

RESEARCH ARTICLE

Population Based Study of the Association Between Binge Drinking and Mortality from Cancer of Oropharynx and Esophagus in Korean Men: the Kangwha Cohort Study

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Abstract

We assessed the association between frequency of heavy binge drinking and mortality from oropharynx and esophagus cancer after controlling for the total volume of alcohol intake among Korean men. The cohort comprised 2,677 male residents in Kangwha County, aged 55 or older in March 1985, for their upper digestive tract cancer mortality for 20.8 years up to December 31, 2005. For daily binge drinkers versus non-drinkers, the hazard ratios (95% CIs) for mortality were 4.82 (1.36, 17.1) and 6.75 (1.45, 31.4) for oropharyngeal and esophageal cancers, respectively. Even after adjusting for the volume of alcohol intake, we found the hazard ratios for frequency of binge drinking and mortality of oropharyngeal or esophageal cancer to not change appreciably: the hazard ratios were 4.90 (1.00, 27.0) and 7.17 (1.02, 50.6), respectively. For esophageal cancer, there was a strong dose-response relationship. The frequency of heavy binge drinking and not just the volume of alcohol intake may increase the risk of mortality from upper digestive tract cancer, particularly esophageal cancer in Korean men. These findings need to be confirmed in further studies with a larger sample size.

Keywords: Binge drinking - alcohol consumption - oropharyngeal and oesophageal cancer - 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 (CDC, 2004). Binge drinking is quite prevalent in Korea. According to The Third Korea National Health and Nutrition Examination Survey in 2005, 46.3 % of male adults were heavy drinkers in Korea (Lee et al., 2010). In some studies, alcohol consumption has been associated with risks of upper digestive tract cancer, liver cancer and colon cancer as well as breast cancer (Gronbaek et al., 1998; Seitz et al., 1998; La Vecchia, 2007; Bongaerts et al., 2008; Fan et al., 2008; Yi et al., 2010).

Binge drinking, defined as having a substantial amount of drinking on one occasion, may increase risk of cancers as well as cardiovascular disease (CVD) (Malyutina et al., 2002; Mokdad et al., 2007; Morch et al., 2007). Our previous study also reported that heavy binge drinkers had higher hazard ratio of death for CVD mortality compared with non-drinkers (Sull et al., 2009). However, there have been few attempts as yet at cohort studies of the association

between binge drinking and upper digestive tract cancer mortality. Some epidemiological studies have found an association between alcohol intake and the cancers of oral cavity, pharynx and pancreases (Bagnardi et al., 2001; Haas et al., 2012; Yaegashi et al., 2014). In this study, we examined the association of heavy binge drinking frequency with the mortality of upper digestive tract cancer after controlling the total volume of alcohol intake among Korean men through over 20.8-years followed-up of the Kangwha cohort data.

Materials and Methods

Study population

The Kangwha County Cancer Registry was started in 1983 when nationwide medical insurance was implemented in the area (Ohrr et al., 1997). The number of Kangwha County residents who were 55 years of age or older in February 1985 was 9,378. Among them, 67.9% or 6,372 residents participated in interviews and measurements of blood pressure and body mass. Details of the Kangwha cohort study have been published elsewhere (Sull et al., 2009). Participants who were not

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followed up after the initial survey (n=78), suffered cancer before (n=7), or had no information on alcohol intake at entry or education, or smoking amount (n=24) were all excluded, and thus the final study population recruited was 6,263 (male, 2,677; female, 3,586). For a small number of women engaged in binge drinking (n=19) and there was not any mortality from cancer of upper digestive tract among them, we included only men in this study. The final study group comprised 2,677 male subjects. The Institutional Review Board of Human Research of Yonsei University approved the study (Approval No. 4-2007-0182). The study subjects were followed up until December 31, 2005, and thus the maximum period of follow-up for mortality was 20.8 years.

Baseline data collection

The primary survey for the Kangwha Cohort was conducted over a month in March 1985. Twenty six trained interviewers performed data collection for a period of one month after one week long training. Each subject was interviewed using a structured questionnaire for demographic characteristics data: education, occupation, health conditions at entry, health behaviors, diet, and other factors. Blood pressure, height, and weight were measured by trained investigators.

Outcome assessment

The cancer was defined according to the 10th edition of the International Classification of Diseases as C01 to C14 (oropharyngeal cancer) and C15 (esophageal cancer). Deaths among subjects from January 1, 1992 to December 31, 2005 were confirmed by matching the information to death records from the National Statistical Office. Follow-up, performed through record linkage at the national level, is complete, except for emigrants. Data for those who died from March 15, 1985 to December 31, 1991 were collected either through calls and visits of trained surveyors twice a year or from records of burial and death certificates of eup- and myeon-offices that are administrative branch offices of local government in Korea.

Estimation of alcohol consumption

Study participants were asked to answer for the question, "Do you drink alcohol?", in "Yes, No". The frequency of drinking was presented as daily, almost daily, 2-3 times a week, 1-4 times a month, or 4-12 times a year. The frequency of drinking were merged to four groups in further analysis: daily, almost daily, few times a month or week (2-3 times a week plus 1-4 times a month or 4-12 times a year), and non-drinkers. The question on the type of alcoholic beverage and the amount of alcohol consumption was given as: "How much (in bottle, glass) do you drink for a type of alcoholic beverage on one occasion?" Study participants were asked to fill in up to two types of alcoholic beverage they usually consume on one occasion. 83.9% of male drinkers filled in one type only and 16.1% two types. Accordingly, binge drinking was defined as having 6 or more drinks in one or two types of alcoholic beverage on one occasion.

To validate those questions on alcohol consumption and examine the change of alcohol consumption patterns,

the research team implemented the second interview with 3,381 survivors in 1994. They were questioned about current drinking status, current drinking frequency, drinking status ten years ago and drinking frequency ten years ago.

Statistical analysis

Continuous variables are shown as means (standard deviations), and were compared using one-way analysis of variance. Categorical variables are shown as counts and percentages, and were compared using χ^2 tests for association. Study participants were divided into drinking group and non-drinking group. The alcohol drinkers were also divided into binge drinkers and non-binge drinkers; they were further divided in accordance with the frequency of binge drinking (daily, almost daily, few times a month or week, non-drinkers). Cox proportional hazards regression models were used to compute hazard ratios of cancer mortality risk using age as the time line. Cox model results were adjusted for age (year of recruitment), history of chronic disease (ever/never), smoking status (never, former, current smokers of 1-19 tobacco/day, and current smokers of ≥ 20 tobacco/day), education status (no education/elementary/high), occupation (agriculture/other), and BMI (as continuous variable) systolic and diastolic blood pressure (as continuous variables). The trend test was also conducted with drinking frequency as an ordinal variable. The outcome of interest was vital status. Hazard ratios (HRs) and 95% confidence intervals (CIs) were expressed for the results. A significance level of $p < 0.05$ was used for all tests. Analyses were performed using SAS Windows Version 9.3.

Results

The general characteristics of binge drinkers, non-binge drinkers, and non-drinkers are shown in Table 1. It was found that binge drinkers tended to be younger than non-drinkers. The association between binge drinking and current smoking among subjects was significant. Moreover, binge drinking have also shown a reliable association with occupation, where the subjects were more likely to have agricultural work. They had also higher mean BMI compared with those non-drinkers and non-binge drinkers, but not statistically significant. What was more consistent was that almost all subjects (98.8%) had received no formal education or had been educated only at an elementary school level. During the 20.8 years of follow-up, a total of 46 men died due to the upper digestive tract cancer (28 oropharyngeal and 18 esophageal).

Table 2 provides hazard ratios of mortality from upper digestive tract cancers in men. Binge drinkers and non-binge drinkers were compared with their non-drinkers. Binge drinkers had higher risks of mortality from oropharyngeal and esophageal cancer. When compared to non-drinkers, binge drinkers were three-fold as likely to die of oropharyngeal cancer. Their hazard ratio (95% CI) of mortality was 3.57 (1.09 to 11.6). When death due to cause of esophageal cancer was considered, the risk of mortality was almost four times (hazard ratio=1.8319, $p=0.028$) higher for binge drinkers. The hazard ratio

Table 1. Baseline Characteristics of the Kangwha Cohort, 1985-2005, According to the Experience of Alcohol Consumption in Korean Men

Characteristics		Non-drinkers (N=932) Mean±SD	Non-Binge drinkers (N=1196) Mean±SD	Binge drinkers (N=549) Mean±SD	F or χ^2 value
Age, year		67.4±7.8	66.1±7.1	64.9±6.5	20.9*
Body mass index, kg/m ²		22.9±23.4	22.4±17.6	23.0±25.3	0.20
Systolic Blood Pressure, mmHg		150.5±74.1	154.3±63.9	154.7±69.4	0.98
Diastolic Blood Pressure, mmHg		76.4±76.9	75.4±63.2	78.2±71.0	0.29
Chronic disease		N (%)	N (%)	N (%)	
Ever	430 (46.1)	544 (45.5)	240 (43.7)	0.84	
Never	502 (53.9)	652 (54.5)	309 (56.3)		
Education					2.92
No	368 (39.5)	488 (40.8)	228 (41.5)		
Elementary	478 (51.3)	617 (51.6)	282 (51.4)		
High	86 (9.2)	91 (7.6)	39 (7.1)		
Occupation					14.7*
Agriculture	580 (62.3)	807 (67.5)	394 (71.8)		
Other	351 (37.7)	389 (32.5)	155 (28.2)		
Smoking					145.4*
Never	266 (28.5)	170 (14.2)	58 (10.6)		
Former	79 (8.5)	90 (7.5)	30 (5.5)		
Current					
1-19 tobacco/day	232 (24.9)	353 (29.5)	112 (20.4)		
≥20 tobacco/day	355 (38.1)	583 (48.8)	349 (63.6)		

*p<0.01

Table 2. Number of Deaths and Adjusted Hazard Ratios of Death from Upper Digestive Tract Cancers (95% Confidence Interval) According to Binge Drinking Among Korean Men

Type of cancer	ICD 10	Non drinkers (n=932)	Alcohol drinkers	
			Non - binge drinkers (n=1196)	Binge drinkers (≥6 drinks) (n=549)
Oropharyngeal cancer	C01-C14			
No. of cases		5	10	13
Person years		23,083	87,916	86,750
HR (95%CI) ¹		1.00	1.58 (0.54-4.63)	4.54 (1.61-12.8)
HR (95%CI) ²		1.00	1.52 (0.51-4.55)	3.57 (1.09-11.6)
HR (95%CI) ³		1.00	1.50 (0.51-4.43)	3.98 (1.38-11.5)
Esophageal cancer	C15			
No. of cases		3	7	8
Person years		3,000	37,916	38,000
HR (95%CI) ¹		1.00	1.89 (0.49-7.35)	5.04 (1.32-19.2)
HR (95%CI) ²		1.00	1.87 (0.48-7.38)	4.62 (1.17-18.3)
HR (95%CI) ³		1.00	1.90 (0.47-7.59)	4.11 (0.89-18.9)

*HR denotes hazard ratio, and CI confidence interval; ¹Adjusted for age only; ²Adjusted for age (recruit year), the history of chronic disease, smoking habits (never, former, 1-19 tobacco/day, and ≥20 tobacco/day), body mass index, and education status, using the Cox proportional hazard model; ³Additionally adjusted for total alcohol consumption**Table 3. Number of Deaths and Adjusted Hazard Ratios of Death from Upper Digestive Tract Cancers (95% Confidence Interval) According to Frequency of Binge Drinking Among Korean Men**

Type of cancer		Non-drinkers (n=932)	Non-binge drinkers (n=1194)	Frequency of binge drinking (≥6 drinks)			p for trend
				Few times a month or week (n=202)	Almost Daily (n=160)	Daily (n=187)	
Oropharyngeal cancer	No. of cases	5	10	3	5	5	
	Person years	23,083	87,916	21,333	32,666	32,750	
	HR (95% CI) ¹	1.00	1.55 (0.53-4.53)	2.52 (0.60-10.5)	5.62 (1.63-19.4)	5.45 (1.58-18.8)	0.016
	HR (95% CI) ²	1.00	1.50 (0.51-4.49)	2.46 (0.58-10.5)	5.06 (1.41-18.2)	4.82 (1.36-17.1)	0.016
	HR (95% CI) ³	1.00	1.59 (0.53-4.79)	2.50 (0.57-10.7)	5.27 (1.24-22.3)	4.90 (1.00-27.0)	0.019
Esophageal cancer	No. of cases	3	7	2	2	4	
	Person years	3,000	37,916	4,916	10,333	22,750	
	HR (95% CI) ¹	1.00	1.79 (0.46-6.91)	2.84 (0.47-17.0)	3.84 (0.64-23.0)	7.07 (1.58-31.6)	0.013
	HR (95% CI) ²	1.00	1.87 (0.48-7.38)	3.14 (0.51-19.4)	3.95 (0.63-25.0)	6.75 (1.45-31.4)	0.007
	HR (95% CI) ³	1.00	2.00 (0.50-8.05)	3.20 (0.51-20.2)	4.17 (0.56-31.0)	7.17 (1.02-50.6)	0.007

*HR denotes hazard ratio, and CI confidence interval; ¹Unadjusted; ²Adjusted for age (recruit year), the history of chronic disease, smoking habits (never, former, 1-19 tobacco/day, and ≥20 tobacco/day), body mass index, and education status, using the Cox proportional hazard model; ³Additionally adjusted for total alcohol consumption

was 4.62 (1.17 to 18.3) for esophageal cancer. There was still significant relationship between binge drinking and oropharyngeal or esophageal cancer mortality, after adjusting for total alcohol consumption.

The effects of frequency of binge drinking on the hazard ratio of mortality in men are shown in Table 3. Binge drinkers had an elevated risk of oropharyngeal and

esophageal cancer death if they had daily binge drinking compared to non-drinkers. The hazard ratio (95%CI) of mortality was 4.82 (1.36 to 17.1) for oropharyngeal cancer, 6.75 (1.45 to 31.4) for esophageal cancer. In case of esophageal cancer, there was strong dose-response relationship between frequency of binge drinking and the cancer mortality (p for trend=0.007). Compared with binge

drinking few times a month or week the risk of esophageal cancer doubled among those drinking daily. When we additionally adjusted for total alcohol consumption, the association with oropharyngeal and esophageal cancer in binge drinkers who drink daily was still significant with a hazard ratio of 4.90 (1.00 to 27.0) and 7.17 (1.02 to 50.6), respectively (Table 3).

Discussion

In the Kangwha Cohort established for people aged 55 or older in 1985, we analyzed binge drinking and mortality from the upper digestive tract cancer. Our study showed that binge drinking was associated with risks of mortality from the oropharyngeal and esophageal cancers. In a meta-analysis on the relationship between alcohol consumption and cancer risk, strong trends in risk were observed for cancers of the oral cavity, pharynx, esophagus and larynx (Bagnardi et al., 2001). A recent study conducted for the Asian population with respect to esophagus cancer, the association was also significantly strong with alcohol consumption, in particular, in heavy drinkers (Ohr et al., 1997; Bagnardi et al., 2001; Malyutina et al., 2002; La Vecchia, 2007; Mokdad et al., 2007; Morch et al., 2007; Fan et al., 2008; Ishiguro et al., 2009; Sull et al., 2009; Yi et al., 2010; Haas et al., 2012). The present study demonstrated that upper digestive tract cancer, including oropharyngeal and esophageal cancers, had a strong relationship with binge drinking.

In this study, binge drinking was defined as having ≥ 6 alcoholic drinks on one occasion. Binge drinkers who consume ≥ 6 drinks on one occasion were associated with mortality from upper digestive tract cancer including oropharynx and esophagus. The highest risk of esophageal cancer mortality, with a 7.17-fold risk of death, was seen among those who were heavy binge drinkers. Our findings support other prospective studies with community-based samples showing that heavy alcohol consumption was associated with oral cavity, pharynx and esophageal cancer mortality (Bagnardi et al., 2001; Haas et al., 2012).

Probable mechanisms for the association between alcohol drinking and upper digestive tract cancer have been presented in several studies (Bagnardi et al., 2001; Haas et al., 2012). It has been reported that the carcinogen of esophageal cancer, with regard to alcohol consumption, is acetaldehyde, a highly reactive and toxic alcohol metabolite (Homann et al., 1997). Acetaldehyde interferes with the DNA repair machinery and directly inhibits O6 methyl-guanyltransferase, an enzyme important for the repair. The inhalation of acetaldehyde has been known to cause bronchial cancer as well as esophageal cancer. Especially, several studies reported the hazards of binge drinking through experiments. After in vivo administration of ethanol, analogous to binge drinking condition, histone H3 modification was found in rat tissues (Kim and Shukla, 2006). A Russian study also reported the association between binge drinking and duodenum ulcer mortality (Razvodovsky, 2007).

This study has several limitations to be discussed. First, alcohol consumption variables data were collected through a questionnaire for the Kangwha Cohort of people

aged 55 or older. Some could raise an issue of validity for this. However, when a Korean study collected alcohol consumption variables data for elderly people through a questionnaire in 1998, its reliability and validity were highly evaluated (Park et al., 1998). Besides, the research team implemented the second interview test with 3,381 survivors in 1994. Percent agreement between drinking status data collected in 1985 and those in 1994 is 87% and Cohen's kappa value is 0.697. They showed substantial agreement between the two data. Second, smoking is a known risk factor for upper digestive tract cancer, including oral cavity, pharynx and esophagus cancer. A rough classification of smoking may become a confounder in our study. To solve this problem, further classification of smoking status was performed as four groups such as never, former, current smokers of 1-19 tobaccos per day, and current smokers of ≥ 20 tobaccos per day. Still, it may have a possibility of residual confounding. Third, despite the larger sample size, some of the subgroups included a relatively small number of individuals. For example, the highest HR for mortality from esophageal cancer among males who had heavy binge drinking was found in a group only with four individuals. The substantial difference between this group and the others could be due to the small group size.

In conclusion, when the mortality risk of binge drinkers was compared to that of non-drinkers, mortality risks from upper digestive tract cancers were high in binge drinkers who drink daily. However, since the study population was people aged 55 or older living in an agricultural community, further studies need to be undertaken to truly understand the risks of binge drinking in the entire population.

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