Body Mass Index and the Risk of Cancers of the Gastric Cardia and Distal Stomach in Shanghai, China

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Abstract

The divergent incidence patterns of gastric cardia and distal stomach cancers suggest different etiologies. Although obesity has recently been linked to cardia cancer in Western populations, its association with distal stomach cancer remains unclear. This study examined the relation of anthropometric measurements to risk by subsites of stomach cancer in a Chinese population. We identified 1124 population-based cases of stomach cancer, ages 20–69 years, newly diagnosed between December 1988 and November 1989 in Shanghai, China. Controls (*n* = 1451) were randomly selected from permanent Shanghai residents and frequency-matched to cases by age and sex. Information on demographic characteristics, height and weight, diet, smoking, and other exposures was obtained by trained interviewers in person. The body mass index (BMI) was calculated as weight in kilograms divided by height in square meters and categorized into quartiles based on the distribution among controls. Odds ratios and 95% confidence intervals were estimated using logistic regression models, simultaneously adjusting for age, education, income, cigarette smoking (men only), alcohol drinking (men only), intake of total calories, and chronic gastric diseases. For gastric cardia cancer, the odds ratios among men were 1.4, 1.5, and 3.0 in the second, third, and fourth quartiles of usual BMI (*P* for trend, <0.01). Among women, elevated risks also were associated with excess weight, but the gradient in risk was not smooth. Risk patterns for usual body weight, maximum BMI, and minimum BMI were similar to those found for usual BMI. For distal stomach cancer, no association with usual BMI was observed among men, but a slightly elevated risk was seen among women. Our observations in China support recent findings in Western populations that obesity contributes to the risk of gastric cardia cancer, especially among men.

Introduction

The incidence of gastric cardia cancer has been increasing in the United States and other Western countries for the past two decades, whereas rates for cancer of the distal stomach have declined (1–6). The divergent trends suggest etiological variation by anatomical subsite, but little information is available on the risk factors involved. Obesity has been associated with an excess risk of gastric cardia cancer in limited case-control studies in Western populations (7–8), and its association with distal stomach cancer has not been well examined (9). In a large population-based case-control study of stomach cancer conducted in Shanghai, China, we evaluated risk factors for stomach cancer by anatomical subsite. Associations with consumption of cigarettes, alcohol, and green tea have been reported earlier (10). Herein we examine the association with self-reported anthropometric variables.

Materials and Methods

This study was part of a large population-based case-control study that also included cancers of the colon and rectum. The methods of this study have been described in detail elsewhere (10). Briefly, cases of stomach cancer were ages 20–69 years, newly diagnosed between December 1, 1988 and November 30, 1989 among permanent residents of the 10 urban districts of Shanghai (henceforth referred to as Shanghai). A standard medical abstract form was used to collect data on the date and methods of diagnosis, histological type, and subsite of tumor. Of the 1722 eligible patients diagnosed with stomach cancer, 353 (20.5%) died before interview, 153 (8.9%) moved away, 19 (1.1%) refused to participate, and 73 (4.2%) were excluded because only clinical diagnostic information was available. Thus, 1124 (770 males and 354 females) patients were included in the present analysis (65.3%). All cases were confirmed by histology (52.1%) or other diagnostic methods including surgery, endoscopy, X-ray, and ultrasound (47.9%). The cases were grouped into three categories: (*a*) cardia [ICD (11) code 151.0]; (*b*) distal stomach (ICD code 151.1–151.8); and (*c*) stomach not otherwise specified (ICD code 151.9). Among men, 145 (18.8%) cancers arose in the cardia, 530 (68.9%) cancers arose in the distal stomach, and 95 (12.3%) cancers were unclassified. Among women, the corresponding numbers were 40 (11.3%), 257 (72.6%), and 57 (16.1%), respectively. Controls were selected from permanent residents of Shanghai,

Received 11/8/96; revised 2/27/97; accepted 3/5/97.

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Table 1 Cutpoints for quartiles of anthropometric variables by sex, Shanghai, China, 1988–1989

	Men				Women			
	Q1[a]	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Usual weight (kg)	≤55	≤60	≤65	>65	≤48	≤52	≤57.5	>57.5
Height (m)	≤1.67	≤1.70	≤1.72	>1.72	≤1.55	≤1.58	≤1.61	>1.61
Usual BMI[b] (kg/m^2)	≤19.38	≤20.77	≤22.15	>22.15	≤19.49	≤21.09	≤22.87	>22.87
Maximum BMI[c] (kg/m^2)	≤20.24	≤21.97	≤23.88	>23.88	≤20.67	≤22.71	≤25.15	>25.15
Minimum BMI[d] (kg/m^2)	≤18.07	≤19.36	≤20.76	>20.76	≤17.46	≤19.05	≤20.81	>20.81

[a] Q, quartile.
[b] BMI based on usual adult weight.
[c] BMI based on maximum adult weight.
[d] BMI based on minimum adult weight.

frequency-matched to the expected distributions by age (5-year category) and sex of both stomach and colorectal cancer cases combined. A systematic random sampling method was used to search the population-based Shanghai Resident Registry files for eligible controls. Of the 1692 eligible controls, 1451 (819 men and 632 women) were interviewed, yielding a response rate of 85.8%.

Each subject was interviewed in person by trained interviewers. A structured questionnaire elicited information on demographic background and residential history, height and weight history, smoking, alcohol drinking, diet, history of selected diseases, family history of cancer, occupation, and other factors. The self-reported anthropometric variables included adult height, usual adult weight, and maximum and minimum weight during adulthood. Maximum weight for women excluded weight during pregnancy. Information within 1 year before interview of cases and controls was excluded.

BMI,[2] computed as weight in kilograms divided by height in square meters (kg/m^2), was used to measure relative weight in this study. Categories of height, weight, and BMI were grouped into quartiles based on distributions among the controls (Table 1). In addition, separate analyses were conducted for usual BMI (BMI based on usual adult weight), using a cutpoint defined as obesity (>25 kg/m^2) in China (12). Risk of stomach cancer associated with BMI was estimated by ORs and 95% CIs, using logistic regression models (13). Dose-response relations were examined by test of linear trends based on quartile variables. All ORs were adjusted for age, monthly family per capita income, educational level, intake of total calories, and history of chronic gastric disease (gastritis and gastric and duodenal ulcers), because all these factors substantially altered the risk estimates of BMI factors in the logistic model. Moreover, ORs for men were also adjusted for cigarette smoking and alcohol drinking, confounding factors that are common among Chinese men but not among Chinese women. Other potential confounding factors, such as fat intake, physical activity, and occupation, were also considered in the multivariate analyses, but they did not alter the associations with BMI.

Results

Compared with controls, patients with gastric cardia cancer tended to have a higher male:female ratio (3.8:1 *versus* 1.3:1), to be older (median age, 61 *versus* 59 years), to have lower monthly incomes (41% of cases *versus* 30% of controls had an average per capita income of 22 yuan/month or less), and to be less educated (61% of cases *versus* 43% of controls had primary school or lower education). Patients with distal stomach cancers also had a higher male:female ratio (2.1:1), were older (median age, 60 years), had lower monthly incomes (35%), and were less educated (47%) compared with controls, but these differences were smaller than those observed between cardia cases and controls.

Among the controls, the mean level of usual BMI was generally similar among smokers and nonsmokers (20.98 *versus* 21.22), among alcohol drinkers and nondrinkers (21.03 *versus* 21.15), and among those with and without a history of chronic gastric diseases (20.66 *versus* 21.25). Furthermore, the BMI increased with advancing age ($r = 0.11$; $P < 0.01$). The usual BMI also was positively correlated with intake of calories ($r = 0.17$; $P < 0.01$) and fat ($r = 0.06$; $P = 0.01$), although the correlation with fat was weak.

Because the magnitude of association between gastric cardia cancer and BMI seemed to differ between men and women, despite a lack of statistically significant gender interaction, and substantial differences in the prevalence of confounding factors existed between the sexes, subsequent results are presented separately by gender. Risks for gastric cardia cancer increased with increasing usual BMI, with ORs being 1.4 (CI, 0.7–2.6), 1.5 (CI, 0.8–2.8), and 3.0 (CI, 1.7–5.4) in the second, third, and highest quartile of usual BMI among men (P for trend test, <0.01; Table 2). Among women, risks were not consistently elevated or statistically significant (ORs = 0.9, 2.0, and 1.4 in the upper three quartiles of usual BMI, respectively (P for trend test, 0.31). When subjects in the highest quartile of usual BMI were further divided by the level of excess weight, risks among the most obese were further elevated to more than 5-fold in men and to nearly 2-fold in women. No clear associations were found between usual BMI and distal stomach cancer except for a 2-fold (CI, 1.1–3.9) excess among obese women.

Table 3 shows the results of other anthropometric measurements in relation to cardia cancer. Among men, risks rose consistently with increasing levels of usual weight, whereas height seemed not to be a risk factor. Among women, risks generally increased with usual weight and height. The associations with maximum and minimum BMIs resembled those observed for usual BMI (data not shown). Risks did not vary consistently with the percentage of change between the minimum and maximum weights.

For the same measures, associations with distal stomach cancer were much weaker than those seen for cardia cancer (data not shown), with no clear trends found for usual weight or height in either men or women. No significant trends in risk were associated with maximum and minimum BMIs, but in the

[2] BMI, body mass index; CI, confidence interval; OR, odds ratio; ICD, International Classification of Diseases.

Table 2 ORs[a] and 95% CIs for cardia and distal stomach cancers and all stomach cancers combined in relation to usual BMI by sex, Shanghai, China, 1988–1989

BMI (kg/m^2)	Men			Women		
	Cases/controls	OR	95% CI	Cases/controls	OR	95% CI
Cardia						
Q1[b]	21/209	1.0		6/156	1.0	
Q2	26/188	1.4	(0.7–2.6)	6/143	0.9	(0.3–3.0)
Q3	30/204	1.5	(0.8–2.8)	13/158	2.0	(0.7–5.6)
Q4	71/211	3.0	(1.7–5.4)	12/159	1.4	(0.5–4.1)
≤25	46/181	2.7	(1.5–4.8)	7/110	1.3	(0.4–4.1)
>25	15/30	5.4	(2.4–12.3)	5/49	1.8	(0.5–6.4)
P for trend[c]			<0.01			0.04
Distal						
Q1	121/209	1.0		50/156	1.0	
Q2	98/188	0.9	(0.7–1.3)	52/143	1.2	(0.7–1.9)
Q3	105/204	0.9	(0.7–1.3)	46/158	1.0	(0.6–1.7)
Q4	124/211	1.1	(0.8–1.6)	64/159	1.6	(1.0–2.7)
≤25	101/181	1.1	(0.7–1.5)	42/110	1.5	(0.9–2.5)
>25	23/30	1.5	(0.8–2.8)	22/49	2.0	(1.1–3.9)
P for trend			0.33			0.02
All sites						
Q1	190/209	1.0		83/156	1.0	
Q2	156/188	0.9	(0.7–1.2)	82/143	1.1	(0.7–1.6)
Q3	184/204	1.1	(0.8–1.4)	76/158	1.0	(0.7–1.5)
Q4	231/211	1.3	(1.0–1.8)	105/159	1.5	(1.0–2.2)
≤25	181/181	1.2	(0.9–1.6)	68/110	1.4	(0.9–2.1)
>25	50/30	2.1	(1.2–3.5)	37/49	1.8	(1.0–3.1)
P for trend			<0.01			0.16

[a] Adjusted for age, education, income, cigarette smoking (men only), alcohol drinking (men only), intake of total calories, and chronic gastric diseases.
[b] Q, quartile. Q1, lowest quartile of BMI; Q4, highest quartile of BMI.
[c] Trend tests did not include subcategories of Q4 (≤25 and >25).

Table 3 ORs[a] and 95% CIs for cardia cancer in relation to usual weight and height by sex, Shanghai, China, 1988–1989

	Men			Women		
	Cases/controls	OR	95% CI	Cases/controls	OR	95% CI
Usual weight (kg)						
Q1[b]	28/247	1.0		4/147	1.0	
Q2	34/262	1.3	(0.8–2.3)	6/127	1.4	(0.4–5.1)
Q3	36/178	2.1	(1.2–3.8)	9/172	1.6	(0.5–5.6)
Q4	40/125	3.5	(1.9–6.1)	18/171	2.7	(0.8–8.6)
P for trend			<0.01			0.04
Height (m)						
Q1	32/199	1.0		4/137	1.0	
Q2	33/193	1.1	(0.6–1.9)	6/146	1.5	(0.4–5.5)
Q3	28/163	1.1	(0.6–2.0)	15/188	3.2	(1.0–10.4)
Q4	45/259	1.3	(0.8–2.7)	12/150	3.1	(0.9–10.6)
P for trend			0.33			0.02

[a] Adjusted for age, education, income, cigarette smoking (men only), alcohol drinking (men only), intake of total calories, and chronic gastric diseases.
[b] Q, quartile.

highest quartiles of both variables, the ORs were 1.5 (CI, 1.1–2.1) and 1.9 (CI, 1.3–2.7), respectively, for men, and 1.7 (CI, 1.0–2.8) and 2.4 (CI, 1.5–4.0), respectively, for women.

When stratified by age, usual BMI was associated with greater risks of cardia cancer among the younger (<60 years) rather than the older (≥60 years) age groups in both men and women (Table 4). No effect modification by other demographic or life-style factors was detected, including education, income, cigarette smoking, alcohol drinking, caloric intake, and a history of chronic gastric diseases (data not shown). The risk of distal stomach cancer in relation to usual BMI was not modified by age group.

Discussion

Although the reasons for the rapid rise in incidence of gastric cardia cancer in the United States and other Western countries remain uncertain (3, 4, 6), the parallel increase in esophageal adenocarcinoma has suggested shared etiological mechanisms (3, 14). A few recent case-control studies of these tumors have

Table 4 ORs[a] and 95% CIs for cardia cancer in relation to usual BMI by age and sex, Shanghai, China, 1988 –1989

	Younger age (<60 yrs)			Older age (≥60 yrs)		
	Cases/controls	OR	95% CI	Cases/controls	OR	95% CI
A. Men						
Usual BMI (kg/m^2)						
Q1[b]	4/100	1.0		17/109	1.0	
Q2	16/101	3.3	(1.0–10.6)	10/87	0.7	(0.3–1.7)
Q3	12/104	2.8	(0.8–9.3)	18/100	1.0	(0.5–2.2)
Q4	25/93	6.5	(2.1–20.6)	36/118	2.1	(1.1–4.2)
P for trend			<0.01			0.01
B. Women						
Usual BMI (kg/m^2)						
Q1	2/87	1.0		4/69	1.0	
Q2	3/91	1.2	(0.2–7.9)	3/52	0.8	(0.2–3.8)
Q3	5/90	2.4	(0.4–14.2)	8/68	1.9	(0.5–7.3)
Q4	5/89	2.4	(0.4–14.1)	7/70	1.2	(0.3–4.7)
P for trend			0.25			0.51

[a] Adjusted for age, education, income, cigarette smoking (men only), alcohol drinking (men only), intake of total calories, and chronic gastric diseases.
[b] Q, quartile.

suggested an association with obesity. Vaughan *et al.* (8) reported increasing risks of adenocarcinoma of the gastric cardia with increasing levels of BMI, with a 2-fold excess risk among those in the 90th percentile. Brown *et al.* (7) reported that men in the highest quartile of BMI had a 3-fold elevated risk of esophageal adenocarcinoma. Kabat *et al.* (9), on the other hand, reported no consistent associations with BMI in a combined group of patients with adenocarcinomas of the esophagus or gastric cardia as compared with a hospitalized control group.

Our finding of significantly elevated risks of gastric cardia cancer with increasing levels of BMI in a Chinese population lends additional support for an etiological role of obesity. The observation is of particular interest in view of the low magnitude of usual BMI distribution (Table 1) in this generally lean population. Although our limited data suggest that risk is not related to weight fluctuation, we could not assess an effect of the anatomical pattern of weight distribution. However, the stronger association with usual BMI among men rather than women suggests that central adiposity, more commonly seen in men (15), may be an important factor. This possibility would be consistent with the higher male:female ratio for cardia cancer compared with that of distal stomach cancer in our data, but additional studies are needed to confirm any gender differences in the risk of cardia cancer associated with BMI. It is not clear why the association between obesity and cardia cancer was more pronounced among the younger age groups rather than among the older age groups. The relationships to body weight, however, could not be attributed to risk factors such as cigarette smoking, alcohol drinking, or history of chronic gastric disease.

The mechanisms by which obesity may increase the risk of gastric cardia and esophageal adenocarcinomas are unclear, but gastroesophageal reflux disease is believed to play a critical role (9, 16). It has been shown that obesity predisposes to gastroesophageal reflux, particularly among obese persons with central fat distribution and an associated elevation in intraabdominal pressure (15, 17). Thus, the upward trends reported for adenocarcinomas of the esophagus and gastric cardia may be due at least partly to increases of body weight in the general population.

Few studies have examined the association between body mass and the risk of distal stomach cancer. Kabat *et al.* (9) found no consistent trend with levels of BMI. Similarly, no clear trends have been noted between weight levels and overall stomach cancer in several cohort studies (18–20). Other studies, however, have reported an inverse association between body weight and overall stomach cancer, presumably related to distal gastric cancers (21, 22). Our study found no significant association between body mass and risk of distal stomach cancer in men, although obese women seemed at slightly increased risk. Thus, the findings to date suggest that a positive association of obesity with stomach cancer risk is confined to tumors of the gastric cardia.

Several potential limitations of this study should be noted. The self-reported height and weight may be subject to recall bias. Underreporting of usual weight may occur among cancer patients with preclinical weight loss, which would bias the risk estimates associated with body mass downward. It is therefore possible that the magnitude of the risks of gastric cardia cancer associated with body mass is underestimated in our study. However, the absence of an effect on distal stomach cancer among men and a slightly elevated risk among obese women, in contrast to previous studies, would argue against a substantial underreporting of weight in our data. Another concern was a low percentage of pathological confirmation for cases. However, exclusion of histologically unconfirmed cases did not materially alter the findings. Although misclassification by subsite of tumor origin was possible, the specificity of findings by subsite and the consistency with limited evidence from previous studies (7, 8) add credence to our findings. Cases with multiple sites of tumor origin (ICD code 151.8) were grouped with the distal subsite, because the majority of stomach cancers occur in the distal portion. However, the reported ORs were not materially altered when cases with multiple sites were excluded in separate analyses. In addition, 353 (20.5%) deceased cases were not interviewed in our study, and the effect of obesity on survival after stomach cancer diagnoses is unclear. Given the diverse findings between cardia and distal stomach cancer, however, it is unlikely that systematic bias due to survival exists in our data. Selection bias due to refusal would be minimum, because only a relatively small proportion of subjects (10.0% of cases and 14.2% of controls) refused to participate.

In summary, our finding of elevated risks of gastric cardia cancer with increasing BMI in a Chinese population with relatively low excess weight supports the notion that obesity predisposes to this tumor. The greater risks of cardia cancer associated with obesity among men rather than women are consistent with the higher male:female ratio for cardia cancer rather than distal stomach cancer seen in our study and in Western populations. We observed no consistent association between obesity and the risk of distal stomach cancer. Additional studies are needed to clarify the mechanisms by which obesity predisposes to adenocarcinomas of the gastric cardia and esophagus, including the role of gastroesophageal reflux disease.

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