

## RESEARCH COMMUNICATION

# Association between Alcohol Consumption and Colorectal Carcinogenesis: an Ecological Study in Korea

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### Abstract

The sharp rise in the incidence rate of colorectal cancer (CRC) in Korea over the past decades may be partly attributed to increase in alcohol consumption. An ecological study was conducted in Korea to determine the association between alcohol consumption and the risk of colorectal cancer. We obtained the CRC incidence rates for the years 1999–2007 from the Korean Central Cancer Registry and the data on national alcohol consumption for the years 1998, 2001, 2005, and 2007 from the reports of the Korea National Health and Nutrition Examination Survey. Pearson's correlation coefficients were determined using data for alcohol intake and CRC incidence rate. People who consumed more than 45 g alcohol/day were defined as heavy drinkers. A significant correlation between alcohol consumption and the CRC incidence rate was observed in men; Pearson's correlation coefficients were statistically significant for men ( $r = 0.99$ ;  $P = 0.001$ ), but not for women ( $r = 0.82$ ;  $P = 0.180$ ). In the <50-year age group, the age-specific incidence rate for men was comparable to that for women, but in the  $\geq 50$ -year age group, it increased rapidly in men. The increase in alcohol consumption appears to be attributable to increase in the number of heavy drinkers among men aged 25–59 years, particularly among men aged 45–49 years. Our findings may aid in predicting future CRC incidence in Korea.

**Keywords:** Colorectal cancer - alcohol - heavy drinker - Korea

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### Introduction

The incidence rate of colorectal cancer (CRC) is increasing sharply in Asia, while it is stabilizing or even declining in most developed countries (Sung et al., 2005; WHSA, 2010). The CRC incidence rate in South Korea is currently among the highest following a rapid increase over the past decades. In 2008, the age-standardized CRC incidence rate was 46.9 per 100,000 men in South Korea, as compared to 41.7 in Japan, 16.3 in China, and 34.1 in the United States (WHSA, 2010). It has been estimated that approximately 70–80% cases of CRC can be attributed to environmental and lifestyle factors, including westernized dietary habits, smoking, and physical inactivity (Willett, 1995; Coyle, 2009; Franco et al., 2005; Lee et al., 2008). Extensive studies on the effects of alcohol consumption suggested that alcohol may be one of the causes of CRC (Cho et al., 2004; Mizoue et al., 2008; Moskal et al., 2007). These studies showed that the CRC risk was significantly higher in heavy drinkers, those who drank >3 drinks/day, than in nondrinkers. Further, genetically-determined susceptibility, through its interaction with other causative factors, may also play an important role in colorectal carcinogenesis (Arasaradnam et al., 2008; Coyle, 2009). It has been proposed that an alcohol-CRC

association may be more apparent in Asian populations than in Western populations partly because of the relatively high prevalence of the slow-metabolizing aldehyde dehydrogenase (ALDH) variant in Asian populations (Moskal et al., 2007; Mizoue et al., 2008).

In this study, we examined the trends in alcohol consumption and CRC incidence over a 10-year period to test the hypothesis that the secular increase in CRC incidence is causally related to the increase in alcohol consumption in the Korean population.

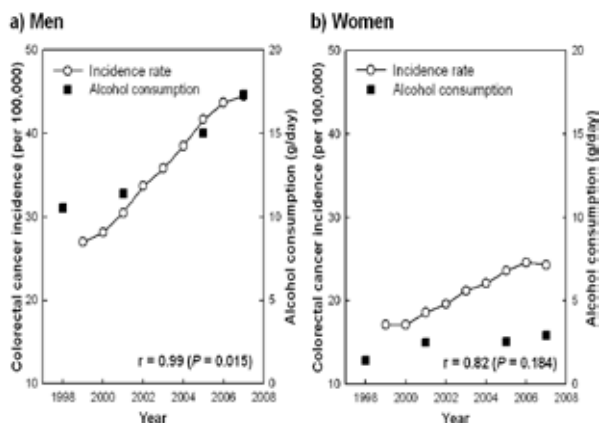
### Materials and Methods

The CRC incidence rates in Korea for the years 1999–2007 were obtained from the Korean Statistical Information Service, which collects data from the Korean Central Cancer Registry. The age-standardized CRC incidence rates were calculated by applying the direct standardization method using age-specific CRC incidence rates and the population of Korea in 1990 as the standard population. We obtained data on alcohol consumption for the years 1998, 2001, 2005, and 2007 from the reports of the Korea National Health and Nutrition Examination Survey. Pearson's correlation coefficients were determined using the alcohol intake data and CRC incidence rates for

men and women, respectively. The trend of age-specific CRC incidence and alcohol consumption was examined using the 5-year age distribution. On the basis of their alcohol consumption, the individuals were categorized into 4 groups (<15, 15–30, 30–45, and ≥45 g alcohol/day) and those who consumed ≥45 g alcohol/day were defined as heavy drinkers. Statistical analyses were performed using SAS statistical software version 9.1 (SAS Institute, Cary, NC), and a 2-sided P-value less than 0.5 was considered significant.

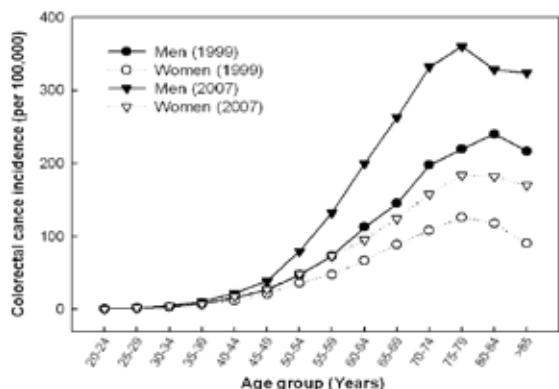
## Results

The CRC incidence rate among men increased markedly with an increase in alcohol consumption (Figure 1). The age-standardized CRC incidence rates between 1999 and 2007 increased from 27.0 to 44.5 per 100,000 men (annual percentage change = 7.0) and from 17.1 to 24.3 per 100,000 women (annual percentage change = 5.3). The daily alcohol consumption between 1999 and 2007 increased from 10.6 to 17.3 g alcohol/day for men and from 1.4 to 2.9 g alcohol/day for women. Pearson's correlation coefficients between CRC incidence rates and alcohol consumption were statistically significant for men ( $r = 0.99$ ;  $P = 0.015$ ), but not for women ( $r = 0.82$ ;  $P = 0.184$ ).



**Figure 1. Trends in the Age-standardized Colorectal Cancer Incidence Rates (per 100,000) and Daily Alcohol Consumption (g/day) for Men (a) and Women (b) in Korea, 1998-2007**

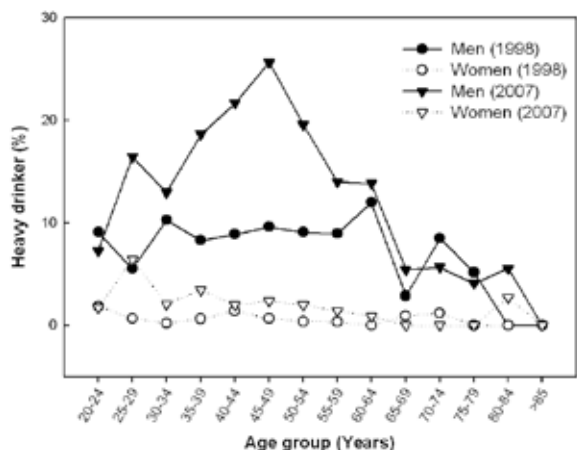
Figure 2 shows the trend of CRC incidence rates among different age groups. The age-specific incidence rates increased with age for both sexes, and the highest CRC incidence rate was observed in the 75–84 year age-group. The age-specific incidence rate for men was comparable to that for women at the age of <50 years, but it increased rapidly from the age of 50 years. We also examined the trend in alcohol consumption by using the 5-year age distribution. In 2007, men aged 45–49 years showed the highest alcohol consumption (28.7 g alcohol/day), followed by those aged 50–54 years (25.9 g alcohol/day). Among women, those in the 25–29 year age-group showed the highest alcohol consumption (7.3 g alcohol/day) (data not shown). We also observed a marker increase in the proportion of people who consumed ≥45 g alcohol/day from 1998 to 2007 among men aged 25–59 years (Figure 3). The percentage of heavy drinkers was highest among men aged 45–49 years, and it is shown that 25.6% men aged 45–49 years consumed ≥45 g alcohol/day in 2007.



**Figure 2. Age-specific Incidence Rates of Colorectal Cancer in 1999 and 2007 by 5-year Age Distribution**

## Discussion

In this ecological study of the Korean population, we found a putative association between alcohol consumption and CRC incidence rate, especially among men. The increase in alcohol consumption in the past decade appears to be attributed to an increase in the number of heavy drinkers in men aged 25–59 years, especially among men in the 45–49 year age group.



**Figure 3 Percentages of Heavy Drinkers in 1998 and 2007 by 5-year Age Distribution**

The findings from many epidemiological studies that investigated the association between alcohol consumption and CRC risk were inconclusive (Otani et al., 2003a; Cho et al., 2004; Chen et al., 2005; Mizoue et al., 2008). However, several studies consistently reported that heavy drinking may elevate the risk of CRC (Cho et al., 2004; Mizoue et al., 2008). A pooled analysis of 8 population-based cohort studies conducted in North America and Europe showed that an increased CRC risk was limited to persons who consumed ≥45 g alcohol/day (approximately ≥3 drinks/day), and reported that a positive association between alcohol consumption and CRC risk was attributable to ethanol rather than to other components in an alcoholic beverage (Cho et al., 2004). Another pooled analysis of 5 population-based cohort studies conducted in Japan showed a clear dose-response relation between

alcohol consumption and CRC risk in men (Mizoue et al., 2008). In the present study, we observed a significant association between CRC incidence rate and alcohol intake; this association may be attributable to an increased proportion of heavy drinkers.

Several biological mechanisms have been proposed to explain the association between alcohol consumption and colorectal carcinogenesis. Acetaldehyde, a highly reactive and toxic alcohol metabolite, may be responsible for alcohol-induced colorectal carcinogenesis (Koivisto and Salaspuro, 1998; Seitz and Stickel, 2009). In addition, alcohol may antagonize methyl-group metabolism, contribute to abnormal DNA methylation (Arasaranam et al., 2008; Mason and Choi, 2005), and interfere with intestinal absorption of potentially anticarcinogenic nutrients (e.g., folate and calcium) (Sanjoaquin et al., 2005). However, we need to consider factors other than alcohol drinking which have changed during the same period and which have possibly influenced cancer incidence. The westernized diet, other behaviors (e.g., smoking and sedentary lifestyle) (de Vries et al., 2010; Mackay and Amos, 2003), and biological factors (e.g., estrogen and obesity) (Cho et al., 2004; Di Leo et al., 2001) may also be responsible for the increased incidence of CRC, in addition to the improvement in diagnostic methods and increasing number of screenings in Korea (Choi et al., 2010).

The CRC incidence rate varies by several factors including age and sex. The present study shows that the CRC incidence rate in men increased rapidly after 50 years of age, and alcohol consumption has increased considerably among men aged 25–54 years, which may be attributed to the increased proportion of heavy drinkers in these age groups. Considering the applicable induction period between genotoxic exposure and the diagnosis of CRC (Giovannucci, 2001), we may assume that those who consumed excessive amounts of alcohol earlier in life will be at the greatest risk of developing CRC later in life. Besides, alcohol drinkers may develop CRC at a younger age than non-drinkers do. A cross-sectional study of 161,172 persons reported that drinking and drinking with smoking lower the age of onset of CRC by 5.2 and 7.8 years, respectively (Zisman et al., 2006). Additionally, a putative association between alcohol consumption and colorectal carcinogenesis in this study was observed only in men. CRC incidence is higher in men than in women in the high-incidence population and in the traditionally low-risk populations with rising CRC incidence (Koo and Leong, 2010). Migrant studies indicate that CRC incidence rises more rapidly in men than in women when people immigrate from low-incidence to high-incidence areas, which indicates that environmental factors may have a different impact on men and women (Grulich et al., 1995; Koo and Leong, 2010).

It has been suggested that the effect of alcohol consumption on colorectal carcinogenesis differs by among Asian and Western populations (Otani et al., 2003a). A stronger association between alcohol drinking and colorectal carcinogenesis is observed in Asian populations (Mizoue et al., 2008). Some studies have proposed that the different distribution of genetic

polymorphisms of alcohol metabolism-related enzymes including ALDH2 is associated with this difference (Otani et al., 2003b; Seitz and Stickel, 2009); higher proportion of Asians including of Japanese, Koreans, and Chinese carry genetic polymorphisms of ALDH2, which encodes an enzyme with decreased activity and cause a high acetaldehyde levels in blood (Seitz and Stickel, 2009). Thus, chronic consumption of ethanol by individuals with this allele results in a significant increase in CRC risk (Seitz and Stickel, 2009). However, recent large-scale studies have challenged this hypothesis (Matsuo et al., 2006; Yin et al., 2007). Therefore, whether the stronger association between alcohol consumption and CRC risk among Koreans can be explained by a genetic difference in the efficiency of metabolizing alcohol among drinkers remains to be confirmed. The observation that the CRC incidence in Asian immigrants to the United States is higher than that in people living in their own countries may imply that genetic predisposition probably interacts with environmental factors or lifestyle modifications (Flood et al., 2000; Lee et al., 2007).

The present study used data spanning only 10 years, and there remains a concern that this sample may not reflect the true time trend because of the lack of consideration of the induction period between exposure to a risk factor and disease detection. Unfortunately, in Korea, the Korean Central Cancer Registry started collecting the data on CRC incidence only since 1999. Further, the data of alcohol consumption on an individual basis collected using the 24-hour recall method was available only for the years 1998, 2001, 2005, and 2007 from the reports of the Korea National Health and Nutrition Examination Survey; from 1969 to 1995, nation-wide data on food consumption were obtained annually on a household basis by using the food weighting method. Compared to other countries, Korea shows the most rapid increase in the CRC incidence rate in the last 10 years (IARC, 2008). Thus, this study is meaningful as it explores the alcohol-CRC relationship among Koreans and could forecast future secular trends and rates of CRC.

This study has several limitations that are inherent to ecologic studies. The unit of observation was a group of people rather than an individual, and thus, the association between alcohol consumption and the CRC incidence observed in the present study may not be true on the individual level. In addition, ecologic studies are encumbered by unavailability of data necessary for adequate control of confounding in the analysis. We also cannot rule out the possibility that our estimates were distorted because of residual confounding. For example, cigarette smoking and alcohol consumption are highly correlated lifestyle factors across populations (Koh et al., 2005) and a positive alcohol-CRC association was observed among smokers but not among nonsmokers in a pooled analysis (Cho et al., 2004). In addition, the lower alcohol consumption in women probably hindered accurate statistical estimation of its effect on CRC risk. Despite these limitations, our study effectively determined the association between exposure distributions and disease occurrence using unique drinking culture and CRC incidence rate among Koreans.

In conclusion, the results of this study suggest a positive alcohol-CRC association in the Korean population. Considering the rapid increase in CRC incidence in Korea, we need to act promptly in order to prevent CRC and to diagnose the disease at an early stage. Therefore, further research will be needed to elucidate the role of genetic and environmental factors in the colorectal carcinogenesis.

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