



Original Article

Population Attributable Fraction of Established Modifiable Risk Factors on Colorectal Cancer in Korea

Sooyoung Cho¹, Aesun Shin^{1,2}¹Department of Preventive Medicine, Seoul National University College of Medicine, Seoul, ²Cancer Research Institute, Seoul National University, Seoul, Korea

Purpose We estimated the population attributable fraction (PAF) of established risk factors for colorectal cancer, to provide evidence for prioritizing cancer prevention policy.

Materials and Methods The exposure prevalence was calculated by using data from the 2005 Korean National Health Examination Survey for tobacco smoking, alcohol consumption, obesity, physical inactivity, and meat intake. Risk estimates (relative risks) were selected from the published meta-analyses. Cancer incidence data from the Korea Central Cancer Registry were used to estimate the preventable number of colorectal cancer cases in 2015.

Results The PAFs of the tobacco smoking, alcohol consumption, obesity, physical inactivity, and consumption of red and processed meat were as follows: 9.2%, 11.1%, 9.1%, 18.9%, and 10.1% for colon cancer and 21.8%, 12.3%, 3.5%, 5.3%, and 9.2% for rectal cancer among men; 1.0%, 1.3%, 2.7%, 12.3% and 9.2% for colon cancer and 1.7%, 2.3%, 0.8%, 7.2%, and 8.3% for rectal cancer among women. The PAFs of selected risk factors were 46.2% for colon and 42.4% for rectum among men, while 24.3% for colon and 18.9% for rectum among women. The attributable numbers of colon and rectal cancer to selected risk factors were 4,028 and 3,049 cases among men, respectively, while 1,644 and 778 cases among women in the year of 2015.

Conclusion Changes in modifiable risk factors could prevent half of the colorectal cancer in the Korean population.

Key words Colorectal neoplasms, Population attributable fraction, Risk Factors, Lifestyle, Republic of Korea

Introduction

Colorectal cancer is the third-most common cancer among men and the second-most common cancer among women worldwide in 2012 [1]. In Korea, the incidence of colorectal cancer has been decreasing recently, with an annual percent change of -4.9% (-5.4% among men and -4.3% among women) from 2012 to 2015 in age-adjusted rates. Nevertheless, the colorectal cancer was still the third-most common cancer among both sexes (age-standardized rates, 40.2 per 100,000 among men and 22.2 per 100,000 among women) in Korea in the year 2015 [2].

Immigrant studies [3,4] have been suggested that environmental factors play a role in the development of colorectal cancer. The World Cancer Research Fund and American Institute of Cancer Research (WCRF/AICR) have reported lifestyle risk factors for colorectal cancer, such as alcohol consumption, obesity, physical inactivity, and processed meat with “convincing” evidence and red meat intake with “probable” evidence [5]. In addition to the findings reported by WCRF/AICR, tobacco smoking has been classified as a group 1 carcinogen for colorectal cancer [6,7]. Whereas rela-

tive risk (RR) is a relative difference estimate, the attributable risk is usually used to address the effect of the risk factor on disease risk from a public health perspective. Korea National Cancer Center reported sex and cancer-specific population attributable fraction (PAF) of infection [8], tobacco smoking [9], alcohol consumption [10], obesity, and physical inactivity [11] using the results from the studies among the Korean population. For colorectal cancer, the PAF attributed to tobacco smoking, alcohol consumption, obesity, and physical inactivity were estimated at 1.5%, 21.6%, 13.4%, and 1.7%, respectively. Although the aforementioned studies have focused on various risk factors on cancers, the estimated PAFs were not comparable with other studies due to the limited number of epidemiological studies conducted in Korea. In particular, estimated PAFs for physical inactivity was far lower than other reports. Besides, the consumption of processed and red meat was not considered.

In the present study, we aimed to provide a more comprehensive estimate of the PAF of colorectal cancer, including well-established risk factors.

Correspondence: Aesun Shin

Department of Preventive Medicine, Seoul National University College of Medicine, 103 Daehak-ro, Jongno-gu, Seoul 03080, Korea
Tel: 82-2-740-8331 Fax: 82-2-747-4830 E-mail: shinaesun@snu.ac.kr

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Materials and Methods

1. Study selection

We used the summary RRs from the most recent meta-analyses in the calculation of PAFs for tobacco smoking, alcohol consumption, physical inactivity, and consumption of red and processed meat. The selection of previous meta-analyses on obesity and colorectal cancer was restricted to the study, which reported the pooled RR for obesity as a categorical variable to calculate PAFs for obesity at the risk level, rather than the average level in the whole population. The study search was conducted in the PubMed databases for all publications up to September 2019 with the restriction on the study which reported the summary RRs stratified for both sex and anatomical subsites, if possible. We extracted studies on pooled RRs and corresponding 95% confidence intervals from the selected meta-analysis. Descriptions of selected studies were shown in S1 Table.

2. Colorectal cancer incidence

We derived the number of incident colon and rectum cancer cases in Korea from the national cancer statistics for the year of 2015 [2]. The statistics on the nationwide cancer incidence were provided by the Korea Central Cancer Registry, which collected the data for cancer incidence using hospital data, 11 population-based registries, and additional medical chart reviews [12]. A detailed method to collect data on cancer incidence was described elsewhere [12].

3. Prevalence of exposure in Korea

With assuming a latency period of more than 10 years, the prevalence of each exposure was estimated in participants aged 20 years or more from the 2005 Korean National Health Examination Survey data [13]. The prevalence of smoking history was estimated using self-reported information. When survey participants responded to the question about the smoking status that they had never smoked, they were classified as a 'never smoker.' When they responded to the question about the current smoking status that they had smoked in the past, they were classified as a 'former smoker.' When they responded to the question about the current smoking status that they smoked every day or smoked occasionally, they were classified as a 'current smoker.' The prevalence of alcohol consumption was estimated based on the proportion of drinkers, and average alcohol consumption was estimated according to the amount consumed among drinkers. When participants responded to the question about alcohol consumption status that they never drank or rarely drank, they were classified as a 'never drinker.' Otherwise, they were classified as an 'ever drinker.' Daily alcohol consumption amounts were calculated based on information reported for

frequency and amount of usual alcohol consumption. Body mass index (BMI) was calculated to assess obesity using measured height and weight. We then classified the normal as whose BMI of < 25 kg per m², overweight as whose BMI of 25-29.9 kg per m² and obese as whose BMI of ≥ 30 kg per m².

The prevalence of physical activity was estimated based on participants' responses to the question about the frequency per week and the duration of each moderate and vigorous physical activity. Moderate physical activity included slow swimming, double tennis, volleyball, badminton, table tennis and carrying light objects and vigorous activity included jogging, mountain climbing, cycling at fast rides, fast swimming, football, basketball, jumping rope, squash, single tennis and carrying heavy objects in the questionnaire. The moderate and vigorous physical activity were included as 4.5 and 6 metabolic equivalent of task (MET) in the calculation of the mean value of MET hour per week.

We estimated the prevalence and amount of red and processed meat consumption for participants who reported information on the consumption of pork, beef, and processed meat in both the food frequency questionnaire and 24-hour recall dietary survey. When the participants responded to the questionnaire about the average frequency of red and processed meat intake as 'rarely' or '6 to 11 times a year,' they were classified as an 'Eating infrequently.' Otherwise, they were classified as 'Eating frequently.' The average amount of red and processed meat consumption was estimated by using 24-hour recall dietary survey data on the weight of food ingredients used in cooking.

4. Statistical analysis

PAFs of risk were calculated by using the following formula for polytomous exposure as proposed by Hanley [14]:

$$PAF = \frac{\text{prevalence} \times (RR - 1)}{\text{prevalence} \times (RR - 1) + 1}$$

For alcohol consumption, physical inactivity and the consumption of red and processed meat, average RRs were calculated based on the mean level of exposure and the RR of the exposure per unit increment for the whole population with assuming a log-linear relationship of exposure and cancer risk [15]:

$$\text{Risk} = \exp[\ln(\text{risk per unit increment}) \times \text{mean level of exposure}]$$

$$PAF = \frac{\text{Risk} - 1}{\text{Risk}}$$

For assumptions about independent exposures and their effects, we also calculated the PAF of risk accounting for interaction among multiple exposures using the following formula where *i* refers to *i*th risk factor [16]:

Table 1. Meta-analyzed relative risks and its corresponding 95% confidence intervals from previous meta analytic studies

Type of risk factors	Men		Women	
	Colon	Rectum	Colon	Rectum
Tobacco smoking [17]				
Never smoker	Reference	Reference	Reference	Reference
Former smoker	1.18 (1.05-1.33)	1.23 (1.01-1.48)	1.19 (1.09-1.30)	1.27 (1.05-1.52)
Current smoker	1.09 (0.92-1.30)	1.36 (1.08-1.71)	1.08 (0.97-1.21)	1.16 (0.97-1.40)
Alcohol consumption [18]				
Daily consumed ethanol contents, per 10 g per day	1.08 (1.06-1.11)	1.09 (1.06-1.12)	1.05 (1.02-1.09)	1.09 (1.04-1.15)
Obesity; defined by body mass index (kg per m²) [20]				
Normal (< 25)	Reference	Reference	Reference	Reference
Overweight (25-29.9)	1.25 (1.14-1.37)	1.08 (0.97-1.20)	1.09 (0.99-1.20)	1.02 (0.88-1.17)
Obese (≥ 30)	1.51 (1.42-1.61)	1.29 (1.19-1.40)	1.16 (1.01-1.34)	1.08 (0.92-1.26)
Physical activity [19]				
Per 20 MET hours per week	0.82 (0.75-0.90)	0.95 (0.88-1.02)	0.88 (0.79-0.97)	0.93 (0.83-1.04)
Consumption of red and processed meat [18]				
Per 100 g per day	1.19 (1.10-1.30)	1.17 (0.99-1.39)	1.19 (1.10-1.30)	1.17 (0.99-1.39)

MET, metabolic equivalent of task.

$$\text{PAF for multiple risk factors} = 1 - \prod_{i=1}^n (1 - \text{PAF}_i)$$

Estimations of exposure prevalence were performed using the SAS SURVEYMEANS and SURVEYFREQ procedures (ver. 9.4, SAS Institute Inc., Cary, NC) to account for the complex survey design and sample weights.

Results

Table 1 presents the meta-analyzed RRs for each risk factor from previous studies [17-20]. The pooled RRs of the former and current smoker for rectal cancer (former smoker, 1.23 [1.01-1.48] among men and 1.27 [1.05-1.52] among women; current smoker, 1.36 [1.08-1.71] among men and 1.16 [0.97-1.40] among women) was higher than those for colon cancer (former smoker, 1.18 [1.05-1.33] among men and 1.19 [1.09-1.30] among women; current smoker, 1.09 [0.92-1.30] among men and 1.08 [1.07-1.21] among women) in both men and women. The risk for alcohol consumed at 10 g per day was not shown a significant difference in anatomical subsites and sex (1.08 [1.06-1.11] for colon and 1.09 [1.06-1.12] for rectum among men; 1.05 [1.02-1.09] for colon and 1.09 [1.04-1.15] for rectum among women). People with overweight (BMI of 25-29.9 kg/m²) and obese (BMI of higher than or equal to 30 kg/m²) had higher risk for colon than those for rectum in both men (overweight, 1.25 [1.14-1.37] for colon and 1.08 [0.97-1.20] for rectum; obese, 1.51 [1.42-1.61] for colon and 1.29 [1.19-1.40] for rectum) and women (overweight, 1.09 [0.99-1.20] for colon and 1.02 [0.88-1.17] for rectum; obese, 1.16 [1.01-1.34] for colon and 1.08 [0.92-1.26] for rectum),

compared to people with normal range of body mass index (less than 25 kg/m²). The pooled RRs of recreational physical inactivity per 20 MET-hours per week were lower for colon than for rectum (0.82 [0.75-0.90] for colon and 0.95 [0.88-1.02] for rectum among men; 0.88 [0.79-0.97] for colon and 0.93 [0.83-1.04] for rectum among women). The same RRs for red and processed meat consumption was extracted for each subsite for both sexes since less than three studies were used to estimate pooled RRs stratified for sex and subsites. The risk for daily consumed red and processed meat per 100 g was increased as 19% (1.19 [1.10-1.30]) for colon and 17% (1.17 [0.99-1.39]) for rectum among both men and women.

Table 2 presented the prevalence of each risk factor in Korea in the year of 2005 by sex. Most men were a former or current smoker (20.1% for never, 27.0% for former, and 52.9% for the current smoker), although most women were never smoker (91.2% for never, 3.0% for former, and 5.8% for the current smoker). The prevalence of ever drinking alcohol (5.2% for never and 94.8% for the ever drinker among men; 19.4% for never and 80.6% for the ever drinker among women) and the mean of ethanol content among ever drinker (mean±standard error; 15.2±0.4 g among men and 2.7±0.2 g among women) were higher among men than among women. More men (31.5% for overweight, 3.6% for obese) showed overweight and obese than women (24.6% for overweight, 3.4% for obese). The prevalence of people who reported their moderate or vigorous physical activities was slightly higher among men (96.8%) than among women (94.7%). The mean value of MET per hour per week was also higher among men (21.1±0.5) than among women (20.5±0.5). The prevalence of consuming red and processed meat (95.0% among men and

Table 2. The weighted frequency and prevalence of risk factors in 2005 by sex using the data from the 2005 Korean National Health Examination Survey

Type of risk factors and corresponding categories	Men	Women
Tobacco smoking		
Never smoker	3,546,946 (20.1)	16,520,472 (91.2)
Former smoker	4,765,369 (27.0)	539,087 (3.0)
Current smoker	9,318,116 (52.9)	1,049,770 (5.8)
Alcohol consumption		
Never drinker	925,278 (5.2)	3,518,845 (19.4)
Ever drinker	16,710,359 (94.8)	14,590,484 (80.6)
Ethanol content among ever drinker (g/day)	15.2±0.4	2.7±0.2
Obesity defined by body mass index (kg/m²)		
Normal (< 25)	11,399,769 (64.9)	12,914,318 (72.0)
Overweight (25-29.9)	5,533,360 (31.5)	4,409,877 (24.6)
Obese (≥ 30)	637,490 (3.6)	615,593 (3.4)
Response to moderate and vigorous physical activity		
Neither	389,169 (3.2)	490,953 (5.3)
Either or both	11,603,750 (96.8)	8,808,993 (94.7)
MET per hour per week	21.1±0.5	20.5±0.5
Consumption of red and processed meat		
Not consumer	219,179 (5.0)	317,207 (7.2)
Consumer	4,146,673 (95.0)	4,062,038 (92.8)
Amount (g/day)	122.3±14.5	110.8±11.0

Values are presented as number (%) or mean±SE. MET, metabolic equivalent of task; SE, standard error.

Table 3. The number and the population attributable risks (%) of the incident colorectal cancer in 2015

Risk factor	Men		Women	
	Colon (n=8,719)	Rectum (n=7,192)	Colon(n=6,765)	Rectum(n=4,114)
Tobacco smoking	802 (9.2)	1,568 (21.8)	74 (1.0)	70 (1.7)
Alcohol consumption	959 (11.0)	885 (12.3)	88 (1.3)	95 (2.3)
Obesity	793 (9.1)	252 (3.5)	183 (2.7)	33 (0.8)
Physical inactivity	1,648 (18.9)	381 (5.3)	832 (12.3)	296 (7.2)
Consumption of red and processed meat	881 (10.1)	662 (9.2)	622 (9.2)	341 (8.3)
All the above risk factors	4,028 (46.2)	3,049 (42.4)	1,644 (24.3)	778 (18.9)

Values are presented as number (%).

92.8% among women) and the mean amount of daily red and processed meat consumption (122.3±14.5 g among men and 110.8±11.0 g among women) were higher among women than among men.

Table 3 shows the PAFs and the number of colorectal cancer cases attributable to risk factors. The highest PAF for colon cancer among men showed for the consumption of physical inactivity (18.9% with 1,648 cases), followed by alcohol consumption (11.0% with 959 cases), red and processed meat (10.1% with 881 cases), tobacco smoking (9.2% with 802 cases), and obesity (9.1% with 793 cases). The consumption of physical inactivity (12.3% with 832 cases) was

shown to the highest PAF for colon cancer among women, followed by red and processed meat (9.2% with 622 cases), obesity (2.7% with 183 cases), alcohol consumption (1.3% with 88 cases), and tobacco smoking (1.0% with 74 cases).

For rectal cancer, the highest PAF showed for tobacco smoking (21.8% with 1,568 cases) among men, followed by alcohol consumption (12.3% with 885 cases), consumption of red and processed meat (9.2% with 662 cases), physical inactivity (5.3% with 381 cases), and obesity (3.5% with 252 cases). Similarly, consumption of red and processed meat (8.3% with 341 cases) showed the highest PAF for rectal cancer among women, followed by physical inactivity (7.2%

with 296 cases), alcohol consumption (2.3% with 95 cases), tobacco smoking (1.7% with 70 cases), and obesity (0.8% with 33 cases). The combined PAFs for the selected risk factors considered in this study were 46.2% for colon cancer (4,028 cases) and 42.4% for rectal cancer (3,049 cases) among men and 24.3% for colon cancer (1,644 cases) and 18.9% for rectal cancer (778 cases) among women, respectively.

Discussion

Of the more than 26,000 colorectal cancer cases in Korea in 2015, over 9.5 thousand cases were attributable for well-known modifiable factors including tobacco smoking, alcohol consumption, obesity, physical inactivity, and the consumption of red and processed meat. The PAFs of selected lifestyle factors among men were higher than among women, with the exception of physical inactivity for rectal cancer. The fraction for colon cancer attributable to tobacco smoking and alcohol consumption were lower than those for rectal cancer among both sexes. In contrast, the fraction for colon cancer attributable to obesity, physical inactivity, and consumption of red and processed meat was higher than those for rectal cancer among both men and women.

We observed that the fraction of colon cancer attributable to tobacco smoking was higher than those of rectal cancer, and the difference of the PAFs to tobacco smoking on subsites of colon/rectum cancer was larger among men than among women. This difference can be explained by higher pooled RRs for rectal cancer than colon cancer and a much higher prevalence of former and current smoking among men than women. Results from this study show higher proportion of colon and rectal cancer attributable to tobacco smoking among men than women, and it is consistent with previous studies in East Asians including Japan [21] (29.7% among men and 5.0% among women), China [22] (8.4% among men and 0.4% among women) and a previous study conducted in Korea [9] (1.5% among men and less than 0.01% among women), due to low proportion of former and current smoker among women. In contrast to the results in East Asians, high PAF among women were observed in European studies [23,24] (6.6% among men and 9.9% among women in the UK; 12% in Norway) and it can be explained by decreasing trends of tobacco smoking among men and increasing trends among women [25].

The PAFs of colon and rectum cancer among men were notably higher than among women due to a higher consumption amounts per day among men than women. The PAFs for alcohol consumption were consistently higher among men than women in the previous studies, including the United Kingdom [23] (15.5% among men and 6.9% among women),

Brazil [26] (8.5% among men and 2.6% among women), Japan [21] (9.0% among men and 2.5% among women), China [22] (8.7% among men and 1.1% among women) and previous study in Korea (8.6% among men and 4.4% among women for colon).

The PAFs for obesity were higher among men than among women for both subsites due to the higher prevalence of overweight and higher meta-analyzed RR among men than among women. PAFs among Asian including Japan [21] (0.8% among men and 1.6% among women), China [22] (4.9% among men and 5.8% among women) and previous [11] (6.8% among men and 6.6% among women) and present study in Korea were lower than those among European population such as United Kingdom [23] (13.6% among men and 12.2% among women) and France [27] (18.0% among men and 17.7% among women for colon; 9.1% among men and 8.6% among women for rectum). These differences could be explained by the prevalence of obesity, which was higher in Europe than in Asia [28].

We observed a little higher PAFs for physical inactivity in colorectal cancer risk, compared with results from other countries (0.3% in Japan [21], 8.9% in China [22], and 3.0% in United Kingdom [23] among men; 0.6% in Japan [21], 9.0% in China [22], and 3.6% in United Kingdom [23] among women). Especially, the PAF for physical inactivity was far higher than that found in previous Korean study [11] (0.8% among men; 0.9% among women). It can be explained by differences in the definition of physical inactivity. Furthermore, although this study and previous study in Korea calculated the PAFs for the same domain of leisure-time (or recreational) physical activity, this study presented a higher fraction of colon/rectum cancer to physical inactivity than the previous study in Korea. The authors of the previous Korean study estimated the pooled RRs for colorectal cancers based on results from Korean studies, while the authors, who reported the meta-analyzed RRs used in this study, estimated the RRs for colon and rectal cancer based on results from studies without restriction on population. S2-S6 Tables list the RRs which were reported on the association between colorectal cancer and lifestyle factors, including smoking, alcohol drinking, obesity, physical activity and (red) meat intake, in Korean population.

Although it was difficult to compare results from China, UK and our study due to the differences on the type of meat, the PAFs for the intake of red and processed meat in our study were similar with those for the intake of high red and processed meat in China [22] (9.1% among men and 7.9% among women) and lower than those for the intake of any meat in the United Kingdom [23] (24.8% among men and 16.4% among women).

We used nationally representative data to estimate the

prevalence of each risk factor and data from the national cancer registry to ascertain the number of incident colorectal cancer cases. Our study has a few limitations. First, we used RRs from the meta-analysis without the restriction of the study area due to the insufficient number of prospective studies to estimate a national-level pooled RR. If there is substantial heterogeneity on the risk estimates depends on the geographic area, it could be a limitation of the study. However, we did not find a substantial difference in risk estimates by geographic areas from the meta-analyses we used for the current study. There were possibilities of misclassification during estimating the prevalence of exposures at each category, as presented in meta-analysis studies. Second, we could not consider the effect of potential interactions between selected risk factors. Combined PAFs of risk factors included in our study were calculated based on the assumption of independence, but there is a possibility that it could be inappropriate to explain the complex etiology of cancer.

We concluded that approximately 44% of men and 22% of women who diagnosed with colon or rectum cancer in 2015 were preventable with modification of lifestyle. Our study suggested that the tobacco smoking and alcohol consumption could account for a high proportion of colorectal cancer cases, especially among men. We also confirmed that the physical inactivity and consumption of red and processed meat had a high proportion of the risk for colon and rectum

cancer among both men and women. In addition, results from this study can support the evidence that lifestyles that were required to modify appropriately may vary according to sex and subsites of colorectal cancer.

Electronic Supplementary Material

Supplementary materials are available at Cancer Research and Treatment website (<https://www.e-crt.org>).

Author Contributions

Conceived and designed the analysis: Shin A, Cho S.

Collected the data: Shin A, Cho S.

Contributed data or analysis tools: Shin A, Cho S.

Performed the analysis: Shin A, Cho S.

Wrote the paper: Shin A, Cho S.

Conflicts of Interest

Conflicts of interest relevant to this article was not reported.

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