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ORIGINAL CONTRIBUTION

Coffee consumption and mortality from all causes of death, cardiovascular disease and cancer in an elderly Spanish population

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Abstract

Purpose The effect of coffee consumption on mortality has been scarcely investigated in the elderly. We assessed the association between coffee consumption and mortality from all-cause, cardiovascular disease (CVD) and cancer, in an elderly population of Spain.

Methods We studied 903 individuals (511 women) aged 65 years and older from two population-based studies, the EUREYE-Spain study and the Valencia Nutritional Survey. Coffee consumption and diet were assessed using a validated food frequency questionnaire. Information on education, anthropometry, sleeping time, smoking, alcohol intake, physical activity and pre-existing disease was collected at baseline. Deaths were ascertained during a 12-year follow-up period, and Cox proportional hazards regression models were used to estimate adjusted hazard ratios (HR).

Results There were 403 deaths during the 12-year period (40% from CVD), 174 of which occurred during the first 6 years. We observed evidence of a lower CVD mortality among coffee drinkers in the first 6 years of follow-up. Drinkers of ≤1 cup of coffee/day and > 1 cup/day showed lower CVD mortality than non-drinkers of coffee, HR 0.82 (95% CI 0.46–1.44) and HR 0.38 (0.15–0.96), respectively (p trend = 0.04). This association of coffee with CVD mortality attenuated after 12 years of follow-up. No significant association was observed with all-cause or cancer mortality, neither for caffeinated and decaffeinated coffee.

Conclusions In this study, coffee consumption was associated with lower CVD mortality in elderly. Although this association should be further investigated, coffee consumption appears to be safe for the elderly since no increased mortality was observed in coffee drinkers.

Keywords Coffee · Caffeinated · Decaffeinated · Mortality · Elderly · Cardiovascular mortality.

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Introduction

Coffee has long been the most consumed beverage in the world and consequently, its health effects have been a subject of interest. Three recently published reviews concluded that coffee consumption was associated with a reduced risk of all-cause and cardiovascular disease (CVD) mortality in adults [1–3], and thus it could be considered as part of a healthy diet [3]. Although long-term adverse effects of coffee on health outcomes were not found, coffee has been considered detrimental due to its caffeine content and acute effects increasing blood pressure [4], insulin resistance [5] and the risk of some cardiovascular diseases [4, 6].

The mechanism by which coffee consumption may reduce mortality is not completely understood, although some of its components such as minerals and polyphenols have antioxidant and anti-inflammatory effects that may be beneficial on human health [3, 7]. Nevertheless, it has been reported that some lifestyle factors such as smoking status could also play a confounding effect in the relation between coffee and mortality [8, 9].

Although some studies reported that coffee consumption was associated with higher mortality in general population [6], or only in men [10, 11], most published studies have shown that regular coffee consumption is associated with a lower incidence of diabetes [12], mental illness [13, 14], and certain types of cancers [3, 15, 16], and with a lower total and CVD mortality [2, 3, 9, 17, 18]. Most of the studies have been carried out in developed countries, mostly using populations with a wide age range [1, 2, 17], but only a few investigated the association in the elderly. Thus, the evidence on the association between coffee and mortality in countries with high life-expectancy and healthy diets such as those in the south of Europe is practically non-existent [19]. To the best of our knowledge, only two studies have evaluated the association between coffee consumption and all-cause or CVD mortality in the elderly [20, 21], both showing an inverse association, although in one study the association appeared to attenuated after 10 years of follow-up [21]. The aim of this study was to assess the association between coffee consumption and all-cause, CVD and cancer mortality in an elderly population in Spain taking into account amount and type of coffee.

Methods

Study population

We analyzed data of 511 women and 392 men ($n = 903$) aged 65 years and above who participated in two population-based surveys in the Valencia Region (Spain): the EUREYE-Spain study and the Valencia Nutrition Survey (VNS). Details of both studies have been published elsewhere [22–24]. Briefly, the EUREYE study was a multi-centre cross-sectional study based on representative samples of elderly people aged 65 years and above from seven European countries in 2000–2001 that enrolled 597 subjects in the province of Alicante in the Valencia Region, Spain. The VNS was a nutrition and examination survey also based on a representative sample of an adult population in the Valencia Region that included 306 participants aged 65 years and above in 1994. In both studies, participants were interviewed by trained fieldworkers using structured questionnaires.

Ethical approval for the studies was given by the Local Ethical Committee of the Hospital of San Juan and the Miguel Hernandez University, Alicante, Spain. Written informed consent was obtained from all subjects.

Coffee and dietary assessment

Dietary information was collected using validated semi-quantitative food frequency questionnaires (FFQ), similar to the Willett questionnaire [25], that were adapted and validated in an adult and elderly population in Spain [26, 27]. The FFQ used in the Valencia Nutrition Survey had 93 food items and the FFQ used in the EUREYE-Spain study included 131 food items since fruit and vegetables were not grouped, and some additional foods were added to make the questionnaire more comparable to other European countries that participated in the EUREYE study. Both FFQ included nine sections for the main food groups: diary; eggs, meat and fish; vegetables; fruits; breads and cereals; oils and fats; sweets and pastry; beverages; and processed foods. The FFQ showed a satisfactory reproducibility and validity when their nutrient and food intake estimates were compared with those from four 1-week dietary records in an adult population in Valencia [27]. The validity correlation coefficients (adjusted for energy intake) ranged from 0.27 for folate intake to 0.67 for calcium intake (average 0.47), and the reproducibility correlation coefficients ranged from 0.30 for carotene intake to 0.65 for calcium intake (average 0.40). The carotenoids and vitamin C intake estimated by the FFQ also showed good correlations with carotenoids and vitamin C in plasma [26]. The 93-item FFQ showed a good reproducibility for total coffee consumption; the correlation coefficient was $r = 0.60$. Participants were asked how often on average they consumed a standard portion size of each food item during the previous year using one of the nine possible consumption frequencies, ranging from “never or less than once per month” to “six or more per day”. The FFQ included two items to collect information on coffee consumption, one item for caffeinated coffee and another for decaffeinated coffee.

A cup of coffee was defined using typical sizes (about 50 ml for expresso cup or 125–150 ml for instant/brewed/ground coffee).

The total coffee consumption in cups per day was calculated as the sum of caffeinated and decaffeinated coffee.

We estimated the adherence to a Mediterranean Diet (MD) for each participant using the relative Mediterranean Diet Score (rMED) [28], which is a variation of the original Mediterranean diet score [29, 30]. Instead of using the median to score each component, in the rMED, the intake in grams of each component, except for alcohol, is referred per 1000 kcals and divided into tertiles. A value of 0, 1, and 2 was assigned to the first, second, and third tertiles of intake, respectively, for the six components that presumably fit the MD: fruits (including nuts and seeds), vegetables (excluding potatoes), legumes, fish, olive oil and cereals (including whole grain). Two components were negatively scored that probably do not fit the MD (lower scoring for the higher intakes): total meat (including processed meat) and dairy products. Owing to the assumed positive effects of moderate alcohol consumption, it was considered as a dichotomous variable using the following ranges: 2 points for moderate consumption (5–25 g/day for women and 10–50 g/day for men) and 0 points for higher or lower consumption. The overall rMED score was calculated for each participant summing the points of the nine components. The scores ranged from 0 to 6 points (low adherence), 7–10 (medium adherence) to 11–18 points (high adherence). Nutrient values and energy intake were primarily obtained from food composition tables from the US Department of Agriculture [31] and other Spanish published sources [32].

Assessment of mortality

The date and cause of deaths during the 12-year follow-up period were confirmed through the National Death Index from the Spanish Statistical Office and the Mortality Registry in the Valencia Region.

The cause of death was coded according to version 10 of the International Classification of Diseases (ICD-10). For analysis purposes, we grouped deaths in three broad categories as follows: cardiovascular disease (ICD-10: I00-I99), cancer (ICD-10 codes: C00-D49), and all-cause mortality including the two first categories and deaths from any other cause.

Other variables

During the interviews, the study participants also provided information on socio-demographic variables, smoking and alcohol consumption, health status, physical activity and other lifestyles. For the analysis, we collected information on potential confounders such as sex, age (65–74 years, ≥ 75 years), study (EUREYE-Spain; Valencia Nutrition Survey), education level (< primary school; ≥ primary school), BMI calculated by dividing measured body weight (kg) by the square of measured body height (m) (< 25, 25–30, ≥ 30 kg/m^2), waist circumference (normal, 78–94 cm in men and 64–80 cm in women; Moderate, 94–102 cm in men and 80–88 cm in women; and Large, > 102 cm in men and > 88 cm in women) [33], smoking (never, ex-smoker, current), self-reported main physical activity (very low; low–moderately active) and physical activity at leisure time (very low, mostly at sitting position; low–moderate–vigorous), total sleeping time in hours per day and pre-existing chronic disease at baseline (self-reported diabetes, high blood cholesterol and high blood pressure). A high level of agreement has been shown between self-reported diseases in the elderly and those documented in the medical record [34, 35].

Statistical analysis

We used relative frequencies (percentages) and Chi-square tests to describe and compare categorical variables, and means, standard deviations and ANOVA tests for continuous variables. We calculated person-years of follow-up for each participant from the date of baseline interview in every survey to the date of death or completion of the 6- and 12-year follow-up, whichever came first. We examined the association between total, caffeinated and decaffeinated coffee consumption and risk of mortality at 6 and 12 years of follow-up. Participants were classified according to their consumption of total coffee as non-drinkers, drinkers of ≤1 cup/day (range 0.1–1.0 cups) and drinkers of > 1 cup/day (range 1.1–5.5). We did not use more categorization for drinkers since the number of participants consuming 2, 3 and 4 or more cups/day was low 40 (4.4%), 140 (15.5%) and 14 (1.6%), respectively. Participants were also classified by the type of coffee in non-consumers, decaffeinated or caffeinated consumption. We used Cox proportional hazards models to estimate hazard ratios (HR) and 95% confidence intervals (95% CI) for each category of coffee consumption in comparison to the lower category (no consumption; ≤ 1 cup/day, > 1 cup/day) from all causes of mortality, CVD and cancer mortality.

Analyses were run separately for each survey to explore the heterogeneity using I^2 and Cochran's Q test [36]. As the results between studies did not show heterogeneity, the results were presented combined, adjusting by study as a dichotomous variable. Two models were presented: a model adjusted for age and sex, and a multivariable model adjusted for the variables mentioned above that have been considered as potential confounders published in the literature and those variables showing p values < 0.20 in bivariate analysis. Total calorie intake was not included in the multivariate analysis since the components of rMED were already adjusted for 1000 kcals. The non-zero slope of the scaled Schoenfield residuals on the time function suggested that the proportional hazard assumption was met. Likelihood ratio test (LRT) was used to test the overall significance of coffee consumption as categorical variable, and trend tests were also used to evaluate dose–response for amount of coffee consumption as a continuous term.

The applied statistical tests were bilateral, and signification was established at 0.05. The statistical analysis was performed with the statistical software R.3.3.2 (R Foundation for Statistical Computing, Vienna, Austria, http://www.r-project.org) and STATA 15® College Station, TX: StataCorp LP.

Results

The baseline characteristics of the participants according to the categories of coffee consumption are shown in Table 1. More than two out of three participants were coffee drinkers, 48% were drinkers of up to 1 cup/daily and 21.5% reported drinking more than one cup of coffee daily. Compared to non-drinkers of coffee, coffee drinkers were more likely to be men, past or present smokers and have a higher education level, moderate–high physical activity at work, and a lower proportion of self-reported hypertension.

Table 2 shows the number of deaths and hazard ratios by amount of coffee consumption. During the 6 years of follow-up (4955.7), we documented 174 deaths, 68 (39%) from CVD and 45 (26%) from cancer. During the overall 12 years of follow-up (8650.0 person-years), we documented 403 deaths, 160 (40%) due to CVD and 90 (23%) due to cancer. Figure 1 shows the cumulative incidence for all-cause and CVD deaths during the study period according to the amount of coffee consumption. In general, coffee drinkers showed curves with lower incidence of deaths than non-drinkers of coffee.

After adjusting for age, sex, survey, educational level, BMI, waist circumference, sleeping time, smoking, self-reported diabetes, high cholesterol and hypertension, adherence to Mediterranean Diet, physical activity at work and at leisure time, we observed evidence of a lower CVD mortality among coffee drinkers after 6 years of follow-up. Compared with non-drinkers of coffee, drinkers of ≤ 1 cup/day and > 1 cup/day showed lower CVD mortality at year 6 of follow-up, HR 0.82 (95% CI 0.46–1.44) and HR 0.38 (0.15–0.96) respectively (p trend = 0.04). A lower all-cause mortality was also observed among drinkers of more than one cup of coffee a day, the age- and sex-adjusted HR was 0.60 (0.38–0.96), although this lost significance in the fully adjusted multivariable model, HR 0.74 (0.45–1.20). No significant association was observed for cancer mortality. After 12 years of follow-up, no association was observed of coffee consumption with all-cause, CVD or cancer mortality.

The association between type of coffee consumption and mortality at 6 and 12 years of follow-up is shown in Table 3. A lower CVD mortality was observed among decaffeinated (32%) and caffeinated (30%) coffee drinkers with respect to non-coffee drinkers at year 6 of follow-up, although the association was not statistically significant. Overall, no statistically significant association was observed between type of coffee and all-cause, CVD or cancer mortality at 6 or 12 years of follow-up.

Discussion

In this study we found an inverse association between coffee consumption and cardiovascular mortality in elderly of 65 years and above in Spain after a 6-year follow-up and after the adjustment for potential confounders. By the end of the 12-year follow-up, the association attenuated and lost statistical significance. This protective effect of coffee was not observed for all-cause or cancer mortality. Regarding type of coffee, caffeinated and decaffeinated coffee drinkers showed a non-significant protective effect for CV mortality although our study may be underpowered to explore the association by type of coffee.

The inverse association between coffee consumption and CVD mortality has been found in many studies with adult populations as shown in several meta-analyses [1, 2, 9, 18, 34] and subsequent studies carried out in different continents [17, 38–41]. However, this association has scarcely been analyzed in the elderly despite the high consumption of coffee observed among them. To our knowledge, only two studies have focused on the association between coffee consumption and total or CVD mortality in an elderly population, both showing lower mortality. In a Finnish study with adults aged 70 and above observed during a 14-year period, a lower total, CVD and cancer mortality was found that was stronger during the first few years and gradually attenuated towards the end of the follow-up [21]. In a prospective study of the first National Health and Nutrition Examination Survey, that included 6594 male and female participants aged 32–86 years, the consumption of caffeinated beverages was associated with lower heart disease mortality among those aged 65 years or more [42]. Our results are consistent with these studies as we observed 62% less CVD mortality among coffee drinkers of more than one cup of coffee a day compared to non-drinkers of coffee at 6 years, and 26% less total mortality as well, although the effect for total mortality was not statistically significant. Similarly to the results of the Finnish study, the association we found for CVD mortality was stronger and significant during the first 6 years

Table 1 Socio-demographic and lifestyle characteristics according to coffee consumption among elderly participants (65 years and above) of the EUREYE-Spain and the Valencia Nutrition Studies in Spain ($n = 903$)

	Total	Coffee consumption			*p* value[1]
		No	≤ 1 cup/day (range 0.01–1.0)	> 1 cup/day (range 1.1–5.5)	
Cups of coffee/day (mean, SD)		0	0.87 (0.27)	2.5 (0.66)	
Study, *n* (%)	903	273 (30.2)	436 (48.3)	194 (21.5)	
EUREYE-Spain	597 (66.1)	173 (63.4)	308 (70.6)	116 (59.8)	0.01
VNS	306 (33.9)	100 (36.6)	128 (29.4)	78 (40.2)	
Sex = women, n (%)	511 (56.6)	183 (67.0)	237 (54.4)	91 (46.9)	< 0.001
Age, *n* (%)					
65–74 years	567 (62.8)	151 (55.3)	276 (63.3)	140 (72.2)	
≥ 75 years	336 (37.2)	122 (44.7)	160 (36.7)	54 (27.8)	< 0.001
Education level, *n* (%)					
< Primary school	588 (65.1)	197 (72.2)	275 (63.1)	116 (59.8)	0.01
≥ Primary school	315 (34.9)	76 (27.8)	161 (36.9)	78 (40.2)	
Body mass index (kg/m^2), *n* (%)					
< 25	167 (18.6)	58 (21.3)	69 (16.0)	40 (20.6)	0.29
25–30	419 (46.7)	117 (43.0)	209 (48.5)	93 (47.9)	
≥ 30	311 (34.7)	97 (35.7)	153 (35.5)	61 (31.4)	
Waist circumference[2], *n* (%)					
Normal	97 (10.9)	26 (9.7)	51 (11.8)	20 (10.5)	0.56
Moderate	204 (22.9)	57 (21.3)	96 (22.2)	51 (26.7)	
Large	590 (66.2)	185 (69.0)	285 (66.0)	120 (62.8)	
Smoking status, *n* (%)					
Never	574 (63.6)	206 (75.7)	266 (61.1)	102 (52.6)	< 0.001
Ex-smoker	206 (22.8)	48 (17.6)	104 (23.9)	54 (27.8)	
Current	121 (13.4)	18 (6.6)	65 (14.9)	38 (19.6)	
Diabetes[3] (yes), *n* (%)	175 (19.4)	50 (18.3)	91 (20.9)	34 (17.5)	0.52
Cholesterol[3] (yes), *n* (%)	181 (20.2)	55 (20.3)	83 (19.1)	43 (22.5)	0.62
Hypertension[3] (yes), *n* (%)	359 (40.1)	120 (44.4)	181 (41.8)	58 (30.2)	< 0.05
Main physical activity, *n* (%)					
Very low	292 (32.3)	104 (38.1)	135 (31.0)	53 (27.3)	0.03
Low–moderately active	611 (67.7)	169 (61.9)	301 (69.0)	141 (72.7)	
Physical activity at leisure time, *n* (%)					
Very low	505 (56.6)	153 (57.5)	244 (56.4)	108 (56.0)	0.76
Low–moderately active	387 (43.4)	113 (42.5)	189 (43.6)	85 (44.0)	
Sleeping time, hours/day (mean SD)	7.8 (2.0)	7.7 (2.2)	7.8 (1.9)	7.9 (1.9)	0.39
rMED, mean (SD)	8.2 (2.4)	8.2 (2.3)	8.2 (2.4)	8.3 (2.5)	0.99

SD standard deviation, *VNS* Valencia nutrition survey, EUREYE-Spain Survey, *BMI* body mass index, *rMED* relative Mediterranean Dietary index

[1]*p* value from Chi-square test (categorical variables) and ANOVA (continuous variables)

[2]Waist circumference: normal (78–94 cm in men and 64–80 cm in women), moderate (94–102 cm in men and 80–88 cm in women), large (> 102 cm in men and > 88 cm in women)

[3]Self-reported diabetes (no/yes), high cholesterol (no/yes) and hypertension (no/yes)

and attenuated at year 12 of follow-up. This attenuation of effect may be related to several factors such as a low number of people available at the end of the study period, a regression dilution because of possible changes of the exposure (e.g., reduction of coffee consumption with age), or a misclassification of the exposure since it was measured at baseline, which altogether may also cause an underestimation of the effect [21, 43].

In addition to its protective effect for CVD mortality, it is also important to note the high prevalence of coffee consumption observed in the elderly population of our study, although the amount of coffee consumption was

Table 2 Associations between level of coffee consumption and all-cause, cardiovascular disease and cancer mortality among elderly participants of EUREYE-Spain study and Valencia Nutrition Survey in Spain

	Coffee consumption				
	No	≤ 1 cup/day	> 1 cup/day	*p* value[2]	*p* trend[3]
Follow-up at 6 years					
All-cause (*n*, %)	273 (30.2)	436 (48.3)	194 (21.5)		
Deaths, *n*	61	86	27		
Person-years	1462.8	2392.7	1100.1		
HR (95% CI)					
Age- and sex-adjusted	1.00	0.85 (0.61–1.18)	0.60 (0.38–0.96)	0.08	0.03
Multivariable[1]	1.00	1.03 (0.72–1.46)	0.74 (0.45–1.20)	0.31	0.29
CVD (*n*, %)	241 (30.3)	382 (47.9)	174 (21.8)		
Deaths, *n*	29	32	7		
Person-years	1366.5	2207.9	1022.4		
HR (95% CI)					
Age- and sex-adjusted	1.00	0.73 (0.44–1.20)	0.37 (0.16–0.86)	0.03	0.01
Multivariable[1]	1.00	0.82 (0.46–1.44)	0.38 (0.15–0.96)	0.08	0.04
Cancer (*n*, %)	222 (28.7)	374 (48.3)	178 (23.0)		
Deaths, *n*	10	24	11		
Person-years	1293.6	2181.1	1047.1		
HR (95% CI)					
Age- and sex-adjusted	1.00	1.34 (0.64–2.82)	1.29 (0.54–3.08)	0.72	0.55
Multivariable[1]	1.00	1.49 (0.67–3.29)	1.46 (0.58–3.67)	0.57	0.41
Follow-up at 12 years					
All-cause (*n*, %)	273 (30.2)	436 (48.3)	194 (21.5)		
Deaths, *n*	129	191	83		
Person-years	2518.9	4185.8	1945.3		
HR (95% CI)					
Age- and sex-adjusted	1.00	0.88 (0.70–1.10)	0.86 (0.65–1.14)	0.45	0.25
Multivariable[1]	1.00	0.97 (0.76–1.23)	0.95 (0.71–1.28)	0.94	0.74
CVD (*n*, %)	200 (30.3)	321 (48.6)	139 (21.1)		
Deaths, *n*	56	76	28		
Person-years	2054.1	3449.1	1558.7		
HR (95% CI)					
Age- and sex-adjusted	1.00	0.83 (0.59–1.18)	0.77 (0.49–1.22)	0.45	0.22
Multivariable[1]	1.00	0.91 (0.62–1.32)	0.83 (0.51–1.32)	0.77	0.47
Cancer (*n*, %)	167 (28.3)	286 (48.5)	137 (23.2)		
Deaths, *n*	23	41	26		
Person-years	1863.9	3163.9	1507.5		
HR (95% CI)					
Age- and sex-adjusted	1.00	1.00 (0.60–1.67)	1.30 (0.74–2.30)	0.55	0.36
Multivariable[1]	1.00	1.06 (0.62–1.83)	1.30 (0.71–2.41)	0.66	0.39

CI confidence interval, *CVD* cardiovascular disease

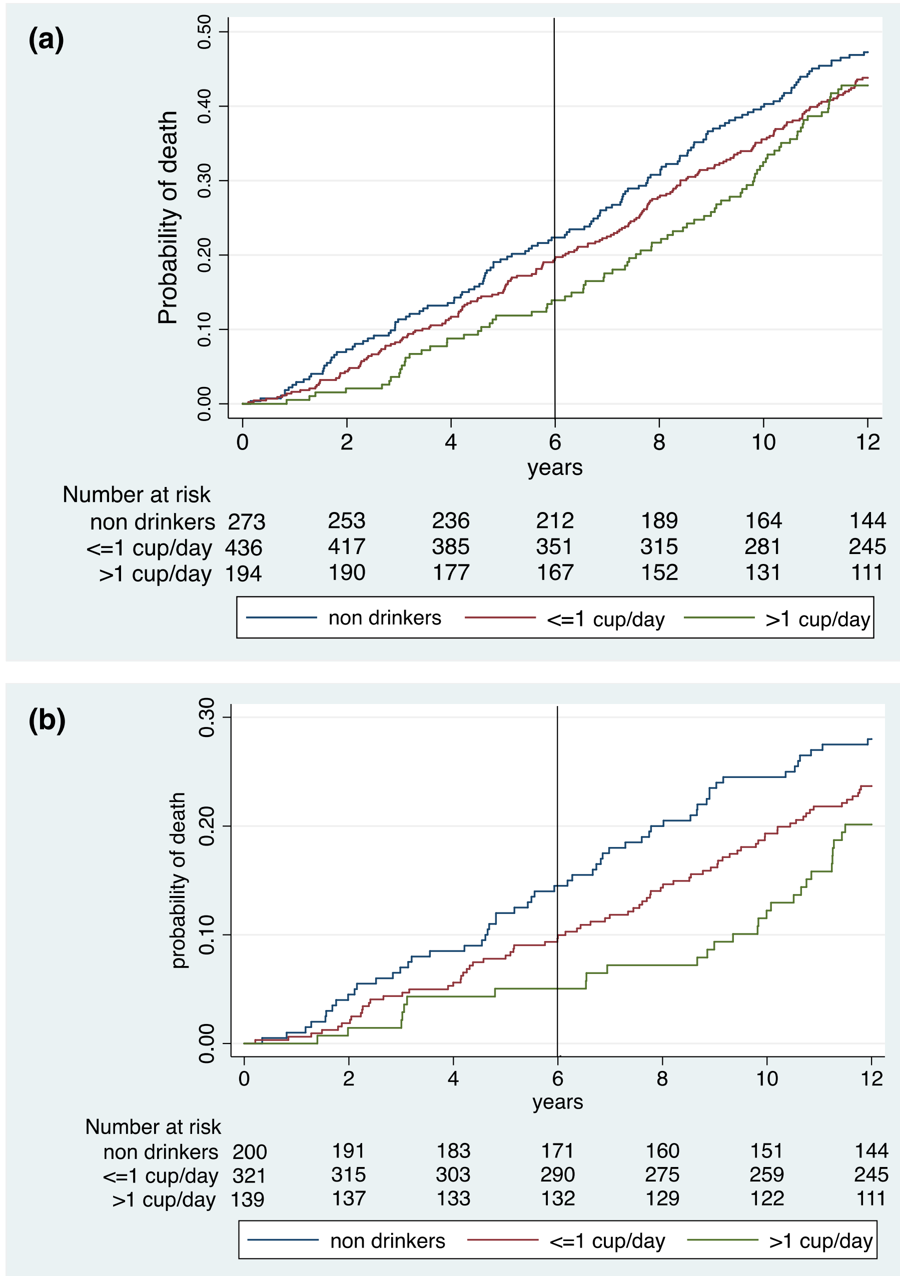
[1]Cox regression model adjusted for age (65–74, ≥ 75 years), sex, study (EUREYE study, Valencia Nutrition Survey), educational level (< Primary, ≥ Primary), BMI (< 25, 25.0–29.9, ≥ 30), waist circumference (normal, moderate and large), sleeping time (h/day), smoking habit (current; past and never), self-reported diabetes (no/yes), high cholesterol (no/yes), hypertension (no/yes), relative Mediterranean Diet, main physical activity (very low, low–moderately active), and at leisure time (low, moderate–high)

[2]*p* value from likelihood ratio test

[3]*p* trend was evaluated for coffee consumption as a continuous term

considerably lower than the observed in the elderly population of the North European and American studies [20, 21]. This may be relevant to make recommendations on coffee drinking as a safe beverage for the elderly not only because of its beneficial effect, but also because no harmful effects were observed either for total or cancer mortality.

Fig. 1 Cumulative incidence of death according to coffee consumption for all-cause (**a**) and cardiovascular disease (**b**) mortality in participants from EUREYE-Spain study and Valencia Nutritional Survey in Spain



The mechanisms by which coffee may reduce CVD mortality are yet unclear although they may relate to the antioxidant benefits of other components apart from caffeine, for instance, the reduction of LDL oxidation that intervenes in the development of atherosclerosis [3], or to phenolic compounds of coffee such as chlorogenic acid that could improve glucose tolerance, or other substances including magnesium or trigonelline that improve insulin sensitivity [7]. Unfortunately, our study was based on the prospective analysis of two cross-sectional studies with no information on biomarkers related to coffee consumption. Regarding the potential carcinogenic effect of some coffee compounds pointed out in some studies, we observed a small increased risk for cancer mortality at 6 years although far from statistically significant and probably due to chance. In any case, our study had a limited sample size for the exploration of an association for total cancer or any specific cancer site. At most, coffee drinking has been considered as a potential effect modifier rather than a risk factor per se [44].

Regarding type of coffee, our questionnaire included two specific questions for caffeinated and decaffeinated coffee. Although we observed 30 and 32% less CVD mortality for the consumption of caffeinated or decaffeinated coffee, the association was not statistically significant. Unfortunately,

Table 3 Associations between type of coffee consumption and all-cause, cardiovascular disease and cancer mortality among elderly participants of EUREYE-Spain study and Valencia Nutrition survey in Spain

	Coffee consumption			
	No	Decaffeinated coffee[1] (range 0.1–4.5 cups/day)	Caffeinated coffee[1] (range 0.1–4.5 cups/day)	*p* value[3]
Cups of coffee/day (mean, SD)		1.2 (0.68)	1.4 (0.87)	
Follow-up at 6 years				
All-cause mortality (*n*, %)	273 (30.2)	290 (32.1)	340 (37.7)	
Deaths, *n*	61	56	57	
Person-years	1462.8	1586.1	1906.7	
HR (95% CI)				
Age- and sex-adjusted	1.00	0.82 (0.57–1.19)	0.73 (0.50–1.06)	0.25
Multivariable[2]	1.00	0.94 (0.63–1.38)	0.95 (0.64–1.40)	0.94
CVD (*n*, %)	241 (30.2)	256 (32.1)	300 (37.7)	
Deaths, *n*	29	22	17	
Person-years	1366.5	1478.1	1752.1	
HR (95% CI)				
Age- and sex-adjusted	1.00	0.68 (0.39–1.18)	0.55 (0.30–1.01)	0.13
Multivariable[2]	1.00	0.68 (0.36–1.26)	0.70 (0.37–1.36)	0.41
Cancer (*n*, %)	222 (28.7)	251 (32.4)	301 (38.9)	
Deaths, *n*	10	17	18	
Person-years	1293.6	1464.7	1763.5	
HR (95% CI)				
Age- and sex-adjusted	1.00	1.38 (0.63–3.03)	1.27 (0.58–2.79)	0.70
Multivariable[2]	1.00	1.58 (0.69–3.62)	1.39 (0.59–3.23)	0.53
Follow-up at 12 years				
All-cause mortality (*n*, %)	273 (30.2)	290 (32.1)	340 (37.7)	
Deaths, *n*	129	132	142	
Person-years	2518.91	2755.3	3375.8	
HR (95% CI)				
Age- and sex-adjusted	1.00	0.92 (0.72–1.17)	0.83 (0.65–1.05)	0.32
Multivariable[2]	1.00	0.95 (0.73–1.22)	0.98 (0.76–1.27)	0.91
CVD (*n*, %)	200 (30.3)	218 (33.0)	242 (36.7)	
Deaths, *n*	56	60	44	
Person-years	2054.1	2315.9	2691.7	
HR (95% CI)				
Age- and sex-adjusted	1.00	0.95 (0.66–1.37)	0.67 (0.45–1.01)	0.10
Multivariable[2]	1.00	0.93 (0.63–1.38)	0.83 (0.54–1.29)	0.72
Cancer (*n*, %)	167 (28.3)	184 (31.2)	239 (40.5)	
Deaths, *n*	23	26	41	
Person-years	1863.9	2033.2	2638.2	
HR (95% CI)				
Age- and sex-adjusted	1.00	1.01 (0.57–1.77)	1.16 (0.69–1.95)	0.79
Multivariable[2]	1.00	1.00 (0.55–1.83)	1.25 (0.72–2.21)	0.64

HR hazard ratio, *CI* confidence interval, *CVD* cardiovascular disease

[1]Any coffee consumption

[2]Cox regression model adjusted for age (65–74, ≥ 75 years), sex, study (EUREYE study, Valencia Nutrition Survey), education (< Primary, ≥Primary school), BMI (< 25, 25.0–29.9, ≥ 30), waist circumference (normal, moderate and large); sleep (h/day), smoking (current; past and never), self-reported diabetes (no/yes), high cholesterol (no/yes), hypertension (no/yes), relative Mediterranean Diet, main physical activity (very low, low–moderately active), and at leisure time (low, moderate–high)

[3]*p* value from likelihood ratio test

our study had limited power to obtain significant associations of this magnitude by type and amount of coffee.

Before accepting our findings, we should consider some limitations in our study. First, we were not able to control for possible changes in coffee consumption during the follow-up, although we assumed that coffee consumption among elderly subjects was a habit that had been adopted years ago and was unlikely to change over the years. Furthermore, it has been suggested that a single assessment could be adequate to assess usual coffee drinking in the medium-to-long-term [9]. Second, a high proportion of participants reported one or more pre-existing chronic diseases at baseline which may influence coffee consumption and early mortality; however, we ran models excluding deaths in the first year and adjusting for the main self-reported diseases and the effect estimates were basically unchanged, although they were less precise (data not shown). Third, the fact that the participants were volunteers might have produced some response bias, although consumption among our study participants was similar to that shown in other studies with an elderly population in the Valencia Region [45].

On the other hand, our study has several strengths. We had well-defined, relatively homogeneous populations, from a Mediterranean area in Spain from which we obtained high-quality information on baseline characteristics, lifestyles, diet and other factors in a personal interview, following standard protocols and validated questionnaires [22–24, 26], and therefore, we were able to obtain adjusted estimates making confounding less likely. In addition, the information on coffee consumption was gathered before the outcome occurred, and therefore, any potential differential misclassification of the main determinant was essentially avoided. However, before generalizing or inferring any causality from our results to an elderly population, we should bear in mind that our study was observational. Thus, before recommending coffee as a safe beverage in elderly people, our results should be further confirmed in other elderly populations, if possible, in large prospective cohort studies, collecting information about methods of coffee preparation and the amount of caffeinated and decaffeinated coffee.

In summary, this study shows that the consumption of more than one cup of coffee a day is associated with lower cardiovascular mortality in the elderly, and has no harmful effects for total or cancer mortality. These results are consistent with the two previous studies, and therefore, coffee consumption appears to be safe for elderly people and may be integrated in a healthy diet. Since coffee consumption is very prevalent in elderly people, further investigation is needed to confirm these findings and to distinguish any differential effects for caffeinated or decaffeinated coffee.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest or any financial interest with study results.

Ethical standards Ethical approval for the studies was given by the Local Ethical Committee of the Hospital of San Juan and the Miguel Hernandez University, Alicante, Spain. Written informed consent was obtained from all subjects.

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