

Alcohol Consumption and Mortality in the Korean Multi-center Cancer Cohort Study

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Objectives: To examine the association between alcohol consumption habit, types of beverages, alcohol consumption quantity, and overall and cancer-specific mortality among Korean adults.

Methods: The alcohol consumption information of a total of 16 320 participants who were 20 years or older from the Korean Multi-center Cancer Cohort were analyzed to examine the association between alcohol consumption habit and mortality (median follow-up of 9.3 years). The Cox proportional hazard model was used to estimate the hazard ratio (HR) of alcohol consumption to mortality adjusting for age, sex, geographic areas, education, smoking status, and body mass index.

Results: Alcohol drinkers showed an increased risk for total mortality compared with never drinkers (HR, 1.72; 95% confidence interval [CI], 1.38 to 2.14 for past drinkers; HR, 1.21; 95% CI, 1.06 to 1.39 for current drinkers), while past drinkers only were associated with higher risk for cancer deaths (HR, 1.84; 95% CI, 1.34 to 2.53). The quantity of alcohol consumed per week showed a J-shaped association with risk of mortality. Relative to light drinkers (0.01 to 90 g/wk), never drinkers and heavy drinkers (>504 g/wk) had an increased risk for all-cause and cancer deaths: (HR, 1.18; 95% CI, 0.96 to 1.45) and (HR, 1.39; 95% CI, 1.05 to 1.83) for all-cause mortality; and (HR, 1.55; 95% CI, 1.15 to 2.11) and (HR, 2.07; 95% CI, 1.39 to 3.09) for all cancer mortality, respectively. Heavy drinkers (>504 g/wk) showed an elevated risk for death from stomach and liver cancers.

Conclusions: The present study supports the existence of a J-shaped association between alcohol consumption quantity and the risk of all-cause and cancer deaths. Heavy drinkers had an increased risk of death from cancer overall and liver and stomach cancer.

Key words: Alcohol drinking, Mortality, Korean Multi-center Cancer Cohort, Korea

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INTRODUCTION

Excessive alcohol consumption causes 75 000 deaths each year in the United States, and it is the third leading preventable cause of death. Binge drinking accounts for more than half of these deaths [1]. High alcohol consumption is positively related to the risk of certain cancers, hypertension, liver diseases, injuries, and violence [2-4]. However, in the elderly, light to moderate alcohol consumption is associated with lower risks for heart disease, diabetes, dementia, psychosocial func-

tioning, and mortality due to cancer [2-4]. Due to a combination of beneficial and harmful effects, the relationship between alcohol consumption dose and all-cause mortality has been depicted as a J-shaped curve [5-7].

Most studies on the effects of alcohol consumption on all-cause or disease-specific mortality [8,9] have been from a Caucasian perspective, and little is known about whether there is a genetic susceptibility to the effects of alcohol on cancer among Asian men and women because it may differ from other populations [4,10,11]. Moreover, a large portion of Korean men drink alcohol extensively, and the prevalence of alcohol dependence and alcohol abuse is much higher in Korea compared to other countries [12].

The aim of this study was to examine the association between alcohol consumption and all-cause and cancer-specific mortality in the Korean population from the Korean Multi-center Cancer Cohort (KMCC) data.

METHODS

Study Population

The KMCC was built based on 4 rural and urban areas to determine the relationship between lifestyle habits, molecular genetic factors, and the risk of cancers. Information on lifestyle, disease history, family history, female reproductive factors, dietary habits, and demographics was collected [13]. Written informed consent was obtained from all of the participants, and the Institutional Board of Human Research at Seoul National University College of Medicine approved the study.

A total of 20 059 subjects participated in the KMCC between 1993 and 2004. Among them, 1570 participants recruited from two areas (Sancheong and Uiryeong) were excluded because no information was available on alcohol consumption habits, 1484 participants who were younger than 20 years old at the baseline of enrollment were excluded, and an additional 685 subjects were excluded due to missing information on alcohol consumption. The number of subjects in the final study population included in the analysis was 16 320.

Information on the date and causes of death was obtained from death certificate data from the Korea National Statistics Office. Cause of death was classified according to the 10th revision of the International Classification of Disease (ICD-10). The ICD-10 codes used to classify specific cancers that had relatively high mortalities in Korea were as follows: all types of cancer (C00-C97), lung cancer (C34), stomach cancer (C16), and

liver cancer (C22).

Estimation of Alcohol Consumption

Alcohol consumption was assessed at cohort entry using a structured questionnaire. Participants were asked to answer questions on whether they ever drank alcoholic beverages; "Yes", "Yes, but not now", or "No" were the answer options to the question, "Have you ever drunk alcohol?", as used in the National Alcohol Survey [14]. Concerning drinking status, participants were divided into 3 groups: never drinkers, past drinkers, and current drinkers, with the latter two also denoted as "drinkers" in this paper. The frequency of consumption was presented as more than 2 times a day, daily, 4 to 6 times a week, 2 to 3 times a week, weekly, 2 to 3 times a month, or less than once a month. The question on the type of alcoholic beverage, which included soju, beer, and raw rice wine (makkoli) and the average amount of alcohol consumption over the past one year was asked as: "How much do you drink of a type of an alcoholic beverage at 1 sitting?" The most frequently consumed alcoholic beverage was soju.

Regarding the type of alcoholic beverages, 'mixed' means drinking two or more kinds of beverages, and 'alone' means drinking only one type of beverage. For example, soju 'mixed' means that soju was consumed with other alcoholic beverages at least one time over the past year. About 39% of the current drinkers consumed soju 'mixed' with other alcoholic beverages in this study.

To calculate the alcohol consumption quantity, we multiplied the amount of alcohol in a drink by the concentration of each beverage and we calculated the frequency of alcohol intake per week and weight of each beverage by multiplying 0.8 by the volume. Concerning the consumption amount, they were divided into 5 groups: nondrinkers, ≤ 90 g/wk, 90.01 to 252 g/wk, 252.01 to 504 g/wk, and > 504 g/wk based on the quartile distribution of cases of death among current drinkers.

Statistical Analysis

To describe the baseline characteristics of the study, participants were compared using the chi-squared test for categorical variables and the *t*-test or ANOVA for continuous variables. Hazard ratios (HRs) and corresponding 95% confidence intervals (CIs) for alcohol consumption groups and their association with overall and disease-specific mortality were obtained with the Cox proportional hazards regression models, and follow-up time was used as a time-scale. The analysis was performed

in both men and women combined due to the small number of female alcohol drinkers.

The associations of interaction between alcohol consumption status, alcohol consumption amount, and other covariates in the final model with sex were tested, and there was no interaction. All models were adjusted for sex, age group (20 to 29, 30 to 39, 40 to 49, 50 to 59, 60 to 69, and ≥ 70 years), 3 geographic areas (Haman, Chungju, plus Youngil and Uljin together), smoking status (never, past, and current), educational level (uneducated, 1 to 12, ≥ 13 years), and body mass index (BMI) in quintile form (< 20.89 , 20.89 to 22.65, 22.66 to 24.30, 24.31 to 26.27, and ≥ 26.28). Sensitivity analyses were performed after excluding the all-cause mortality that had occurred in the first 2 years of follow-up. Analyses were performed with SAS version 9.2 (SAS Inc., Cary, NC, USA).

RESULTS

The general characteristics of the study population are shown in Table 1. Past and current drinkers were more likely to be male, whereas never drinkers were mostly female. Those of the old age group (age 60 years and older) were more likely to be past or current drinkers, whereas those in the 30 to 39 and 40 to 49 age groups were more likely to be current drinkers. Never drinkers were more likely to be never smokers, past and current drinkers were more likely to be smokers, and past and current drinkers were more likely to have low BMI (≤ 24.3).

Never, past, and current drinkers were all more likely to be negative than positive for diabetes. However, participants with hypertension were more likely to be past drinkers than never drinkers or current drinkers, while alcohol consumption status and prevalence of diabetes and hypertension were not signifi-

Table 1. General characteristics of the study population at the time of recruitment

	n (%)	Never drinker ¹	Past drinker	Current drinker	p-value
Total	16 320 (100)	9766 (59.8)	638 (3.9)	5916 (36.3)	
Sex					<0.001
Male	6405 (39.3)	1782 (18.2)	508 (79.6)	4115 (69.6)	
Female	9915 (60.7)	7984 (82.8)	130 (20.4)	1801 (30.4)	
Age					<0.001
20-29	563 (3.4)	205 (2.1)	12 (1.9)	346 (5.8)	
30-39	1756 (10.8)	888 (9.1)	35 (5.5)	833 (14.1)	
40-49	3146 (19.3)	1892 (19.4)	65 (10.2)	1189 (20.1)	
50-59	4184 (25.6)	2622 (26.8)	145 (22.7)	1417 (23.9)	
60-69	4696 (28.8)	2930 (30.0)	233 (36.5)	1533 (25.9)	
≥ 70	1975 (12.1)	1229 (12.6)	148 (23.2)	598 (10.1)	
Educational attainment (y)					<0.001
No formal education	3526 (21.6)	2473 (25.8)	139 (22.0)	914 (15.5)	
1-12	12 205 (74.8)	6942 (72.3)	480 (75.8)	4783 (81.3)	
≥ 13	381 (2.3)	182 (1.9)	14 (2.2)	185 (3.2)	
Missing	208 (1.3)				
Smoking habit					<0.001
Never smoker	10 187 (62.4)	7816 (81.9)	159 (25.0)	2212 (37.5)	
Ex-smoker	1510 (9.2)	414 (4.3)	223 (35.0)	873 (14.8)	
Current smoker	4378 (26.8)	1313 (13.8)	255 (40.0)	2810 (47.7)	
Missing	245 (1.5)				
Body mass index					<0.001
< 20.89	4044 (24.8)	2337 (23.9)	192 (30.1)	1515 (25.6)	
20.89-22.65	3075 (18.8)	1744 (17.9)	124 (19.4)	1207 (20.4)	
22.66-24.30	3062 (18.8)	1825 (18.7)	105 (16.5)	1132 (19.1)	
24.31-26.27	3071 (18.8)	1890 (19.4)	106 (16.6)	1075 (18.2)	
≥ 26.28	3068 (18.8)	1970 (20.2)	111 (17.4)	987 (16.7)	

Values are presented as n (%). The sum of the column percentage might exceed 100 because each is a rounded-up value.

¹Column percentage.

cantly related (data not shown).

During the mean follow-up of 9.3 years with 151 402.4 person-years, 1209 deaths were observed. Among them, 505 were cancer deaths, and the leading causes were lung cancer (n = 123), stomach cancer (n = 93), and liver cancer (n = 85).

Table 2 shows the HRs of the all-cause and cancer-specific mortalities according to alcohol drinking habit. Past drinkers (HR, 1.72; 95% CI, 1.38 to 2.14) and current drinkers (HR, 1.21; 95% CI, 1.06 to 1.39) had a significantly higher risk for all-cause mortality. In the past drinker group, significantly higher risks for mortality from all types of cancer, stomach cancer, and liver cancer were observed (overall cancer: HR, 1.84; 95% CI, 1.34 to 2.53; stomach cancer: HR, 2.30; 95% CI, 1.17 to 4.51; liver cancer: HR, 3.18; 95% CI, 1.50 to 6.71) compared to never drinkers. Among current drinkers, no statistically significant association was found for cancer mortality. Past drinkers did not have a significant relationship to death due to lung cancer. In addition, current drinkers also did not have a significant relationship to death due to all types of cancer, and lung, stomach, and liver cancer when added to the multivariate models, which included age, sex, and other risk factors, whereas current drinkers adjusted for age only had a statistically significant relationship with the same causes of death.

Table 3 shows the hazard ratios for the all-cause and cancer-specific mortalities according to alcohol consumption amount. The risk of total mortality increased according to weekly alcohol consumption quantity in drinkers (>90, ≤252 g/wk, HR, 1.29; 95% CI, 0.99 to 1.66; >252, ≤504 g/wk, HR, 1.31, 95% CI; 1.00 to 1.71; >504 g/wk, HR, 1.39; 95% CI, 1.05 to 1.83), although there was a marginally, not statistically, significant increased risk among never drinkers (HR, 1.18; 95% CI, 0.96 to 1.45). Compared to current drinkers of 0.01 to 90 g/wk, the risk of cause-specific mortalities increased significantly in heavy drinkers and nondrinkers. An association was found among non-drinkers with all types of cancer (HR, 1.55; 95% CI, 1.15 to 2.11) and lung cancer (HR, 2.07; 95% CI, 1.05 to 4.08), and heavy drinking (>504 g/wk) increased the risk of all types of cancer (HR, 2.07; 95% CI, 1.39 to 3.09), stomach cancer, and liver cancer. Alcohol consumption of 90.01 to 252 g/wk increased the risk of mortality due to all types of cancer and lung cancer specifically. Alcohol consumption of 252.01 to 504 g/wk also increased the risk of all types of cancer. However, drinking did not show a significant relationship with mortality caused by the cancers mentioned above when the mortality values were adjusted for the education level and geographical area.

Table 4 shows the hazard ratios of total mortality according

Table 2. Hazard ratios and 95% confidence intervals for all-cause and cancer deaths according to alcohol consumption status in the KMCC study subjects from 1993 to 2004 (n = 16 320)

Cancer deaths	ICD-10	No. of deaths	Alcohol consumption status		
			Never drinker	Past drinker	Current drinker
All-cause deaths	A00-Z99	1209	568 ¹	112	529
	Model 1 ²		1.0	1.72 (1.38, 2.14)	1.21 (1.06, 1.39)
	Model 2 ³		1.0	2.51 (2.05, 3.08)	1.89 (1.67, 2.13)
Cancer deaths					
All cancers	C00-C97	505	222	56	227
	Model 1		1.0	1.84 (1.34, 2.53)	1.09 (0.88, 1.35)
	Model 2		1.0	3.40 (2.53, 4.56)	2.08 (1.72, 2.50)
Lung and bronchus	C34	123	52	12	59
	Model 1		1.0	1.28 (0.66, 2.47)	0.94 (0.62, 1.42)
	Model 2		1.0	3.09 (1.65, 5.81)	2.34 (1.61, 3.41)
Stomach	C16	93	35	14	44
	Model 1		1.0	2.30 (1.17, 4.51)	1.14 (0.70, 1.87)
	Model 2		1.0	5.34 (2.86, 9.95)	2.54 (1.63, 3.96)
Liver	C22	85	34	11	40
	Model 1		1.0	3.18 (1.50, 6.71)	1.27 (0.75, 2.15)
	Model 2		1.0	4.78 (2.41, 9.45)	2.30 (1.45, 3.63)

KMCC, Korean Multi-center Cancer Cohort; ICD-10, the 10th revision of the International Classification of Disease.

¹Number of deaths for each specific cause divided by the alcohol consumption status. ²Adjusted for age, sex, body mass index, smoking habit, geographic area, and educational attainment. ³Adjusted for age.

to type of alcoholic beverages. Total mortality showed a statistically significant relationship with drinking soju alone (HR, 1.23; 95% CI, 1.04 to 1.46) and raw rice wine alone (HR, 1.54; 95% CI, 1.10 to 2.16), whereas other beverages did not show a statistically significant relationship. Drinking raw rice wine with other

beverages (raw rice wine mixed) was marginally significant (HR, 1.19; 95% CI, 0.96 to 1.47). Mixed soju drinkers were not significantly related to total mortality; mixed beer and mixed raw rice wine drinkers also were not significantly related to death due to all-cause death when added to the multivariate

Table 3. Hazard ratios and 95% confidence intervals for all-cause and cancer deaths according to alcohol consumption amount per week (g) in the KMCC study subjects from 1993 to 2004 (n = 15 683)

Cancer deaths	ICD-10	No. of deaths	Alcohol consumption amount per week (g)				
			Never drinker	0.01-90	90.01-252	252.01-504	>504.01
All-cause deaths ¹	A00-Z99	1122	680 ² 1.18 (0.96, 1.45) ³	112 1.0	128 1.29 (0.99, 1.66) ³	108 1.31 (1.00, 1.71)	94 1.39 (1.05, 1.83)
Cancer deaths ⁴							
All cancers	C00-C97	482	278 1.55 (1.15, 2.11)	51 1.0	57 1.70 (1.16, 2.49)	50 1.84 (1.24, 2.72)	46 2.07 (1.39, 3.09)
Lung and bronchus	C34	114	64 2.07 (1.05, 4.08)	10 1.0	18 2.59 (1.19, 5.63)	12 2.12 (0.91, 4.92)	10 2.09 (0.87, 5.03)
Stomach	C16	90	49 1.94 (0.91, 4.15)	8 1.0	13 2.37 (0.98, 5.74) ³	9 2.06 (0.79, 5.35)	11 2.93 (1.18, 7.31)
Liver	C22	82	45 1.74 (0.80, 3.76)	8 1.0	10 1.95 (0.77, 4.97)	8 1.99 (0.72, 5.18)	11 3.50 (1.40, 8.78)

The amount of beverages consumed by past drinkers was treated as 0 g/wk, and 15 683 subjects' alcohol consumption quantities were available. KMCC, Korean Multi-center Cancer Cohort; ICD-10, the 10th revision of the International Classification of Disease.

¹Model 1: adjusted for age, sex, body mass index, smoking habit, geographic area, and educational attainment. ²Number of deaths due to all-cause deaths and all-cancer deaths. ³Marginal significance $0.05 \leq p < 0.1$. ⁴Model 2: adjusted for age, sex, body mass index, and smoking habit.

Table 4. HR and 95% CI for all-cause deaths according to the type of alcohol beverage in the KMCC study subjects from 1993 to 2004 (n = 15 683)

Type of beverage ¹	Total	Alcohol consumption amount per week (g) ¹	No. of deaths	Model	HR (95% CI)	
Never drinker	9766	0	568		1.0	
Soju	Mixed	2308	151.8	146	Model 1 ²	1.09 (0.89, 1.33)
					Model 2 ³	1.63 (1.36, 1.96)
	Alone	2287	232.8	248	Model 1	1.23 (1.04, 1.46)
					Model 2	2.12 (1.82, 2.46)
Beer	Mixed	1806	54.2	67	Model 1	0.90 (0.69, 1.18)
					Model 2	1.32 (1.02, 1.70)
	Alone	383	47.2	10	Model 1	0.77 (0.41, 1.45)
					Model 2	0.99 (0.53, 1.86)
Raw rice wine	Mixed	1158	168	120	Model 1	1.19 (0.96, 1.47) ⁴
					Model 2	1.74 (1.43, 2.12)
	Alone	252	243.6	38	Model 1	1.54 (1.10, 2.16)
					Model 2	1.77 (1.27, 2.46)
Sake, wine	Mixed	359	56.9	17	Model 1	0.74 (0.45, 1.20)
					Model 2	1.06 (0.66, 1.72)
	Alone	46	170.5	2	Model 1	0.52 (0.13, 2.09)
					Model 2	0.75 (0.19, 2.99)

HR, hazard ratio; CI, confidence interval; KMCC, Korean Multi-center Cancer Cohort.

¹The intake levels of each individual alcoholic beverage among the drinkers. ²Adjusted for age, sex, body mass index, smoking habit, geographic area, and educational attainment. ³Adjusted for age. ⁴Marginal significance $0.05 \leq p < 0.1$.

model including for age, sex, and other risk factors, whereas those adjusted for age only were statistically significant.

DISCUSSION

In this analysis, we found J-shaped associations between the amount of alcohol consumed and the risk of mortality due to all causes, overall cancer, and liver cancer. The J-shaped association between alcohol consumption and all-cause mortality is well established so far, whereby light to moderate drinkers have a lower mortality rate, and heavy drinkers have a higher mortality rate [15,16]. The J-shaped association has been suggested to explain the cardioprotective effect of moderate drinking including the effects on lipids and hemostatic factors [17,18], and this explanation was partially reasonable in light of the results of this study because total mortality included death due to coronary heart disease.

In a cohort study of Japanese physicians, the relative risk of all-cause mortality was 30% higher in heavy drinkers than non-drinkers [19]. Among our study participants, when the amount of alcohol consumption became higher, the risk of total death compared to the 0.01 to 90 g/wk consumption level increased significantly, and all-cause mortality in heavy drinkers increased relatively, which might have resulted in the quite high mortality from overall cancer that was found.

In our study, we found that past drinkers had a higher mortality due to overall cancer, stomach cancer, and liver cancer. Alcohol consumption of more than 90 g/wk also increased the risk of death from overall cancer and lung cancer (90.01 to 252 g/wk), and an increased risk was shown for overall cancer, stomach cancer, and liver cancer (>504 g/wk). Alcohol has been classified as a group 1 carcinogen by the International Agency for Research on Cancer. It is consistently reported to increase the risk of cancers in the oral cavity, pharynx, larynx, esophagus, colon, liver, and female breast [20]. In a study in the US, heavy consumption of alcohol at the study baseline and at age 45 was associated with more than doubling the risk for lung squamous cell carcinoma (HR for ≥ 3 drinks/d at the study baseline, 2.54; 95% CI, 1.36 to 4.73; *p*-trend, 0.002), but not for lung adenocarcinoma [21]. However, it is often difficult to separate the effects of heavy alcohol intake and smoking in observational studies because the two are highly correlated; the mechanism from alcohol that promotes lung cancer is unclear, and the findings on the relationship between alcohol and lung cancer are mixed in the literature and need to be further in-

vestigated with experimental studies in order to confirm the association [22]. In this study, we did not include pack-year, duration of smoking, or passive smoking; hence, the results of this study on the relationship between alcohol and lung cancer might have been due to not sufficiently adjusting for the above factors. In a pooled analysis study based on 4 prospective cohort studies encompassing 174 719 participants in Japan, a significantly increased risk for primary liver cancer among heavy drinkers in both sexes was observed [23]. In a cohort study among 1.34 million Koreans, alcohol consumption was positively associated with the risk of death from stomach cancer [24]. In another cohort study in Korea, a marginally increased risk of stomach cancer among those with a salt preference was found [25]. However, in much of the literature, a confirmed association was scarce, and unequivocal evidence on the effects of salt intake on death from gastric cancer remains controversial, so we did not include that dietary factor in the final model. We also did not find the impact of alcohol drinking on death due to colorectal cancer, pancreatic cancer, biliary tract cancer, or esophageal cancer. However, the number of participants with these cancers was so small that it would not be statistically significant (data not shown).

In this study, we found that Korea's traditional beverages, soju and raw rice wine, increased the risk of total mortality. In a study from Australia, for males, the HRs for beer increased with the amount consumed (*p*-trend, 0.05) to a maximum of 1.56 for those who consumed 60 g/d or more [26]. Studies have shown that the risk of all-cause death and overall cancer increases according to the type of alcoholic beverage, and wine has been found to have a protective effect on total mortality [27]. However, some studies did not find any difference in risk according to type of alcoholic beverage, and there was some possibility that the positive association in the above results was attributable to the alcohol concentration of each beverage, or that the most frequently consumed beverage in each region performed studies above tended to be the one with the highest association [28].

Our study also has notable strengths. First, our mortality data was collected from the National Death Certificate System, which covers more than 90% of the deaths in the Korea. Second, we found that soju increased the risk of total mortality among drinkers. Although soju is a traditional and very popular beverage in Korea, it has not yet been studied properly. Therefore, this study is valuable for promoting awareness on the risks of excessive drinking of soju in Korea.

This study has several limitations. First, because alcohol consumption was assessed at the baseline only, we could not consider the changes in drinking habits over time. The validity of the results could have increased if we had performed repeated measures because the alcohol consumption patterns might have changed after the enrollment period. However, repeated measures could not weaken the significant association between alcohol consumption and total and cause-specific mortalities in this study, but would help to reinforce the association more clearly. Second, the number of subjects and follow-up duration were limited in the analysis of mortality for medium- to low-rate cancers. Third, we cannot rule out the possibility that our results were affected by residual confounding factors, for example, pack-years of smoking, passive smoking, and salt preference.

Despite these limitations, our study determined the association between exposure distributions and mortality using unique drinking culture as well as total and cancer-specific mortalities among Koreans. In addition, considering reverse causation, we excluded the all-cause mortalities that have occurred in the first 2 years of follow-up, and we had consistent results from the sensitivity analysis.

In conclusion, consuming alcohol may increase the risk of total mortality and mortality due to a specific cancer, particularly among soju drinkers. Significant relationships between alcohol amount and overall mortality, and mortality from lung, stomach, and liver cancer also exist. Considering the mortality according to alcohol consumption in Korea, we need to take proper measures in order to prevent deaths due to all-cause death and cancer arising from drinking, and measures addressed to the general population to increase the exposure to information on alcohol consumption in proper amounts would have more public health implications than control measures focused primarily on high alcohol consumers. Furthermore, further research might be needed to confirm the effects of the type of beverage on mortality.

CONFLICT OF INTEREST

The authors have no conflicts of interest with the material presented in this paper.

REFERENCES

1. Sull JW, Yi SW, Nam CM, Choi K, Ohrr H. Binge drinking and

hypertension on cardiovascular disease mortality in Korean men and women: a Kangwha cohort study. *Stroke* 2010;41(10):2157-2162.

2. Ferreira MP, Weems MK. Alcohol consumption by aging adults in the United States: health benefits and detriments. *J Am Diet Assoc* 2008;108(10):1668-1676.
3. Karlamangla AS, Sarkisian CA, Kado DM, Dedes H, Liao DH, Kim S, et al. Light to moderate alcohol consumption and disability: variable benefits by health status. *Am J Epidemiol* 2009;169(1):96-104.
4. Mukamal KJ, Rimm EB. Alcohol consumption: risks and benefits. *Curr Atheroscler Rep* 2008;10(6):536-543.
5. Bongaerts BW, van den Brandt PA, Goldbohm RA, de Goeij AF, Weijnenberg MP. Alcohol consumption, type of alcoholic beverage and risk of colorectal cancer at specific subsites. *Int J Cancer* 2008;123(10):2411-2417.
6. Fan Y, Yuan JM, Wang R, Gao YT, Yu MC. Alcohol, tobacco, and diet in relation to esophageal cancer: the Shanghai Cohort Study. *Nutr Cancer* 2008;60(3):354-363.
7. La Vecchia C. Alcohol and liver cancer. *Eur J Cancer Prev* 2007;16(6):495-497.
8. Fan AZ, Russell M, Dorn J, Freudenheim JL, Nochajski T, Hovey K, et al. Lifetime alcohol drinking pattern is related to the prevalence of metabolic syndrome. *The Western New York Health Study (WNYHS)*. *Eur J Epidemiol* 2006;21(2):129-138.
9. Sung KC, Kim SH, Reaven GM. Relationship among alcohol, body weight, and cardiovascular risk factors in 27,030 Korean men. *Diabetes Care* 2007;30(10):2690-2694.
10. Kim S, Popkin BM, Siega-Riz AM, Haines PS, Arab L. A cross-national comparison of lifestyle between China and the United States, using a comprehensive cross-national measurement tool of the healthfulness of lifestyles: the Lifestyle Index. *Prev Med* 2004;38(2):160-171.
11. Zheng W, Chow WH, Yang G, Jin F, Rothman N, Blair A, et al. The Shanghai Women's Health Study: rationale, study design, and baseline characteristics. *Am J Epidemiol* 2005;162(11):1123-1131.
12. Min S, Noh S, Shin J, Ahn JS, Kim TH. Alcohol dependence, mortality, and chronic health conditions in a rural population in Korea. *J Korean Med Sci* 2008;23(1):1-9.
13. Yoo KY, Shin HR, Chang SH, Lee KS, Park SK, Kang D, et al. Korean Multi-center Cancer Cohort Study including a Biological Materials Bank (KMCC-I). *Asian Pac J Cancer Prev* 2002;3(1):85-92.
14. Greenfield TK, Kerr WC, Bond J, Ye Y, Stockwell T. Graduated Fre-

- frequencies alcohol measures for monitoring consumption patterns: results from an Australian national survey and a US diary validity study. *Contemp Drug Probl* 2009;36(3-4):75056015.
15. Fuchs CS, Stampfer MJ, Colditz GA, Giovannucci EL, Manson JE, Kawachi I, et al. Alcohol consumption and mortality among women. *N Engl J Med* 1995;332(19):1245-1250.
 16. Thun MJ, Peto R, Lopez AD, Monaco JH, Henley SJ, Heath CW Jr, et al. Alcohol consumption and mortality among middle-aged and elderly U.S. adults. *N Engl J Med* 1997;337(24):1705-1714.
 17. Zakhari S. Alcohol and the cardiovascular system: molecular mechanisms for beneficial and harmful action. *Alcohol Health Res World* 1997;21(1):21-29.
 18. Rimm EB, Williams P, Fosher K, Criqui M, Stampfer MJ. Moderate alcohol intake and lower risk of coronary heart disease: meta-analysis of effects on lipids and haemostatic factors. *BMJ* 1999;319(7224):1523-1528.
 19. Kono S, Ikeda M, Tokudome S, Nishizumi M, Kuratsune M. Cigarette smoking, alcohol and cancer mortality: a cohort study of male Japanese physicians. *Jpn J Cancer Res* 1987;78(12):1323-1328.
 20. International Agency for Research on Cancer. IARC strengthens its findings on several carcinogenic personal habits and household exposures; 2009 [cited 2012 Sep 17]. Available from: http://www.iarc.fr/en/media-centre/pr/2009/pdfs/pr196_E.pdf.
 21. Chao C, Li Q, Zhang F, White E. Alcohol consumption and risk of lung cancer in the VITamins And Lifestyle Study. *Nutr Cancer* 2011;63(6):880-888.
 22. Bandera EV, Freudenheim JL, Vena JE. Alcohol consumption and lung cancer: a review of the epidemiologic evidence. *Cancer Epidemiol Biomarkers Prev* 2001;10(8):813-821.
 23. Shimazu T, Sasazuki S, Wakai K, Tamakoshi A, Tsuji I, Sugawara Y, et al. Alcohol drinking and primary liver cancer: a pooled analysis of four Japanese cohort studies. *Int J Cancer* 2012;130(11):2645-2653.
 24. Kim MK, Ko MJ, Han JT. Alcohol consumption and mortality from all-cause and cancers among 1.34 million Koreans: the results from the Korea national health insurance corporation's health examinee cohort in 2000. *Cancer Causes Control* 2010;21(12):2295-2302.
 25. Kim J, Park S, Nam BH. Gastric cancer and salt preference: a population-based cohort study in Korea. *Am J Clin Nutr* 2010;91(5):1289-1293.
 26. Baglietto L, English DR, Hopper JL, Powles J, Giles GG. Average volume of alcohol consumed, type of beverage, drinking pattern and the risk of death from all causes. *Alcohol Alcohol* 2006;41(6):664-671.
 27. Gronbaek M, Becker U, Johansen D, Gottschau A, Schnohr P, Hein HO, et al. Type of alcohol consumed and mortality from all causes, coronary heart disease, and cancer. *Ann Intern Med* 2000;133(6):411-419.
 28. Bagnardi V, Blangiardo M, La Vecchia C, Corrao G. A meta-analysis of alcohol drinking and cancer risk. *Br J Cancer* 2001;85(11):1700-1705.