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ORIGINAL REPORT

Effects of Excess Weight on Cancer Incidences Depending on Cancer Sites and Histologic Findings Among Men: Korea National Health Insurance Corporation Study

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Authors' disclosures of potential conflicts of interest are found at the end of this article.

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ABSTRACT

Purpose

The effects of excess weight on the development of cancers are controversial, and little is known for populations outside the United States and Europe. We conducted this study to assess the effects of excess weight with a large cohort of Koreans.

Methods

We assessed the relationship between body mass index (BMI) and various cancers in a 10-year follow-up cohort of 781,283 Korean men who were free of prior cancer at baseline. Weight and height were measured, and questionnaires related to health behaviors and medical history were completed. Data on newly developed cancers were obtained from two organizations in Korea. A proportional hazards model was used to examine the relationship between BMI and cancer.

Results

Adenocarcinoma in the colon and rectosigmoid, hepatocellular carcinoma, cholangiocarcinoma, adenocarcinoma in the prostate, renal cell carcinoma, papillary carcinoma in the thyroid, small-cell carcinoma in the lung, non-Hodgkin's lymphoma, and melanoma had positive dose-dependent relationships with BMI (all $P < .05$). Although no linear trend was found ($P = .267$), obese men who never smoked with a BMI of ≥ 30 kg/m^2 had an increased risk of developing gastric adenocarcinoma (relative risk = 1.73). Other cancers, such as leukemia, multiple myeloma, and gallbladder and pancreatic cancer, did not show significant associations.

Conclusion

These findings show that, even in Koreans, obesity clearly increases the risk of many types of cancers and the strength of the associations varies with the organ and histologic type. Because these obesity-related cancers are reported to be rapidly increasing in Korea and many other Asian countries, controlling obesity epidemics could be an effective tool for preventing these cancers in these areas.

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INTRODUCTION

Obesity and cancer are major public health problems with global significance. The prevalence of obesity has increased to epidemic proportions in recent decades,[1] and cancer remains one of the leading causes of death in Western and many Asian countries.[2,3]

Hundreds of previous studies by scientists working in Western countries have examined the association between body weight and cancer.[4-8] They have demonstrated that excess weight increases the risk of colon, kidney, esophagus (adenocarcinoma), endometrial, and postmenopausal breast cancer.[4-17] Some epidemiologic studies have suggested that cancers at other sites, such as the liver, gallbladder, thyroid, prostate, pancreas, ovary, leukemia, and cervix, are associated with excess weight, but the results for these cancers are inconsistent.[4-8,18-23] Recently, some investigators have suggested new associations between body weight and additional cancers, such as multiple myeloma, melanoma, non-Hodgkin's lymphoma, and others.[8,23-26] These newly identified obesity-related cancers suggest that more types of cancer are associated with body weight than had previously been thought to be the case.

This evidence supports the idea that controlling obesity can be an important tool for preventing a number of cancers among the populations of modern societies. However, this assertion needs further investigation, as well as verification that it is applicable to populations other than those in developed Western societies, given that almost all of the data on this issue thus far have been obtained from Western populations. Compared with whites, Asians tend to have relatively small body frames; their lifestyles, genetic backgrounds, and general environments also differ. Different epidemiologic characteristics for cancers have been reported from many Asian countries. Consequently, the effects of body weight on the development of cancer in Asians might differ from those in whites. Nevertheless, this assumption has not been verified, and data on this topic are scarce. We have conducted an investigation to clarify the association between obesity and cancer, according to organ site and histologic type, by examining data from a large cohort of Korean men.

METHODS

Study Population

Our patients were civil servants and private school workers and their dependants, who were members of the Korea National Health Insurance Corporation (KNHIC). The KNHIC provides medical insurance for all Koreans, and all Koreans are legally obliged to become members of this national insurance system. All members are eligible for a general health status examination every 2 years, and for some populations, like our study patients, this examination is obligatory by law. Of the possible patients, 824,138 men who were aged 20 years old or older and who had undergone medical examinations in 1992 were selected. Excluding nonresponders to questionnaires and those who had a previous cancer (total, 5.2%), 781,283 men were finally selected as study patients. We restricted our analyses to men because the women in the KNHIC study were generally younger than the men, and the number of cancer patients was too small for detailed analyses.

Data Collection

The body mass index (BMI) was used as an index of adiposity. BMI is calculated as the weight in kilograms divided by the height in meters squared. The data on body weight and height were collected by direct measurements at medical institutions equipped with facilities and staff approved by the regulations defined by the KNHIC.[27] The subjects were categorized into six groups by BMI: less than 18.5, 18.5 to 22.9, 23.0 to 24.9, 25.0 to 26.9, 27.0 to 29.9, and $\geq$ 30.0 kg/m^2. This classification corresponds to the classification proposed by WHO for the Western-Pacific region and with the classifications adopted by previous studies on Asians.[28] Because the number of incident cancer cases among men with a BMI $\geq$ 30 kg/m^2 was too small to be analyzed in detail, we did not classify this range of BMI further. Several categories of BMI were combined if a single category was found to have insufficient patients to produce sufficient statistical power. We set the BMI of 18.5 to 22.9 kg/m^2 as a reference for comparison because it is considered to be the normal range in the guidelines for Asians issued by WHO Western-Pacific region and others.[28]

The questionnaire included questions pertaining to age, smoking status, alcohol consumption, family history of cancer or other diseases, personal medical history, exercise (frequency and duration), and area of residence. Examinees were required to reply 3 to 4 days before each examination. The questionnaires were self-administered, and trained staff reviewed the completed questionnaires.

End Points

First, we obtained data on verified incident cancer patients for the period between the date of the initial medical examination in 1992 and December 31, 2001, from the Korea Central Cancer Registry (KCCR), using each individual's personal identification number. The KCCR is a hospital-based cancer registration system involving 75 (94%) of the 80 Korean university hospitals and 120 (96%) of the 125 teaching hospitals nationwide in 2001. These hospital-based reports have been estimated as covering at least 80% of the newly diagnosed malignancies in Korea.[29] In this system, the histologic types of cancer, which are confirmed by pathologists, must also be reported. The diagnoses of cancers, including histologic types, are coded according to the second revision of the International Classification of Diseases for Oncology.[30]

To reduce the number of missing patients and to improve accuracy, we also obtained data from the KNHIC in addition to that from the KCCR. Comparison of these two types of data identified an additional 9.1% of discrepant patients from the KNHIC data, and we tried to refine these patients. Because all hospitals in Korea are reimbursed only after bills that include the final diagnosis and treatment for each patient are submitted to the KNHIC and membership in this national insurance system is a legal obligation for all Koreans, we expected that almost all the data on new cancer patients would be included in this database. However, some of the additional 9.1% of cancer patients found in the KNHIC data might have been caused either by false registration of noncancer patients or failure of real patient registration in the KCCR. Of these discrepant cancer patients, only those whose cancer was confirmed by medical bills or reports of chemotherapy, conservative therapy, surgery, or death certificates were included in our analyses to improve accuracy (the KNHIC data increased the cancer incident patients by 5.9%). Because the histologic types of these additional patients were unavailable, we classified the histologic diagnoses of these patients as unknown or other. In the cases of death, multiple cancers, and others, we censored these patients at the time of the first occurrence.

The histologic types were classified based on the clinical significance and prevalence of each cancer in Korea,[29] as well as according to the WHO classification of tumors.[30] Lesions in the distal esophagus and gastric cardia were combined into one lesion, and lesions in the sigmoid and rectum were also combined. Because it is often difficult to determine where a large lesion

Table 1. Age-Adjusted Incidence Rate and Multivariate Relative Risk of Cancer According to Body Mass Index Among the Whole Study Population

Type of Cancer	Body Mass Index: < 18.5 kg/m²	18.5-22.9 kg/m²	23.0-24.9 kg/m²	25.0-26.9 kg/m²	27.0-29.9 kg/m²	≥ 30.0 kg/m²	*P* for Trend
All cancers							.753
No. of incident cancer cases	369	8,211	5,618	3,271	1,284	196	
Person-years of follow-up	126,551.6	3,576,563.5	2,185,952.8	1,237,087.5	483,194.9	59,333	
Age-standardized rate*	280.2	255.3	244.6	247.4	246.4	317.1	
Relative risk†	0.99	1.00	0.98	1.00	0.99	1.26	
95% CI	0.89 to 1.11	—	0.95 to 1.02	0.96 to 1.04	0.93 to 1.05	1.10 to 1.46	
Upper and middle esophageal cancer							< .001
No. of incident cancer cases	6	87	38	22	6	—	
Person-years of follow-up	128,205.8	3,610,201.2	220,866.2	1,249,744.6	548,237.3	—	
Age-standardized rate*	4.0	2.7	1.6	1.6	1.0	—	
Relative risk†	1.21	1.00	0.63	0.64	0.38	—	
95% CI	0.49 to 2.99	—	0.43 to 0.92	0.40 to 1.02	0.17 to 0.87	—	
Distal esophageal and gastric cardia cancer							.03
No. of incident cancer cases	7	125	67	42	13	—	
Person-years of follow-up	128,186.9	3,610,080.8	2,207,979.8	1,249,679.3	548,221.6	—	
Age-standardized rate*	4.5	3.8	2.8	3.1	2.4	—	
Relative risk†	1.10	1.00	0.77	0.83	0.59	—	
95% CI	0.49 to 2.50	—	0.57 to 1.04	0.58 to 1.18	0.34 to 1.05	—	
Stomach cancer							.066
No. of incident cancer cases	106	2,392	1,479	917	343	56	
Person-years of follow-up	127,683.9	3,600,418.2	2,202,265.4	1,246,220.4	486,801.1	59,894.5	
Age-standardized rate*	72.2	73.2	63.6	68.7	64.7	88.2	
Relative risk†	0.96	1.00	0.88	0.95	0.90	1.25	
95% CI	0.78 to 1.18	—	0.82 to 0.94	0.88 to 1.03	0.80 to 1.01	0.96 to 1.63	
Colon cancer excluding rectosigmoid cancer							.001
No. of incident cancer cases	14	359	316	190	63	11	
Person-years of follow-up	128,132.8	3,607,253.0	2,205,446.9	1,248,175.4	487,547.0	60,046.0	
Age-standardized rate*	10.1	9.7	13.3	14.3	11.2	18.9	
Relative risk†	1.00	1.00	1.24	1.33	1.07	1.92	
95% CI	0.62 to 1.63	—	1.07 to 1.43	1.13 to 1.57	0.83 to 1.38	1.15 to 3.22	
Rectosigmoid cancer							.003
No. of incident cancer cases	20	606	480	326	117	14	
Person-years of follow-up	129,921.7	3,606,952.6	2,204,456.4	1,247,605.3	487,431.8	60,039.9	
Age-standardized rate*	14.5	18.5	20.5	24.3	22.3	21.9	
Relative risk†	0.64	1.00	1.06	1.29	1.15	1.08	
95% CI	0.36 to 1.13	—	0.92 to 1.22	1.10 to 1.52	0.91 to 1.46	0.56 to 2.10	
Liver cancer excluding intrahepatic ductal cancer							.025
No. of incident cancer cases	54	1,422	1,006	583	240	42	
Person-years of follow-up	127,900.6	3,603,268.4	2,203,137.5	1,246,855.0	487,030.9	59,913.7	
Age-standardized rate*	40.3	43.5	43.1	43.4	45.4	66.0	
Relative risk†	0.84	1.00	1.04	1.04	1.07	1.56	
95% CI	0.63 to 1.10	—	0.96 to 1.13	0.94 to 1.14	0.93 to 1.23	1.15 to 2.12	
Gallbladder cancer							.586
No. of incident cancer cases	7	62	70	29	14	—	
Person-years of follow-up	128,102.5	3,606,477.4	2,208,256.7	1,249,357.3	547,346.4	—	
Age-standardized rate*	4.8	1.9	3.0	2.2	2.4	—	
Relative risk†	2.44	1.00	1.55	1.15	1.25	—	
95% CI	1.12 to 5.34	—	1.10 to 2.20	0.74 to 1.80	0.70 to 2.24	—	
Intra- and extrahepatic biliary tract cancer							.005
No. of incident cancer cases	9	192	164	108	38	6	
Person-years of follow-up	128,112.7	3,604,198.4	2,204,138.6	1,247,055.3	487,930.7	60,041.9	
Age-standardized rate*	5.6	6.0	7.0	7.9	7.1	9.6	
Relative risk†	0.90	1.00	1.22	1.40	1.24	1.64	
95% CI	0.45 to 1.83	—	0.99 to 1.50	1.11 to 1.78	0.87 to 1.75	0.73 to 3.70	

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Table 1. Age-Adjusted Incidence Rate and Multivariate Relative Risk of Cancer According to Body Mass Index Among the Whole Study Population (continued)

Type of Cancer	Body Mass Index: < 18.5 kg/m²	18.5-22.9 kg/m²	23.0-24.9 kg/m²	25.0-26.9 kg/m²	27.0-29.9 kg/m²	≥ 30.0 kg/m²	*P* for Trend
Pancreatic cancer							.564
No. of incident cancer cases	5	203	153	74	26	5	
Person-years of follow-up	128,216.5	3,609,769.3	2,207,627.0	1,249,555.5	488,027.5	60,104.9	
Age-standardized rate*	3.9	6.3	6.5	5.5	4.9	8.7	
Relative risk†	0.53	1.00	1.07	0.87	0.78	1.04	
95% CI	0.22 to 1.29	—	0.86 to 1.32	0.67 to 1.15	0.51 to 1.18	0.39 to 2.81	
Lung cancer							< .001
No. of incident cancer cases	66	1,072	651	333	127	15	
Person-years of follow-up	127,950.0	3,606,223.1	2,205,642.2	1,248,481.3	487,613.0	60,063.8	
Age-standardized rate*	47.7	33.4	27.5	24.6	23.5	23.6	
Relative risk†	1.26	1.00	0.88	0.80	0.78	0.77	
95% CI	0.98 to 1.61	—	0.80 to 0.97	0.70 to 0.90	0.65 to 0.94	0.47 to 1.30	
Kidney cancer							< .001
No. of incident cancer cases	3	220	162	114	58	5	
Person-years of follow-up	128,233.9	3,609,583.0	2,207,565	124,932.2	487,900.2	60,108.1	
Age-standardized rate*	2.5	6.6	7.0	8.5	11.0	7.8	
Relative risk†	0.26	1.00	1.11	1.31	1.82	1.42	
95% CI	0.06 to 1.03	—	0.89 to 1.38	1.02 to 1.67	1.37 to 2.52	0.59 to 3.46	
Bladder cancer							.629
No. of incident cancer cases	19	236	202	106	44	3	
Person-years of follow-up	128,154.7	3,609,613.6	2,207,329.1	1,249,416.4	487,935.8	60,120.9	
Age-standardized rate*	11.9	7.2	8.7	7.8	8.6	4.8	
Relative risk†	1.76	1.00	1.20	1.12	1.16	0.70	
95% CI	1.09 to 2.84	—	0.99 to 1.45	0.89 to 1.41	0.83 to 1.61	0.22 to 2.19	
Prostate cancer							.001
No. of incident cancer cases	6	136	127	83	30	5	
Person-years of follow-up	128,209.6	3,610,199.8	2,207,813.3	1,249,548.8	488,039.1	60,113.9	
Age-standardized rate*	3.7	4.2	5.3	6.2	5.7	8.0	
Relative risk†	0.66	1.00	1.26	1.46	1.39	1.92	
95% CI	0.27 to 1.62	—	0.99 to 1.61	1.11 to 1.92	0.93 to 2.06	0.78 to 4.68	
Brain cancer							.442
No. of incident cancer cases	4	105	69	32	21	3	
Person-years of follow-up	128,215.2	3,610,016.8	2,207,918.3	1,249,687.6	488,045.2	60,118.2	
Age-standardized rate*	3.5	3.0	3.0	2.4	3.9	4.8	
Relative risk†	1.07	1.00	1.09	0.84	1.47	1.79	
95% CI	0.39 to 2.93	—	0.79 to 1.50	0.55 to 1.28	0.90 to 2.38	0.57 to 2.66	
Hodgkin's lymphoma							.241
No. of incident cancer cases	0	13	8	6	4	—	
Person-years of follow-up	128,238.3	3,610,504.5	2,208,170.4	1,249,806.8	548,242.4	—	
Age-standardized rate*	0.0	0.4	0.4	0.5	0.7	—	
Relative risk†	—	1.00	0.92	1.22	1.79	—	
95% CI	—	—	0.38 to 2.23	0.46 to 3.22	0.55 to 6.56	—	
Non-Hodgkin's lymphoma							.04
No. of incident cancer cases	4	11	92	54	29	—	
Person-years of follow-up	128,225.9	3,610,125.9	2,207,856.1	1,249,614.0	548,146.0	—	
Age-standardized rate*	2.9	3.5	4.0	3.9	5.3	—	
Relative risk†	0.72	1.00	1.13	1.18	1.54	—	
95% CI	0.23 to 2.28	—	0.85 to 1.51	0.84 to 1.65	0.99 to 2.75	—	
Leukemia							.683
No. of incident cancer cases	2	86	67	32	10	3	
Person-years of follow-up	128,232.0	3,610,185.9	2,207,898.1	1,249,683.6	488,098.2	60,113.5	
Age-standardized rate*	1.1	2.5	2.9	2.5	2.0	4.5	
Relative risk†	0.64	1.00	1.25	1.01	0.75	2.03	
95% CI	0.16 to 2.61	—	0.90 to 1.75	0.66 to 1.55	0.38 to 1.51	0.64 to 6.44	

(continued on following page)

Table 1. Age-Adjusted Incidence Rate and Multivariate Relative Risk of Cancer According to Body Mass Index Among the Whole Study Population (continued)

Type of Cancer	Body Mass Index < 18.5 kg/m²	18.5-22.9 kg/m²	23.0-24.9 kg/m²	25.0-26.9 kg/m²	27.0-29.9 kg/m²	≥ 30.0 kg/m²	*P* for Trend
Multiple myeloma							.612
No. of incident cancer cases	2	36	45	14	6	—	
Person-years of follow-up	128,230.1	3,610,442.8	2,208,004.2	1,249,780.2	548,241.4	—	
Age-standardized rate*	1.8	1.1	1.9	1.0	1.09	—	
Relative risk†	1.19	1.00	1.72	0.96	0.98	—	
95% CI	0.29 to 4.96	—	1.11 to 2.68	0.51 to 1.77	0.30 to 3.32	—	
Melanoma							.007
No. of incident cancer cases	0	19	11	13	8	—	
Person-years of follow-up	128,238.3	3,610,496.9	2,208,155.3	1,249,762.4	548,224.5	—	
Age-standardized rate*	0.0	0.6	0.5	1.0	1.51	—	
Relative risk†	—	1.00	0.80	2.01	2.82	—	
95% CI	—	—	0.35 to 1.81	0.96 to 4.2	1.15 to 6.70	—	
Thyroid cancer							< .001
No. of incident cancer cases	3	72	70	53	28	—	
Person-years of follow-up	128,219.7	3,610,217.0	2,207,897.3	1,249,579.8	548,143.3	—	
Age-standardized rate*	2.8	2.1	3.2	4.1	5.2	—	
Relative risk†	0.82	1.00	1.52	2.00	2.23	—	
95% CI	0.20 to 3.34	—	1.07 to 2.14	1.38 to 2.89	1.40 to 3.55	—	
Other cancers							< .001
No. of incident cancer cases	42	853	514	247	113	20	
Person-years of follow-up	128,064.8	3,607,120.6	2,206,095.5	1,248,797.1	487,717.2	60,055.4	
Age-standardized rate*	29.5	25.2	22.9	18.4	21.4	29.8	
Relative risk†	1.11	1.00	0.93	0.78	0.81	1.12	
95% CI	0.77 to 1.51	—	0.82 to 1.03	0.68 to 0.94	0.67 to 1.01	0.71 to 1.81	

NOTE. No. of incident cancer cases/person-years of follow-up.
*The rate is per 100,000 person-years, adjusted to the age distribution of the entire study population.
†The Cox proportional hazards model was used, with adjustment for age (as continuous variable in years), smoking status (nonsmoker, former smoker, current smoker), average amount of alcohol consumed per day (none, 0.1 to 14.9, 15.0 to 29.9, or ≥ 30.0, g/d), frequency of regular exercise for more than 30 minutes during a week (0 to 2, 3 to 4, or ≥ 5 times per week), family history of cancer (yes or no/unknown), and residency area (urban or rural) at baseline.

involving both sites started, many previous studies have combined these sites[5,8,14,31]; thus, we have also combined these sites.

Statistical Analysis

We divided the BMI into six categories and calculated the age-adjusted incidence rates for each category of BMI, standardized to the entire study population. Person-years of follow-up were calculated as the time elapsed from the date of the health assessment in 1992 to the date of cancer incidence, to the date of death, or to the end of 2001. We used the Cox proportional hazards regression model to examine the relationship between BMI and the risk of cancer and to adjust for other potential risk factors reported at baseline. We assessed the multivariate relative risk (RR) associated with the development of cancer for each category of BMI, relative to the reference category (BMI = 18.5 to 22.9 kg/m^2), with 95% CIs (Tables 1, 2, and 3). Tests for linear trends were performed across the BMI categories and by testing the significance of the term using the likelihood ratio test. Covariates included in our analyses were age (a continuous variable in years), smoking status (nonsmoker, former smoker, or current smoker), average amount of alcohol consumed per day (none, 0.1 to 14.9, 15.0 to 29.9, or ≥ 30.0 g/d), frequency of regular exercise, which means recreational activity and exercise over 30 minutes during a week (none to two, three to four, or ≥ five times per week), family history of cancer (yes or no/unknown), and residency area (urban or rural) at baseline. Because smoking is a well-known risk factor for many cancers and has an inverse relationship with BMI, we analyzed the data for those who had never smoked in Table 3. We also present the results in relation to the specific histologic types in Tables 2 and 3 but only for those types with statistical significance to reduce the table size.

The population-attributable fraction (PAF) was calculated when cancer showed a statistically significant association with BMI in our study. The PAF of each cancer was estimated for obese (BMI ≥ 25.0 kg/m^2) persons compared with patients of normal weight (BMI = 18.5 to 22.9 kg/m^2), according to the BMI classification defined by WHO for the Western-Pacific region and by others.[28] The PAF was calculated using the following equation: $pd \times [(mRR - 1)/mRR]$, where mRR is the multivariate RR adjusted for the covariates mentioned earlier, and pd is the proportion of patients exposed to the risk factors.[32] Ninety-five percent CIs of adjusted PAF were estimated.[33] We used SAS (version 8.0; SAS Institute Inc, Cary, NC) for the statistical analyses, and a two-sided $P < .05$ was considered statistically significant.

RESULTS

We found that men with a BMI ≥ 30 kg/m^2 had a 26% increase in risk for all types of cancer compared with men with

Table 2. Age-Adjusted Incidence Rate and Relative Risk of Cancer Having Significant Associations With Excess Weight Depending on Pathologic Findings Among the Entire Study Population

Type of Cancer	Body Mass Index < 18.5 kg/m²	18.5-22.9 kg/m²	23.0-24.9 kg/m²	25.0-26.9 kg/m²	27.0-29.9 kg/m²	≥ 30.0 kg/m²	*P* for Trend
Squamous cell carcinoma in upper and middle esophagus							.002
No. of incident cancer cases	5	82	35	22	6	—	
Person-years of follow-up	128,205.8	3,610,201.2	2,208,066.2	1,249,744.6	548,237.3	—	
Age-standardized rate*	3.3	2.5	1.5	1.6	1.0	—	
Relative risk†	1.02	1.00	0.61	0.67	0.4	—	
95% CI	0.37 to 2.78	—	0.41 to 0.90	0.42 to 2.07	0.17 to 0.92	—	
Squamous cell carcinoma in distal esophagus and gastric cardia							< .001
No. of incident cancer cases	3	51	22	11	1	—	
Person-years of follow-up	128,186.9	3,610,080.8	2,207,979.8	1,249,679.3	548,221.6	—	
Age-standardized rate*	2.2	1.6	0.9	0.8	0.2	—	
Relative risk†	1.35	1.00	0.61	0.53	0.11	—	
95% CI	0.42 to 4.34	—	0.37 to 1.00	0.27 to 1.02	0.01 to 0.76	—	
Adenocarcinoma in colon excluding rectosigmoid							.005
No. of incident cancer cases	6	185	166	98	26	6	
Person-years of follow-up	128,132.8	3,607,253.0	2,205,446.9	1,248,175.4	487,547.0	60,046.0	
Age-standardized rate*	4.5	5.0	6.9	7.1	5.4	9.3	
Relative risk†	0.95	1.00	1.23	1.31	1.08	1.64	
95% CI	0.56 to 1.62	—	1.05 to 1.44	1.10 to 1.57	0.82 to 1.42	0.90 to 2.98	
Adenocarcinoma in rectosigmoid							.007
No. of incident cancer cases	11	400	299	204	74	9	
Person-years of follow-up	129,921.7	3,606,952.6	2,204,456.4	1,247,605.3	487,431.8	60,039.9	
Age-standardized rate*	8.3	12.1	12.8	15.2	14.1	14.4	
Relative risk†	0.56	1.00	1.04	1.25	1.16	1.2	
95% CI	0.31 to 1.10	—	0.90 to 1.21	1.06 to 1.49	0.90 to 1.49	0.62 to 2.32	
Hepatocellular carcinoma							.006
No. of incident cancer cases	34	1,009	733	420	185	29	
Person-years of follow-up	127,900.6	3,603,268.4	2,203,137.5	1,246,855.0	487,030.9	59,913.7	
Age-standardized rate*	25.1	30.8	31.5	31.4	35.1	46.2	
Relative risk†	0.77	1.00	1.06	1.06	1.16	1.53	
95% CI	0.54 to 1.08	—	0.96 to 1.17	0.94 to 1.18	0.99 to 1.36	1.06 to 2.22	
Cholangiocarcinoma in intra- and extrahepatic biliary tract							< .001
No. of incident cancer cases	5	142	111	85	33	6	
Person-years of follow-up	128,112.7	3,603,268.4	2,204,138.6	1,247,055.3	487,030.7	60,014.9	
Age-standardized rate*	3.3	4.4	4.7	6.2	6.1	9.6	
Relative risk†	0.6	1.00	1.12	1.5	1.46	2.24	
95% CI	0.22 to 1.63	—	0.87 to 1.43	1.15 to 1.97	1.00 to 2.14	0.99 to 5.07	
Squamous cell carcinoma in lung							< .001
No. of incident cancer cases	29	403	245	111	45	4	
Person-years of follow-up	127,950.0	3,606,223.1	2,205,642.2	1,248,481.3	487,613.0	60,063.8	
Age-standardized rate*	22.0	12.7	10.3	8.2	8.4	6.6	
Relative risk†	1.43	1.00	0.89	0.71	0.74	0.55	
95% CI	0.98 to 2.09	—	0.76 to 1.04	0.58 to 0.88	0.54 to 1.00	0.21 to 1.48	
Adenocarcinoma in lung							.014
No. of incident cancer cases	16	312	202	89	31	5	
Person-years of follow-up	127,950.0	3,606,223.1	2,205,642.2	1,248,481.3	487,613.0	60,063.8	
Age-standardized rate*	11.3	9.6	8.5	6.7	5.7	7.5	
Relative risk†	1.06	1.00	0.92	0.72	0.65	0.89	
95% CI	0.63 to 1.77	—	0.77 to 1.11	0.57 to 0.92	0.45 to 0.94	0.37 to 2.15	

(continued on following page)

Table 2. Age-Adjusted Incidence Rate and Relative Risk of Cancer Having Significant Associations With Excess Weight Depending on Pathologic Findings Among the Entire Study Population (continued)

Type of Cancer	Body Mass Index < 18.5 kg/m^2	18.5-22.9 kg/m^2	23.0-24.9 kg/m^2	25.0-26.9 kg/m^2	27.0-29.9 kg/m^2	≥ 30.0 kg/m^2	*P* for Trend
Small-cell carcinoma in lung							.04
No. of incident cancer cases	11	151	98	67	25	4	
Person-years of follow-up	127,950.0	3,606,223.1	2,205,642.2	1,248,481.3	487,613.0	60,063.8	
Age-standardized rate*	7.7	4.7	4.1	4.9	4.5	6.6	
Relative risk†	1.48	1.00	0.95	1.18	1.10	1.49	
95% CI	0.8 to 2.73	—	0.73 to 1.22	0.89 to 1.58	0.72 to 1.69	0.55 to 4.02	
Renal cell carcinoma							< .001
No. of incident cancer cases	2	173	128	86	49	5	
Person-years of follow-up	128,234.0	3,609,583.1	2,207,565.7	1,249,332.1	487,900.2	60,108.1	
Age-standardized rate*	1.8	5.2	5.5	6.4	9.4	7.8	
Relative risk†	0.29	1.00	1.06	1.23	1.89	1.62	
95% CI	0.07 to 1.17	—	0.84 to 1.34	0.94 to 1.61	1.37 to 2.60	0.66 to 3.94	
Adenocarcinoma in prostate							< .001
No. of incident cancer cases	5	11	106	75	25	5	
Person-years of follow-up	128,209.6	3,610,199.8	2,207,813.3	1,249,548.8	488,039.1	60,113.9	
Age-standardized rate*	3.0	3.5	4.5	5.6	4.7	8.0	
Relative risk†	0.63	1.00	1.25	1.56	1.37	2.27	
95% CI	0.23 to 1.72	—	0.96 to 1.64	1.17 to 2.10	0.89 to 2.12	0.92 to 5.55	
Papillary cell carcinoma in thyroid							< .001
No. of incident cancer cases	2	47	49	36	18	—	
Person-years of follow-up	128,219.7	3,610,217.0	2,207,897.3	1,249,579.8	548,143.3	—	
Age-standardized rate*	1.8	1.4	2.2	2.8	3.3	—	
Relative risk†	0.66	1.00	1.60	2.14	2.23	—	
95% CI	0.09 to 4.83	—	1.04 to 2.45	1.35 to 3.37	1.25 to 3.99	—	

NOTE. Presented cancers in this table were those having statistical significance with excess weight, and cancers having no associations are omitted to reduce table size.

*The rate is per 100,000 person-years, adjusted to the age distribution of the entire study population.

†The Cox proportional hazards model was used, with adjustment for age (as continuous variable in years), smoking status (nonsmoker, former smoker, or current smoker), average amount of alcohol consumed per day (none, 0.1 to 14.9, 15.0 to 29.9, or ≥ 30.0 g/d), frequency of regular exercise for more than 30 minutes during a week (0 to 2, 3 to 4, or ≥ 5 times per week), family history of cancer (yes or no/unknown), and residency area (urban or rural) at baseline.

a normal weight (BMI = 18.5 to 22.9 kg/m^2), even after statistical control of confounding factors. However, we failed to prove a linear trend with increasing BMI (Table 1). Of our study subjects, 26.8% were classified as having never smoked (Table 4). In the group who never smoked, a significant positive linear trend was observed, and men with a BMI ≥ 30 kg/m^2 had an increased risk for cancer of 62% (Table 3).

We confirmed that, in Koreans, excess weight could increase the risk of cancer in the colon, rectosigmoid, and kidney in a dose-dependent manner. We also found significant dose-dependent relationships between BMI and cancers of the liver, prostate, and thyroid, melanoma, and non-Hodgkin's lymphoma. We could not demonstrate associations for other cancers, such as gallbladder, pancreatic, bladder, and brain cancer, leukemia, Hodgkin's lymphoma, and multiple myeloma. Biliary tract cancer, excluding the gallbladder, was newly found to be associated with BMI. Stomach cancer had an increased risk at BMI ≥ 30 kg/m^2 only in the group who never smoked, but no dose-dependent relationship was observed. Esophageal and lung cancers had inverse dose-response relationships with BMI (Tables 1 and 3).

We also examined the detailed relationship between excess weight and the risks of each cancer according to histologic type. Significant positive linear trends were found for adenocarcinoma of the colon and rectosigmoid, hepatocellular carcinoma, cholangiocarcinoma, adenocarcinoma of the prostate, renal cell carcinoma, and papillary cell carcinoma of the thyroid. For hepatocellular carcinoma, an increased RR of 1.53 (95% CI, 1.06 to 2.22) was observed after statistical control for hepatitis B viral infection status (data not shown). However, the other histologic types of liver cancers did not show any relationship with BMI (Table 2).

Negative relationships with BMI were found for adenocarcinoma and squamous cell carcinoma of the lung and squamous cell carcinoma of the esophagus and gastric cardia (Table 2), but these associations disappeared in the group who never smoked. Small-cell lung cancer showed a positive linear trend with BMI (Table 2), but we could not corroborate this association in the group who never smoked because of the small incidence of patients (n = 6).

For BMI ≥ 25 kg/m^2, the estimated percent PAF for each obesity-related cancer ranged from 2.1% to 18.4% in

Table 3. Age-Adjusted Incidence Rate and Relative Risk of Cancer Having Significant Associations With Excess Weight Depending on Specific Organ Sites and Pathologic Findings Among Patients Who Never Smoked

	Body Mass Index						
Type of Cancer	< 18.5 kg/m²	18.5-22.9 kg/m²	23.0-24.9 kg/m²	25.0-26.9 kg/m²	27.0-29.9 kg/m²	≥ 30.0 kg/m²	*P* for Trend
All cancers							< .001
No. of incident cancer cases	33	1,365	1,096	718	286	46	
Person-years of follow-up	31,412.4	927,867.0	606,667.7	348,803.0	132,879.7	16,171.2	
Age-standardized rate*	119.9	169.5	169.1	184.6	187.3	253.1	
Relative risk†	0.69	1.00	1.01	1.11	1.14	1.62	
95% CI	0.48 to 0.96	—	0.93 to 1.10	1.01 to 1.22	1.01 to 1.30	1.22 to 2.16	
Stomach cancer							.336
No. of incident cancer cases	9	440	291	207	86	21	
Person-years of follow-up	31,513.5	931,178.8	609,464.3	350,555.1	133,531.8	16,268.9	
Age-standardized rate*	37.4	54.1	44.4	52.4	54.9	108.4	
Relative risk†	0.60	1.00	0.82	0.96	1.04	2.05	
95% CI	0.31 to 1.15	—	0.7 to 0.95	0.81 to 1.14	0.82 to 1.31	1.32 to 3.19	
Adenocarcinoma in stomach							.267
No. of incident cancer cases	6	335	245	161	73	14	
Person-years of follow-up	31,513.5	931,147.8	609,464.3	350,555.1	133,531.8	16,268.9	
Age-standardized rate*	24.8	41.7	37.2	40.4	46.6	73.7	
Relative risk†	0.52	1.00	0.88	0.95	1.14	1.73	
95% CI	0.23 to 1.15	—	0.75 to 1.04	0.79 to 1.15	0.88 to 1.47	1.01 to 2.96	
Colon cancer excluding rectosigmoid cancer							.038
No. of incident cancer cases	2	95	97	75	18	4	
Person-years of follow-up	31,550.4	932,400.9	609,919.7	350,951.2	133,813.2	16,335.2	
Age-standardized rate*	6.3	10.2	15.2	19.9	12.4	21.5	
Relative risk†	0.66	1.00	1.24	1.58	1.02	1.75	
95% CI	0.16 to 2.67	—	0.93 to 1.66	1.16 to 2.16	0.66 to 1.62	0.64 to 4.78	
Adenocarcinoma in colon excluding rectosigmoid							.04
No. of incident cancer cases	2	77	42	64	16	3	
Person-years of follow-up	31,550.4	932,337.9	609,919.7	350,951.2	133,707.4	16,335.2	
Age-standardized rate*	6.3	8.23	7.2	17.7	10.9	18.3	
Relative risk†	0.78	1.00	0.89	1.64	1.20	1.89	
95% CI	0.19 to 3.19	—	0.33 to 2.90	1.17 to 2.30	0.67 to 2.54	0.55 to 5.63	
Rectosigmoid cancer							.039
No. of incident cancer cases	2	102	84	51	33	—	
Person-years of follow-up	31,552.8	932,337.1	609,988.3	351,001.5	150,056.9	—	
Age-standardized rate*	6.9	12.4	12.9	13.6	21.1	—	
Relative risk†	0.29	1.00	1.04	1.08	1.72	—	
95% CI	0.04 to 2.06	—	0.77 to 1.40	0.77 to 1.53	1.21 to 2.48	—	
Adenocarcinoma in rectosigmoid							.168
No. of incident cancer cases	2	90	73	42	28	—	
Person-years of follow-up	31,550.4	932,337.9	609,919.7	350,951.2	150,042.6	—	
Age-standardized rate*	6.9	11.0	11.2	11.0	13.9	—	
Relative risk†	0.33	1.00	1.02	0.99	1.57	—	
95% CI	0.05 to 2.32	—	0.74 to 1.39	0.68 to 1.43	1.01 to 2.46	—	
Liver cancer excluding intrahepatic ductal cancer							.042
No. of incident cancer cases	7	264	234	138	60	6	
Person-years of follow-up	31,527.6	932,100.2	609,840.7	350,901.3	133,668.7	16,328.6	
Age-standardized rate*	24.0	32.6	35.7	35.3	39.4	32.1	
Relative risk†	0.66	1.00	1.12	1.13	1.29	1.13	
95% CI	0.29 to 1.48	—	0.93 to 1.35	0.91 to 1.40	0.96 to 1.73	0.50 to 2.54	
Hepatocellular carcinoma							.042
No. of incident cancer cases	4	203	169	106	44	4	
Person-years of follow-up	31,527.6	932,100.2	609,840.7	350,901.3	133,668.7	16,328.6	
Age-standardized rate*	14.8	25.0	25.8	27.1	29.0	22.3	
Relative risk†	0.66	1.00	1.12	1.13	1.29	1.13	
95% CI	0.29 to 1.48	—	0.93 to 1.35	0.91 to 1.40	0.96 to 1.73	0.50 to 2.54	

(continued on following page)

Table 3. Age-Adjusted Incidence Rate and Relative Risk of Cancer Having Significant Associations With Excess Weight Depending on Specific Organ Sites and Pathologic Findings Among Patients Who Never Smoked (continued)

Type of Cancer	Body Mass Index < 18.5 kg/m^2	18.5-22.9 kg/m^2	23.0-24.9 kg/m^2	25.0-26.9 kg/m^2	27.0-29.9 kg/m^2	≥ 30.0 kg/m^2	*P* for Trend
Kidney cancer							.004
No. of incident cancer cases	0	42	41	32	12	3	
Person-years of follow-up	31,564.1	932,889.2	610,469.7	351,241.0	133,818.2	16,340.7	
Age-standardized rate*	0.0	5.2	6.3	7.8	8.2	17.6	
Relative risk†	—	1.00	1.32	1.78	1.59	3.53	
95% CI	—	—	0.84 to 2.08	1.10 to 2.87	0.80 to 3.13	1.08 to 11.50	
Renal cell carcinoma							.01
No. of incident cancer cases	0	35	30	27	10	3	
Person-years of follow-up	31,654.1	932,889.3	610,469.7	351,241.0	133,818.2	16,340.7	
Age-standardized rate*	0.0	4.3	4.6	6.6	7.0	17.6	
Relative risk†	—	1.00	1.03	1.63	1.57	3.85	
95% CI	—	—	0.62 to 1.7	0.98 to 2.72	0.77 to 3.19	1.18 to 12.62	
Thyroid cancer							.004
No. of incident cancer cases	0	23	21	21	9	—	
Person-years of follow-up	31,564.1	932,937.3	610,535.5	351,267.8	150,179.7	—	
Age-standardized rate*	0.0	2.7	3.3	5.7	6.1	—	
Relative risk†	—	1.00	1.29	2.35	2.14	—	
95% CI	—	—	0.70 to 2.40	1.28 to 4.33	0.94 to 4.85	—	
Papillary cell carcinoma in thyroid							.036
No. of incident cancer cases	0	14	15	14	5	—	
Person-years of follow-up	31,564.1	932,937.3	610,535.5	351,267.8	150,179.7	—	
Age-standardized rate*	0.0	1.6	2.3	3.9	3.3	—	
Relative risk†	—	1.00	1.37	2.39	1.65	—	
95% CI	—	—	0.65 to 2.89	1.13 to 5.04	0.54 to 5.04	—	

NOTE. Presented cancers in this table were those having statistical significance with excess weight, and cancers having no associations are omitted to reduce table size.
*The rate is per 100,000 person-years, adjusted to the age distribution of the entire study population.
†The Cox proportional hazards model was used, with adjustment for age (as continuous variable in years), average amount of alcohol consumed per day (none, 0.1 to 14.9, 15.0 to 29.9, or ≥ 30.0 g/d), frequency of regular exercise for more than 30 minutes during a week (0 to 2, 3 to 4, or ≥ 5 times per week), family history of cancer (yes or no/unknown), and residency area (urban or rural) at baseline.

the entire population and from 4.2% to 23.1% in the group who never smoked. Overall, obesity (BMI ≥ 25 kg/m^2) accounts for 0.2% of all cancers in the entire population and 3.4% of cancers in the group who never smoked (Table 5).

DISCUSSION

Cancers vary in their incidence by more than an order of magnitude across ethnic groups or nations; moreover, many Asians, including Koreans, have smaller bodies.[28] Therefore, the relationship between BMI and cancers in Koreans may differ from (generally recognized as a lesser relationship) the relationship in whites. However, contrary to our expectations, we found similar relationships for Korean patients compared with Western populations.

Colon and kidney cancer, which have previously been well documented as obesity-related cancers, showed significant positive dose-dependent relationships with increasing BMI. Cancers of the prostate, thyroid, and liver, melanoma, and non-Hodgkin's lymphoma, which had showed conflicting results,[4-8,24,25] also had significant positive dose-dependent relationships with increasing BMI. In addition, we found a new association between excess weight and biliary tract cancer, which, to our knowledge, has not yet been reported. Recently, the incidences of colon, rectosigmoid, thyroid, prostate, kidney, and other cancers have increased in Korea and in many other Asian countries.[29] So, we could infer that the perceived increase in the prevalence of obesity in many Asian countries,[28] including Korea,[34] would explain, to a certain extent, why these cancers are increasing rapidly.

We could not demonstrate associations for some cancers (pancreatic, gallbladder, and esophageal cancers) previously known to be associated with excess weight. Gallbladder cancer frequently develops in conjunction with stones and is significantly associated with BMI in women.[4,20] One recent study demonstrated a significant association between gallbladder cancer mortality and BMI in men,[8] but we failed to demonstrate this relationship in Korean men, even after considering specific histologic types. Similarly, although pancreatic cancer was also known to be related with excess weight,[35]

Table 4. Base-Line Characteristics of Entire Study Population and the Subpopulation of Patients Who Never Smoked in 1992

Characteristic	Entire Population	Never Smoked
No.	781,283	209,389
Age, years		
Mean	40.1	39.7
Standard deviation	9.9	9.3
Body mass index, kg/m^2		
Mean	23.2	23.9
Standard deviation	2.5	2.5
Family history of cancers, %		
Yes	16.3	20.3
No or unknown	83.7	79.7
Residency, %		
Urban	76.4	80.3
Rural	23.6	19.7
Exercise frequency per week, %*		
< 3/week	89.6	83.9
≥ 3/week and < 5/week	6.3	9.1
≥ 5/week	4.1	7.0
Average alcohol consumption per day, %		
None	16.3	22.3
< 15 g/d	38.2	52.1
15-30 g/d	19.4	16.1
≥ 30 g/d	26.1	9.5
Smoking status, %		
Never	26.8	100
Ex-smoker	14.3	—
Current smoker	58.9	—

*Exercise is defined as aerobic exercise for more than 30 minutes until sweating.

we could not demonstrate this relationship. The reason for failing to demonstrate this relationship is unclear, but we expect that further investigations will be able to reveal these associations considering other possible confounding factors, such as gallstone history and other factors.

Hepatocellular carcinoma is far more common in Korea than in Western countries because of the higher prevalence of hepatitis B viral infection.[36] Although previous reports on the relationship between obesity and hepatocellular carcinoma were limited,[18] we found a clear dose-dependent association and increased risk in the obese population (BMI ≥ 30 kg/m^2), even after statistical control of the hepatitis B viral infection status. Gastric adenocarcinoma is also prevalent in Korea.[29] This cancer had an elevated RR in obese (BMI ≥ 30 kg/m^2) patients only in the group who never smoked but did not show a dose-dependent relationship. Although our findings suggest an association between obesity and gastric adenocarcinoma, the failure to demonstrate a dose-dependent relationship, a lack of previous evidence, and the possibility of a chance association prevented us from reaching a definite conclusion.

Recent evidence suggests that adiposity influences different cancer cell types differently within the same organ.[14,37] In our study, depending on histologic type, each cancer showed a different association with excess weight. Some cancers showed relationships with certain histologic types only, and others showed reverse relationships. Lung cancer is a good example. Small-cell lung cancer showed a positive dose-dependent relationship with increasing BMI, whereas squamous and large-cell lung cancers showed negative relationships. Although it is possible that these findings are chance associations, one recent report from a US population also found that small-cell lung cancer had a positive dose-dependent relationship with central obesity.[37] The reason for these different associations is not clear, but they seem to be confounded by smoking and other

Table 5. Population-Attributable Fractions (%) of Obesity-Related Cancer in This Study Population by Specific Cancer Sites

	Entire Population		Never Smoked	
Cancer Types	%	95% CI	%	95% CI
Colon cancer without rectosigmoid cancer	6.1	2.1 to 10.0	9.5	0.3 to 17.8
Rectosigmoid cancer	5.7	1.6 to 9.7	6.4	0.1 to 12.3
Thyroid cancer	18.4	9.0 to 26.8	23.1	5.4 to 37.5
Kidney cancer	11.2	4.8 to 17.1	14.7	1.5 to 26.1
Liver cancer	2.1	0.3 to 3.8	4.2	0.0 to 8.4
Intra- and extrahepatic biliary tract cancer	7.9	2.0 to 13.5	—	—
Prostate cancer	9.6	3.1 to 15.6	—	—
Non-Hodgkin's lymphoma	6.2	0.2 to 12.1	—	—
Melanoma	22.9	0.1 to 41.1	—	—
Total obesity-related cancers*	5	2.4 to 7.6	6.5	2.1 to 10.7
All cancers†	0.2	−0.4 to 0.8	3.4	1.5 to 5.3

NOTE. Classification of body mass index was based on the guideline for Asians proposed by WHO Western-Pacific region and others.[28] Obesity was defined as body mass index of ≥ 25.0 kg/m^2.
*Total obesity-related cancers are summation of above cancers having significant positive dose-dependent relationship with body mass index. In the entire population, nine types of cancers were included (colon, rectosigmoid, liver, biliary tract, kidney, and prostate cancer, Non-Hodgkin's lymphoma, melanoma, and thyroid cancer). In the never-smoked population, five types of cancer were included (colon, rectosigmoid, liver, kidney, and thyroid cancer).
†All cancers are included in total cancers, including obesity-related and obesity-unrelated cancers.

unknown factors.[37,38] Another example is distal esophageal and gastric cardia cancer. In our study, squamous cell carcinoma at this site showed a significant negative association with excess weight, whereas adenocarcinoma did not. According to many previous reports, adenocarcinoma at this site has a positive dose-dependent relationship with BMI, whereas esophageal squamous carcinoma is more profoundly influenced by smoking, with an inverse relationship with BMI.[14] Reflux of gastric acid as a result of increased intra-abdominal pressure is thought to be the main mechanism explaining the relationship between esophageal adenocarcinoma and obesity.[31] However, we failed to demonstrate this relationship for the following two possible reasons: obesity in Koreans severe enough to evoke considerable gastric acid reflux is rare (only 2.6% of Koreans had BMI of $\geq$ 30 kg/m^2 in 1998),[34,39] and *Helicobacter pylori* infection, which has an inverse association with esophageal adenocarcinoma,[40] is prevalent in Koreans.[41]

Much epidemiologic data strongly support the associations between excess weight and certain cancers, but the underlying mechanisms explaining these associations are still uncertain. Increased blood levels of sex steroid, insulin, insulin-like growth factor, leptin, adipocytokine, and increased intra-abdominal pressure (esophageal adenocarcinoma) in obese people have been suggested to explain the associations of obesity with cancers.[5,42] However, data on this issue are still limited and unclear. Further research is needed to elucidate these mechanisms. Although we could not attest this hypothesis only from our data, we did find that interesting associations exist according to histologic type. With the understanding that mechanisms of these associations can be varied depending on their histologic types and that previous data suggested important clues from these associations,[14,37] we expect that our report considering histologic types can contribute to future research and also to a clearer understanding of the relationship between body weight and cancers.

Because smoking is not only a risk factor for certain cancers, but also has an inverse relationship with BMI, we also present the results as they pertain to nonsmokers. Although analyses restricted to nonsmokers may produce more refined results, as noted by other researchers,[8] some unique characteristics of this group need to be considered. In patients who never smoked, covariates, such as exercise, alcohol, and other factors, could differ from the general population, so careful consideration of these covariates is needed to interpret the study results, especially when extrapolating them to broader populations. Therefore, we did not pay more attention to the results from nonsmokers when interpreting and discussing our results.

The PAF of all cancers from obesity (BMI $\geq$ 25.0 kg/m^2) in our study was much smaller (only 0.2% for the entire population and 3.4% for the group who never smoked; Table 5) than that of Western countries,[4] whereas each cancer known to be associated with obesity had a much higher PAF. This discrepancy was attributed to the fact that the most common cancers in Korea are not closely related to excess weight. Stomach cancer is the most prevalent cancer in Korea (24.1% of all cancers for all Korean men from KCCR in 2001), and lung cancer is the second most prevalent cancer (16.0% of all cancers).[29] These cancers showed no dose-dependent relationship or inverse relationship with increasing BMI. After restricting our analyses to the obesity-related cancers and summarizing the cancers with positive associations with increasing BMI, we obtained higher values of PAF (5.0% for the entire population and 6.5% for the group who never smoked) in our study population, which are in accord with previous results from Western countries.[4]

The impact of weight change on the risk of cancer is another important issue to consider because weight gain and loss could be time-dependent covariates in our analyses. A recent study reported that intentional weight loss reduced the risk of obesity-related cancer, whereas unintentional weight loss episodes were not associated with decreased cancer risk.[43] We could not conduct analyses with time-dependent variables because the questionnaires, which contained important time-dependent covariates such as smoking, alcohol, and exercise, given to the subjects were modified during the study period as a result of administrative problems in the KNHIC. Further study is needed to examine time-dependent variables.

The comprehensiveness of cancer case reporting in our study is another consideration. According to surveys of the KCCR, at least 80% of newly developed cancers in Korea are reported.[29] However, this is only an average percentage that can be applied to all subjects in Korea; it does not apply, necessarily, to our study patients. In Korea, the jobs held by our patients are regarded as stable and secure jobs, and there are low rates of leaving or job changing; moreover, all the patients had to be members of KNHIC by law, and their health examination was mandatory. Therefore, this population was relatively easy to follow and should constitute a source of relatively precise information. Therefore, we postulated that more than 80% of the cancer patients, by far, with respect to our patients, were included in the KCCR data; in addition, we matched these data with data of KNHIC, which provides medical insurance to almost all people in Korea, to reduce missing patients. Although we cannot be confident that 100% were included, we expect that almost all patients were included in our study. In addition, occult (prevalent) cancers are also an important issue to be considered. We initially tried to find patients with new cancers that arose in the initial 2 years and found a small number of incident patients (663 patients in the first year and 1,430 patients in the second year). But we could not find any significant differences between the results of analyses including cancers in the initial 2 years and analyses excluding these cancers. We assumed that this was because of the fact that many of the occult cancer patients were diagnosed and excluded through their health status examination in 1992.

One advantage of our study is that actual measurements of height and weight were made by trained individuals. This is preferred over self-reported data, which have been used frequently in a number of well-known large-scale cohort studies, because heavier individuals tend to underreport their weight.[44]

In summary, like western populations, excess weight seems to be associated with many types of cancers for Koreans, and there may prove to be different associations depending on histologic type. This suggests that the increasing levels of obesity among Korean and Asian populations will result in these populations being exposed to a greater risk of cancer. Considering that obesity-related cancers are increasing rapidly in Asian countries, more attention should be paid to controlling obesity in these areas to prevent these cancer epidemics.

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Authors' Disclosures of Potential Conflicts of Interest

The authors indicated no potential conflicts of interest.

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