistic models adjusted on both age and alcohol. Adjustment on alcohol was performed according to the best fit of the model, including alcohol either as a continuous variable, or as a quadratic term, or as both continuous and a quadratic term. In the fully adjusted models, we further adjusted on saturated fatty acids, dietary fiber, alcohol-free energy, tobacco, leisure-time exercise, education level, and body mass index. For tHcy, the fully adjusted model also included folate, and vitamins B6 and B12 intakes, and coffee consumption. Unconditional logistic regression

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estimated the odds ratio (OR) and 95 percent confidence intervals (CI) of having abnormal values of the studied factor, for each cluster relative to the low drinkers cluster. Tests were based on the likelihood ratio test statistic, the importance of main effects was assessed by using the Wald chi-square test statistic, and two sided tests and $p < 0.05$ were used for statistical significance.

Results

Table 1 describes mean intake of selected nutrients by cluster. Low drinkers were quite similar to abstainers, with low energy, fat and saturated fat intakes, and high fiber and beta carotene intakes. All other clusters had lower intakes of fiber and beta carotene, and higher intakes of fat and saturated fat.

Table 2 provides the comparison between the 'low drinkers' and the other clusters, as regards anthropometric or clinical risk factors for cardiovascular disease. The 'abstainers' and 'local wines' clusters were very similar to the 'low drinkers' cluster regarding all risk factors. The 'high quality wines' cluster had a statistically significant risk of overweight, high waist circumference and high waist-to-hip ratio. For the 'beer and cider' cluster, only the non-adjusted OR for waist circumference was statistically significant (OR = 1.5, 95 % CI: 1.0, 2.1). The 'table wines' cluster was significantly associated with a high waist-to-hip ratio (OR = 2.4, 95 % CI: 1.4, 4.2). All associations with anthropometric measurements disappeared after adjustment on alcohol intake.

Regarding blood pressure, no cluster was significantly different from the low-drinkers cluster. However, in the fully adjusted model, the high quality wines cluster was inversely associated with risk of hypertension (OR = 0.5, 95 % CI: 0.4, 0.8).

Table 3 provides the comparison between the 'low drinkers' pattern and the other clusters, as regards biological risk factors for cardiovascular disease. The 'abstainers' pattern displayed a significant risk of low apolipoprotein A-I, which disappeared after alcohol adjustment. They also had a significantly increased risk of high tHcy, which became borderline significant (p = 0.06) after adjustment on intakes of vitamins B6 and B12, folate, saturated fatty acids, dietary fiber, alcohol-free energy, alcohol, and coffee, exercise, education level, tobacco, and body mass index (OR = 1.6, 95 % CI: 1.0, 2.8). The 'high quality wines' cluster had a decreased risk of high lipoprotein(a) (OR = 0.8, 95 % CI: 0.6, 1.0), but statistical significance slightly decreased after full adjustment. This cluster also had an increased risk of high tHcy, which became non-statistically significant after full adjustment. A significant association with low apolipoprotein A-I appeared after alcohol adjustment, as well as after full adjustment. The 'beer and cider' cluster was associated with high tHcy (OR = 1.8, 95 % CI: 1.1,

Table 1 Mean (standard deviation) daily intake of selected macro- and micronutrients by drinking pattern

Nutrient	Low drinkers n = 670	Abstainers n = 329	High quality wines n = 584	Beer and cider n = 190	Digestives n = 54	Local wines n = 238	Table wines n = 61	*p*-value*
Alcohol (g)	15.7 (8.9)	1.9 (1.6)	31.6 (17.1)	33.2 (17.0)	33.5 (20.6)	36.2 (18.6)	46.2 (14.7)	< 0.0001
Alcohol-free energy (Kcal)	2,142 (472)	2,092 (487)	2,187 (434)	2,212 (473)	2,082 (400)	2,193 (450)	2,255 (560)	0.006
Total lipids (g)	92.2 (22.7)	89.8 (23.3)	97.5 (22.4)	98.3 (24.4)	93.1 (19.1)	95.4 (21.7)	97.8 (30.5)	< 0.0001
Monounsaturated fatty acids (g)	32.6 (8.0)	31.5 (8.1)	34.8 (8.2)	35.0 (8.7)	33.0 (6.8)	34.0 (7.9)	34.8 (11.1)	< 0.0001
Polyunsaturated fatty acids (g)	12.9 (4.1)	12.5 (3.9)	13.3 (3.8)	13.5 (4.3)	12.3 (3.4)	13.2 (4.1)	13.6 (5.3)	0.03
Saturated fatty acids (g)	39.5 (11.4)	38.8 (12.1)	42.1 (11.3)	42.2 (12.0)	40.7 (9.5)	40.8 (10.8)	41.9 (13.9)	< 0.0001
Total carbohydrates (g)	228.1 (63.4)	229.6 (66.2)	215.7 (58.8)	229.1 (60.1)	206.1 (53.8)	224.3 (61.4)	224.8 (65.9)	0.001
Starch (g)	132.0 (42.7)	128.8 (45.4)	125.1 (40.7)	132.0 (43.5)	119.0 (38.3)	129.4 (39.6)	142.5 (49.7)	0.005
Total proteins (g)	94.8 (18.8)	93.0 (21.4)	99.0 (19.1)	99.0 (23.4)	92.9 (15.2)	97.9 (21.4)	104.0 (26.0)	< 0.0001
Animal proteins (g)	67.0 (14.6)	66.1 (18.3)	72.2 (15.8)	70.4 (18.9)	67.5 (13.0)	70.0 (17.9)	72.6 (19.7)	< 0.0001
Vegetable proteins (g)	27.8 (8.6)	26.9 (8.8)	26.6 (7.7)	28.6 (8.8)	25.4 (6.3)	27.9 (7.9)	31.4 (11.3)	0.0002
Dietary fiber (g)	13.2 (5.1)	14.1 (6.1)	12.4 (4.4)	12.0 (4.3)	11.3 (4.3)	12.8 (4.9)	12.1 (4.8)	< 0.0001
Beta-carotene (mg)	3.6 (2.1)	3.7 (2.1)	3.3 (1.8)	3.2 (1.8)	3.1 (1.6)	3.2 (1.7)	3.2 (1.7)	0.0008
Iron (mg)	13.5 (3.1)	11.9 (3.1)	14.9 (3.3)	14.5 (3.8)	14.3 (2.9)	15.3 (3.4)	17.4 (4.1)	< 0.0001
Vitamin A (µg)	889.0 (657.0)	811.0 (562.4)	987.3 (745.7)	951.5 (666.5)	1,048.4 (798.6)	962.2 (646.2)	1,046.9 (626.4)	0.002
Vitamin B9 (µg)	304.8 (82.5)	305.8 (90.2)	308.6 (81.7)	307.7 (81.0)	299.4 (65.7)	309.5 (78.2)	313.9 (90.2)	0.93
Vitamin C (mg)	91.0 (43.5)	90.8 (45.9)	89.9 (40.5)	83.2 (41.1)	83.5 (37.2)	90.8 (38.2)	83.9 (39.7)	0.25
Vitamin E (mg)	11.3 (4.1)	11.2 (3.8)	11.4 (3.8)	11.1 (4.2)	11.0 (3.7)	11.3 (3.9)	10.9 (4.3)	0.92

* Analysis of variance

Table 2 Age-adjusted OR[a] and 95% CI[a] of abnormal anthropometric or clinical values according to pattern of drinking versus the 'low drinkers' pattern

	Type of analysis	Low drinkers n = 670	Abstainers n = 329		High quality wines n = 584		Beer and cider n = 190		Digestives n = 54		Local wines n = 238		Table wines n = 61	
		OR	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Body mass index	n1/n2[b]	261/313	126/160		269/233		82/78		27/19		98/106		32/24	
≥25 kg/m^2 vs. < 25	Non-alcohol adjusted[c]	1.0	1.0	0.7, 1.3	1.4**	1.1, 1.8	1.3	0.9, 1.8	1.7	0.9, 3.2	1.1	0.8, 1.5	1.6	0.9, 2.8
	Alcohol adjusted[c]	1.0	1.1	0.8, 1.5	1.1	0.9, 1.5	1.0	0.7, 1.5	1.4	0.8, 2.7	0.9	0.6, 1.2	1.1	0.6, 2.0
	Fully adjusted[c]	1.0	1.0	0.7, 1.4	1.1	0.8, 1.5	0.9	0.6, 1.4	1.0	0.5, 2.0	0.9	0.6, 1.3	1.1	0.6, 2.1
Waist-to-hip ratio	n1/n2	148/426	67/220		165/337		52/108		17/29		60/144		26/30	
≥0.95 vs. < 0.95	Non-alcohol adjusted	1.0	0.9	0.6, 1.2	1.4*	1.1, 1.8	1.4	1.0, 2.1	1.7	0.9, 3.2	1.2	0.8, 1.7	2.4**	1.4, 4.2
	Alcohol adjusted	1.0	1.1	0.8, 1.5	1.1	0.8, 1.5	1.1	0.7, 1.6	1.4	0.7, 2.6	0.9	0.6, 1.3	1.6	0.9, 2.9
	Fully adjusted	1.0	1.0	0.7, 1.5	1.1	0.8, 1.5	0.9	0.6, 1.4	0.9	0.4, 1.9	0.8	0.6, 1.3	1.3	0.7, 2.5
Waist circumference	n1/n2	178/396	83/204		191/311		63/97		20/26		72/132		24/32	
≥94 cm vs. < 94	Non-alcohol adjusted	1.0	0.9	0.7, 1.2	1.4*	1.1, 1.8	1.5*	1.0, 2.1	1.7	0.9, 3.2	1.2	0.8, 1.7	1.6	0.9, 2.8
	Alcohol adjusted	1.0	1.2	0.9, 1.6	1.0	0.8, 1.4	1.1	0.7, 1.6	1.3	0.7, 2.4	0.8	0.6, 1.2	1.0	0.5, 1.7
	Fully adjusted	1.0	1.0	0.7, 1.5	0.9	0.7, 1.3	0.9	0.6, 1.4	1.1	0.5, 2.1	0.8	0.5, 1.2	1.0	0.6, 2.0
Hypertension	n1/n2	258/305	115/172		217/290		76/97		24/22		93/117		24/18	
Diastolic > 90 and/or	Non-alcohol adjusted	1.0	0.8	0.6, 1.1	0.9	0.7, 1.1	0.9	0.7, 1.3	1.3	0.7, 2.5	0.9	0.6, 1.2	1.4	0.7, 2.7
Systolic > 140 mmHg	Alcohol adjusted	1.0	0.9	0.7, 1.2	0.8	0.6, 1.0	0.8	0.6, 1.2	1.2	0.6, 2.2	0.8	0.5, 1.1	1.1	0.6, 2.2
	Fully adjusted	1.0	0.8	0.5, 1.1	0.5***	0.4, 0.8	0.7	0.4, 1.0	0.8	0.4, 1.7	0.7	0.4, 1.0	0.9	0.4, 2.0

* $p < 0.05$, Wald chi-square test
** $p < 0.01$, Wald chi-square test
*** $p < 0.001$, Wald chi-square test
[a] *OR* odds ratio; *CI* confidence interval
[b] *n1/n2* abnormal/normal values for the studied factors
[c] *Non-alcohol adjusted* adjusted on age only; *Alcohol adjusted* adjusted on age and alcohol intake; *Fully adjusted* adjusted on age, education level, intakes of alcohol, saturated fatty acids, dietary fiber, and alcohol-free energy, tobacco, exercise, and body mass index (for the latter, except when studying body mass index, waist circumference, or waist-to-hip ratio)

Table 3 Age-adjusted OR[a] and 95% CI[a] of abnormal biological values according to pattern of drinking versus the 'low drinkers' pattern

	Type of analysis	Low drinkers n = 670	Abstainers n = 329		High quality wines n = 584		Beer and cider n = 190		Digestives n = 54		Local wines n = 238		Table wines n = 61	
		OR	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Apolipoprotein A-I	n1/n2[b]	93/574	75/253		82/502		23/165		10/44		22/215		5/55	
≤1.3 g/L vs. > 1.3	Non-alcohol adjusted[c]	1.0	1.8***	1.3, 2.6	1.0	0.7, 1.4	0.9	0.5, 1.4	1.4	0.6, 2.7	0.7	0.4, 1.0	0.6	0.2, 1.4
	Alcohol adjusted[c]	1.0	1.0	0.6, 1.5	1.6*	1.1, 2.3	1.4	0.8, 2.3	2.1*	1.0, 4.4	1.1	0.6, 1.8	1.3	0.4, 3.3
	Fully adjusted[c]	1.0	1.1	0.7, 1.8	1.6*	1.0, 2.5	1.5	0.8, 2.8	3.1*	1.2, 7.3	0.9	0.4, 1.7	0.8	0.2, 2.6
Apolipoprotein B	n1/n2	163/504	76/252		159/425		48/140		13/41		65/172		24/36	
≥1.35 g/L vs. < 1.35	Non-alcohol adjusted	1.0	0.9	0.7, 1.3	1.2	0.9, 1.5	1.1	0.7, 1.5	1.0	0.5, 1.9	1.2	0.8, 1.6	2.0*	1.1, 3.4
	Alcohol adjusted	1.0	1.0	0.8, 1.4	1.0	0.8, 1.4	0.9	0.6, 1.4	0.9	0.4, 1.6	1.0	0.7, 1.4	1.6	0.9, 2.9
	Fully adjusted	1.0	1.0	0.7, 1.5	1.0	0.7, 1.4	0.9	0.5, 1.4	0.4	0.1, 1.1	0.9	0.6, 1.3	1.4	0.7, 2.7
Cholesterol	n1/n2	344/325	148/180		316/268		88/101		23/31		123/114		33/27	
> 2.4 g/L vs. ≤2.4	Non-alcohol adjusted	1.0	0.8	0.6, 1.3	1.1	0.9, 1.4	0.8	0.6, 1.1	0.7	0.4, 1.3	1.0	0.7, 1.3	1.1	0.6, 1.9
	Alcohol adjusted	1.0	0.8	0.6, 1.1	1.0	0.8, 1.3	0.8	0.5, 1.1	0.7	0.4, 1.2	0.9	0.6, 1.2	0.9	0.5, 1.7
	Fully adjusted	1.0	0.9	0.6, 1.2	1.0	0.7, 1.3	0.7	0.5, 1.1	0.4*	0.2, 0.8	0.8	0.5, 1.1	0.8	0.4, 1.5
Triacylglycerol	n1/n2	133/536	74/254		129/455		40/149		17/37		52/185		19/41	
> 1.5 g/L vs. ≤1.5	Non-alcohol adjusted	1.0	1.2	0.9, 1.6	1.1	0.9, 1.5	1.1	0.7, 1.6	1.9*	1.0, 3.3	1.1	0.8, 1.6	1.9*	1.0, 3.3
	Alcohol adjusted	1.0	1.2	0.9, 1.7	1.0	0.8, 1.3	0.9	0.6, 1.4	1.6	0.8, 2.9	1.0	0.6, 1.4	1.4	0.8, 2.6
	Fully adjusted	1.0	1.3	0.9, 2.0	0.8	0.6, 1.2	0.9	0.5, 1.5	1.1	0.5, 2.5	0.7	0.4, 1.1	1.1	0.5, 2.3
Lipoprotein(a)	n1/n2	169/491	88/233		121/456		51/135		13/41		56/175		12/49	
> 0.3 g/L vs. ≤0.3	Non-alcohol adjusted	1.0	1.1	0.8, 1.5	0.8*	0.6, 1.0	1.1	0.8, 1.6	0.9	0.5, 1.7	0.9	0.6, 1.3	0.7	0.3, 1.3
	Alcohol adjusted	1.0	1.1	0.8, 1.5	0.8	0.6, 1.0	1.1	0.8, 1.7	1.0	0.5, 1.8	0.9	0.6, 1.4	0.7	0.3, 1.4
	Fully adjusted	1.0	0.8	0.6, 1.2	0.8	0.5, 1.1	1.3	0.9, 2.1	1.1	0.5, 2.4	1.0	0.6, 1.4	0.5	0.2, 1.2
Homocysteine	n1/n2	129/136	84/57		136/94		44/26		14/6		58/40		18/9	
≥10 µmol/L vs. < 10	Non-alcohol adjusted	1.0	1.6*	1.0, 2.0	1.5*	1.1, 2.2	1.8*	1.1, 3.1	2.5	1.0, 7.3	1.5	0.9, 2.4	2.1	0.9, 5.0
	Alcohol adjusted	1.0	1.5	1.0, 2.4	1.6*	1.1, 2.3	1.9*	1.1, 3.3	2.6	1.0, 7.7	1.6	0.9, 2.6	2.2	0.9, 5.5
	Fully adjusted	1.0	1.6	1.0, 2.8	1.3	0.8, 2.1	1.5	0.8, 2.9	4.9*	1.2, 33.3	1.6	0.9, 2.9	1.8	0.6, 5.1

* $p < 0.05$, Wald chi-square test
** $p < 0.01$, Wald chi-square test
*** $p < 0.001$, Wald chi-square test
[a] *OR* odds ratio; *CI* confidence interval
[b] *n1/n2* abnormal/normal values for the studied factors
[c] *Non-alcohol adjusted* adjusted on age only; *Alcohol adjusted* adjusted on age and alcohol intake; *Fully adjusted* adjusted on age, education level, intakes of alcohol, saturated fatty acids, dietary fiber, and alcohol-free energy, tobacco, exercise, and body mass index; for homocysteine, additional adjustment on intakes of coffee, and vitamins B6, B9 and B12

3.1); the association was independent of alcohol but became non-statistically significant after further adjustment. The 'digestives' cluster was significantly associated with high triacylglycerol, and borderline significantly associated with high tHcy. Adjustment on alcohol intake decreased the association with triacylglycerol; full adjustment enhanced the positive association with low apolipoprotein A-I (OR = 3.1, 95 % CI: 1.2, 7.3) and high tHcy (OR = 4.9, 95 % CI: 1.2, 33.3), and a negative association with cholesterol (OR = 0.4, 95 % CI: 0.2, 0.8). The 'local wines' cluster was not associated with any biological risk factor in any model, except for a non-significant association with hyperglycemia. The 'table wines' cluster was significantly associated with high apolipoprotein B and high triacylglycerol, but the associations decreased and became non-significant after alcohol adjustment. There was no significant association between any of the patterns and the ApoB/ApoAI ratio, mixed hyperlipidemia or fasting glucose.

Discussion

This study of drinking patterns associated with cardiovascular risk factors had two main objectives. Its first objective was to identify groups of individuals at a specifically high risk of atherosclerotic vascular disease, for public health purposes, using the age-adjusted models. The second objective was to investigate the respective role of alcohol itself and of other features of the cluster including preference in alcoholic drinks, as well as other environmental and socio-demographic features, using alcohol-adjusted and fully adjusted models.

Regarding the raw relationship between cardiovascular risk factors and drinking patterns, we identified table wine drinkers as being at a particularly high risk of atherosclerotic vascular disease. Although a small group, therefore with a low power for finding significant associations, subjects from this cluster combined a significantly high risk of high apolipoprotein B, and high triacylglycerol, as well as of high waist-to-hip ratio. We had previously characterized this group regarding socioeconomic characteristics [12]. They were the highest alcohol consumers, had the lowest level of education, spent the most time watching television, had the lowest level of leisure physical activity, but the highest level of global physical activity. Only one fourth of them had never smoked, and they tended to smoke heavily. In this study, most associations decreased after adjustment on alcohol, suggesting that the most deleterious feature of these subjects was their high alcohol intake. In addition, they had a non-alcohol related increased risk of high tHcy, although not statistically significant at the 5 % level. This absence of statistical significance may be due to a low power, as they represented only 61 men. Our study was based on volunteers, and subjects with a low socio-economic level tend to be underrepresented in this kind of study. Our findings suggest that these subjects should be considered as a group at a particularly high risk of atherosclerotic vascular disease, and should be given specific preventive advice.

On the other hand, the 'local wines' pattern appeared to be at a low risk of cardiovascular disease for most markers except for non-significant high tHcy and hyperglycemia. Despite a higher mean alcohol intake than the low drinkers (36.2 versus 15.7), risk factors were at a very similar level to our reference group, i. e. the 'low drinkers'. Both the 'local wines' and the 'table wines' groups mostly drank wine; therefore our data suggest that quality of wine as well as other behavioral features of the groups could be of importance. Compared to the 'table wines' group, 'local wines' subjects had more leisure time exercise and smoked less [12].

Drinkers of high quality wines differed from the two above-described groups in that they were at a low risk of high lipoprotein(a). This suggests a specific effect of some components of high quality red wine, the most consumed high quality wines in France. Polyphenols, in particular resveratrol, contained in red wine, but also in champagne [19], have been demonstrated to have specific effects on plasma lipids [20, 21], although this is still controversial [22]. In our study, the ratio of red to white wine consumption was over 10 in the 'high quality wines' cluster. Indeed, a specific effect of red wine, as opposed to white wine, on lipoprotein(a) concentrations has been observed in an intervention study [23]. In our study, lipoprotein(a) was not associated with alcohol intake itself, similarly to others [24, 25], while an inverse relationship has been described in an Italian population of hypertensive subjects [26], as well as in a Finnish population of moderate drinkers [27]. Our data suggest that differences in types of alcoholic drinks between studies may explain these discrepancies.

High tHcy has been found associated with alcohol intake, especially in subjects with hard liquor consumption [28], although others observed no effect [29]. In our study, alcohol itself was not associated with tHcy, as described in a previous analysis within the SU.VI.MAX cohort [14], and as demonstrated here by an absence of effect of alcohol adjustment on the calculated OR. However, all clusters were at a higher risk of high tHcy than the low drinkers pattern, irrespective of folate intake. The association was only borderline significant for the 'digestives', 'local wines' and 'table wines' clusters but it was of the same magnitude as for the other clusters. This absence of statistical significance may be due to the limited power of our study regarding tHcy, as it has been determined only in a subset of subjects. Abstainers also displayed a high risk of high tHcy, thus suggesting that characteristics other than folate intake or type of alcoholic drinks may determine tHcy. Many studies described a positive association between coffee consump-

tion and tHcy [30–34]. In our study, coffee consumption did not explain the observed high tHcy, neither in 'abstainers', nor in the other clusters, as adjustment for coffee did not modify the findings.

Alcohol is a strong determinant of apolipoprotein A-I concentration [1], as was also observed in this study. The lowest risk of low apolipoprotein A-I was observed in the 'table wines' cluster, i. e. the group with the highest mean alcohol intake, while the highest risk of low apolipoprotein A-I was observed in the 'abstainers' cluster. In some clusters, the beneficial effect of alcohol on apolipoprotein A-I could be counterbalanced by other characteristics, related either to the type of alcoholic drink, to other features of the diet or to other behavioral characteristics of the cluster. When adjusting on alcohol intake, drinkers of high quality wines and of digestives incurred an increased risk of low apolipoprotein A-I.

Some of the effects associated with our clusters of drinking habits could be related to differences in dietary habits between clusters. It has been demonstrated that eating habits differ according to quantity or type of alcohol consumption [35, 36]. However, adjustment on several nutrients potentially related to cardiovascular risk factors did not modify our findings, thus suggesting that there may be some true effect of beverage preference. To our best knowledge, this is the first study based on cluster analysis of drinking habits and not on an a priori definition of the groups according to their preferential intake of wine, beer or spirits, as is usually performed [37, 38]. In France, nearly all drinkers of alcoholic beverages drink some wine, therefore wine drinkers cannot be studied as a specific group. This study enabled us to demonstrate that quality and type of wine may determine groups at different risk of cardiovascular disease.

We chose to investigate abnormal versus normal values for the studied risk factors, both because it had a relevance for the medical profession, and because for some variables, treated subjects with normal values had to be reclassified as abnormal. However, we also performed linear regression on the variables that were not modified by treatments, and results were similar.

As a conclusion, our study enabled us to determine groups at high risk of cardiovascular disease, based on preference of alcoholic beverages. Our findings may also serve as a basis for future studies of the effect of specific alcoholic beverages on markers of cardiovascular disease.

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