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Association between esophageal cancer in middle-aged and elderly patients and body mass index and waist-to-hip ratio

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Abstract

Objective: This study determined the relationship between esophageal cancer in middle-aged and elderly patients and body mass index (BMI) and waist-to-hip ratio (WHR).

Methods: A hospital-based case-control study was adopted. Two hundred eighty-two patients who were diagnosed with esophageal cancer through clinical endoscopy, X-ray examination, or histopathologic evaluation, and underwent surgery or received chemotherapy were enrolled as cases. The control group consisted of 282 patients without any cancers or esophageal diseases who were hospitalized during the same period in the same hospital. Face-to-face interviews were conducted using standard survey forms, and the height, weight, waist circumference, and hip circumference were measured to calculate the BMI and WHR. The odds ratio (OR) and 95% confidence interval (CI) between the patient BMI and WHR and esophageal cancer were estimated using a multi-factor logistic regression model.

Results: There was no statistical difference between the case and control groups with respect to age, gender, occupation, educational background, place of residence, and history of high blood pressure ($P>0.05$); however, there were more cases who smoked cigarettes and consumed alcohol than controls ($P<0.05$). Single-factor logistic regression analysis showed that the risk for esophageal cancer in overweight and obese patients was 1.53- and 1.82-fold that of normoweight patients, respectively. The risk for esophageal cancer in patients with a WHR in the highest quartile was 1.85-fold the control patients with a WHR in the lowest quartile. After confounding factors, such as gender and age, were adjusted, multi-factor logistic regression analysis indicated that the risk for esophageal cancer in overweight and obese patients increased by 59.4% (OR=1.594) and 78.2% (OR=1.782), respectively, when compared with normoweight patients.

Conclusion: BMI and WHR are important risk factors for esophageal cancer. Overweight and obese patients are at increased risk for esophageal cancer. Maintaining a normal weight may be a factor in preventing esophageal cancer.

Keywords: Esophageal cancer, Body mass index (BMI), Waist-to-hip ratio (WHR), Case-control study

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Introduction

Esophageal cancer refers to malignant lesions formed by the abnormal proliferation of esophageal squamous or glandular epithelium. Esophageal cancer is a common malignant tumor in some countries and regions worldwide. China has a high incidence rate of esophageal cancer, and also one of the highest

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mortality rates of esophageal cancer. According to the world cancer incidence and death report of 2012 released by the International Agency for Research on Cancer (IARC) on 25 August 2014, there were 455,784 cases of esophageal cancer worldwide with 223,306 cases in China (48.99%), and 400,156 deaths worldwide with 197,472 deaths in China (49.35%) [1].

According to the "Malignant Tumor Incidence Rate and Death Analysis of Registry Area in China," which was released by the National Cancer Center, there were 287,632 cases of esophageal cancer in 2010, of which 204,449 were men and 83,183 were women. During the same year, there were 208,473 deaths associated with esophageal cancer, of which 148,865 were men and 59,608 were women [2]. The incidence of esophageal cancer (overall, 21.88/100,000; males, 30.38/100,000; and females, 12.96/100,000) ranks fifth, following lung, breast, gastric, and liver cancers. The esophageal cancer mortality rate ranks fourth amongst cancer-related deaths (overall, 15.85/100,000; male, 22.12/100,000; and female, 9.29/100,000). The urban incidence of esophageal cancer (overall, 16.55/100,000; male, 23.92/100,000; and female, 8.81/100,000) ranks sixth, and the mortality rate ranks fifth (overall, 12.19/100,000; male, 17.84/100,000; and female, 6.26/100,000). The rural incidence of esophageal cancer (overall, 27.29/100,000; male, 36.95/100,000; and female, 17.17/100,000) ranks fourth, following lung, gastric, and liver cancers, and the mortality rate (overall, 19.58/100,000; male, 26.47/100,000; and female, 12.36/100,000) ranks fourth, following lung, liver, and gastric cancers.

With social and economic development, the standard of living and dietary structure of residents in China have undergone changes, and the incidence and mortality rates of esophageal cancer have decreased in urban areas. In areas with a high incidence of esophageal cancer, after 30 years of concerted efforts for prevention and control, the incidence and mortality rates of esophageal cancer have decreased, but the incidence and mortality rates are still at an unacceptably high level, resulting in a heavy burden on society and the economy, and seriously affecting the development of the local social economy [3]. Despite the high rate of morbidity associated with esophageal cancer, as well as the pain and burden, the etiology and natural history remain uncertain. Research has shown that the genesis of esophageal cancer may result from the effects of a number of factors, such as nitrosamines, mould and mould toxin contamination, nutritional imbalance, an unhealthy lifestyle, dietary habits, and genetic predisposition [4, 5]. In addition, domestic and international epidemiologic studies also indicate that the genesis of esophageal cancer is mainly related to environmental and dietary factors, including a limited intake of fresh fruits and vegetables and a poor intake of multiple micronutrients [6, 7]. There are scarce reports on the relationship between obesity (an increase in body mass index [BMI] and waist-to-hip ratio [WHR]) and esophageal cancer, and the reported results are inconsistent [8, 9]. Therefore, a hospital-based case-control study method was designed involving a group of patients with and without esophageal cancer. The differences in general demographic characteristics and physical measures (height, weight, waist circumference [WC] and hip circumference [HC]) in the two groups of patients were investigated to determine the relationship between esophageal cancer and obesity, and to provide a scientific basis for the prevention and control of esophageal cancer, as well as the implementation of intervention measures.

Subjects and methods

Subjects

Two hundred eighty-two patients with esophageal cancer ≥40 years of age who were admitted to the Oncology Department and Department of Chest Surgery of the First Affiliated Hospital of Liaoning Medical College, the Third Affiliated Hospital of Liaoning Medical College, and Jinzhou Central Hospital between September 2012 and March 2013 were enrolled as cases. The inclusion criteria were as follows [7]: (1) males and females ≥40 years old; (2) permanent residents of Jinzhou; (3) diagnosed with esophageal cancer >3 months previously by clinical endoscopy, X-ray examination, or histopathologic evaluation; (4) underwent surgery because of esophageal cancer in 1 of the above-mentioned 3 hospitals; (5) diagnosed with esophageal cancer through clinical histopathologic examination and received chemotherapy; and (6) willing to complete the questionnaire. To increase the comparability of the two groups and control the influence of confounding factors on the results, 1 control case was assigned for each case according to age (±5 years), gender, and place of residence. The patients in the control group were hospitalized

in the same hospital during the same time period; 282 patients without esophageal disease or other digestive tract cancers, but diagnosed with other esophageal diseases comprised the control group. The inclusion criteria for the control group were as follows: (1) same gender as the patients in the case group; (2) age ±5 years of case patients; (3) no esophageal cancer or other digestive tract diseases; (4) no medications for esophageal or other digestive tract diseases within 3 months; (5) no digestive tract cancers; and (6) those who were willing to complete the questionnaire. All of the subjects signed informed consent.

Methods

Face-to-face interviews were conducted using a standard questionnaire self-designed to collect demographic data (age and gender), lifestyle (smoking cigarettes, consuming alcohol, and physical exercise), social and economic status (education, occupation, and family income), personal history of disease (hypertension, diabetes, and cardiovascular disease), and family history of esophageal cancer, and the investigators who had received professional training measured the height and weight using standard methods. The patients wore light clothing without shoes during measurement of the height and weight. The height was rounded to the nearest cm, and the weight was rounded to the nearest 100 g. The WC was measured with the patient in the upright position with the feet 25–35 cm apart, and a soft tape was placed at the midpoint on the line between the inferior border of the lumbar ribs and the iliac crest without compressing the skin and encircling the abdomen. After the subjects sat down for ≥ 5 min, the blood pressure was measured 3 times, and the mean of last two readings was taken for data analysis.

Judgment criteria

The adult BMI criteria in China [10] are divided into the following 4 groups: underweight, BMI≤18.50 kg/m^2; normoweight, BMI=18.50–23.99 kg/m^2; overweight, BMI=24.00–27.99 kg/m^2; and obese, BMI≥28.00 kg/m^2. The WHR was calculated according to the following formula: WHR=WC in cm/HC in cm. The WHR was classified as follows: normal, males with a WHR≤0.9 and females with a WHR≤0.88; and obese, males with a WHR>0.9 and females with a WHR>0.88. Based on the BMI and WHR values, the study patients were divided into four quartiles (Q1–Q4) for BMI and WHR, which were expressed as continuous variables. To reduce the influence of extreme values (too high or too low) on the results of this study, the median values of the four BMI and WHR quartiles were utilized; within the same quartiles, the linear trend test was performed. In current epidemiologic studies, BMI is often utilized as an index to define generalized obesity, and WC or WHR is used as an index to define centripetal or abdominal obesity [11].

Measurement and control of potential confounding factors

It has been reported that gastroesophageal reflux disease (GERD) is an important risk factor for the onset of esophageal cancer, but GERD is not related to BMI [7, 12]. To further control the influence of confounding factors on the study results, patients in the control group completed an additional comprehensive questionnaire on potential confounding factors, including GERD-type symptoms. The GERD-related questions were as follows: (1) evaluate symptoms during the recent 6 months, including whether or not "heartburn, indigestion, or stomach pain is present"; (2) whether or not middle or upper abdominal discomfort occurs frequently; (3) during the intake of food, whether or not antacids are taken to relieve symptoms; (4) whether or not abdominal discomfort or pain is related to posture (such as, the recumbent position or lumbar flexion); (5) whether or not antacid drugs are taken frequently; and (6) whether or not there is a history of a diagnosis of esophageal hiatal hernia. After the preliminary analysis, GERD-type symptoms were defined if the answer to the following questions was yes: (1) whether or not "heartburn, indigestion, or abdominal pain is present"; (2) position is in the upper abdomen; and (3) antacids are taken to relieve symptoms. If there were GERD-type symptoms, such a control was excluded.

Statistical methods

Statistical analyses were performed using SPSS 16.0 software. A t-test was used for numerical variable data expressed as the mean±standard deviation ($\bar{x} \pm s$). A χ^2-test was used for categorical data to determine whether or not there was a difference

in the distribution of general characteristics of the two groups. The ORs and 95% confidence intervals (CIs) for the BMI and WHR of study subjects and the risk of esophageal cancer were estimated using a multi-factor logistic regression model. A $P<0.05$ indicated a statistical difference.

Results

Comparison of demographic characteristics

There were 282 patients in the case group with an age range from 42 to 76 years and a mean age of 55.27±10.16 years. There were 282 patients in the control group with an age range from 42 to 76 years and a mean age of 55.18±10.33 years. There was no statistical difference between the two groups with respect to age, gender, occupation, educational background, place of residence, and history of high blood pressure ($P>0.05$). The family income of the patients in the case group was lower than the control group ($\chi^2=5.356$, $P<0.05$). A higher number of patients in the case group smoked cigarettes and consumed alcohol than patients in the control group ($P<0.05$). The percentage of patients in the case group with diabetes was also higher than the control group ($\chi^2=11.445$, $P=0.001$; Table 1).

Comparison of measured values

The mean BMI in the case group (24.43±3.40 kg/m^2) was higher than the control group (22.79±3.30 kg/m^2; $P<0.01$). The mean BMI values in the case group in each age group were greater than the control group; there was a significant difference between the two groups in the 45-, 50-, 65-, and 76-year age groups ($P<0.05$). The mean WHRs in the males in the case group (0.96±0.05) were significantly higher than the control group (0.91±0.05; $P<0.01$). The mean WHRs in the females in the case group (0.95±0.05) was higher than the control group (0.90±0.07; $P<0.01$). Similarly, after the WHRs were grouped by age, there was a significant difference between the two groups in the 50– and 55–59-year age groups ($P=0.001$); middle-aged women (42–49 year age group) had the most significant difference ($P=0.001$; Table 2).

Relationship between BMI and WHR with esophageal cancer

The results of logistic regression analysis on single factors showed that the risk for esophageal cancer in overweight and obese patients in the case group was1.53 times (95% CI, 1.032–2.524) and 1.82 times (95% CI, 1.163–2.857) that of normoweight patients, and the risk for esophageal cancer in patients within the highest WJR quartile was 1.85 times that of patients within the lowest WHR quartile (95% CI, 1.165–2.941). After confounding factors, such as gender and age, were adjusted, multiple-factor logistic regression analysis showed that the risk for esophageal cancer in overweight and obese patients increased by 59.4% (OR=1.594; 95% CI, 1.058–2.587) and 78.2% (OR=1.782; 95% CI, 1.101–2.786), respectively, when compared with normoweight patients in the control group. When compared with patients within the lowest WHR quartile, the risk for esophageal cancer of patients within the second highest, third highest, and highest quartiles of WHR increased by 4.8%, 32.6%, and 36.5%, respectively (Table 3).

Discussion

There was no statistical significance between the two groups with respect to age, gender, occupation, educational background, place of residence, and history of hypertension, which is consistent with the extant literature [5, 7]. A meta-analysis was conducted on the relationship between cigarette smoking and alcohol consumption and esophageal cancer (included in Reference 14), and the results showed that the combined OR of smoking and high expression of p53 protein and p53 gene change in esophageal cancer (high expression of p53 protein+p53 gene mutation) was 1.99 (95% CI, 1.30–3.06), 1.64 (95% CI, 1.13–2.37; $P<0.05$) [13]. Both the duration of cigarette smoking and consumption of alcohol exhibited a positive dose-response relationship with the the risk for esophageal cancer; domestic and international research reports are consistent in this regard [14–16]. The current study also showed that the proportion of patients in the case group with a history of diabetes was higher than the control group, which is basically consistent with other investigators' results. A meta-analysis was conducted on the link between diabetes and esophageal cancer (included in Reference 6) [17], and the results showed that for both men and women, the number of patients with diabetes in the case group was significantly higher than the control group, and the OR value of female diabetic patients was higher than male diabetic patients (female,

Table 1. Demographic characteristics of the study subjects

Study factors	Case group [*n* (%)]	Control group [*n* (%)]	χ^2	*P*-value
Age (years)			1.226	0.593
42–	44 (15.60)	46 (16.31)		
50–	97 (34.40)	93 (32.98)		
60–	108 (38.30)	111 (39.36)		
≥70	33 (11.70)	32 (11.35)		
Gender			0.677	0.856
Male	193 (68.44)	193 (68.44)		
Female	89 (31.56)	89 (31.56)		
Occupation			1.483	0.171
Worker	85 (30.14)	88 (31.21)		
Farmer	110 (39.01)	106 (37.59)		
Intelligentsia	33 (11.70)	27 (9.57)		
Other	54 (19.15)	61 (21.63)		
Educational background (years)			2.361	0.429
Primary school and below	48 (17.02)	43 (15.25)		
Junior middle school	155 (54.97)	161 (57.09)		
Senior high school	53 (18.79)	49 (17.38)		
Junior college and higher	26 (9.22)	29 (10.28)		
Place of residence				
City	81 (28.72)	87 (30.85)	2.832	0.357
Rural	106 (37.59)	112 (39.72)		
Other	95 (33.69)	83 (29.43)		
Household income per capita (RMB/month)			5.356	0.024
<1000	25 (8.87)	12 (4.25)		
1000–	126 (44.68)	97 (34.40)		
2000–	115 (40.78)	153 (54.26)		
≥3000	16 (5.67)	20 (7.09)		
Smoking			5.114	0.013
Non-smoker	121 (42.91)	157 (55.67)		
Ever-smoker	37 (13.12)	23 (8.16)		
Current smoker	124 (43.97)	102 (36.17)		
Alcohol consumption			7.652	0.006
Non-drinker	64 (22.70)	81 (28.72)		
Former drinker	25 (8.86)	27 (9.58)		
Current drinker	193 (68.44)	174 (61.70)		
History of hypertension			0.833	0.734
Yes	128 (45.39)	125 (44.33)		
No	154 (54.61)	157 (55.67)		
History of diabetes			11.445	0.001
Yes	66 (23.40)	43 (15.25)		
No	216 (76.60)	239 (84.75)		

Table 2. Distribution and comparison of BMI and WHR at different ages between the case and control group ($\bar{x}\pm s$)

Age (years)	BMI				Male WHR				Female WHR			
	Case group	Control group	*t*	*P*-value	Case group	Control group	*t*	*P*-value	Case group	Control group	*t*	*P*-value
42–	23.68±4.12	23.37±3.17	1.53	0.827	0.92±0.03	0.91±0.06	0.63	0.527	0.96±0.02	0.86±0.13	6.76	0.001
45–	24.16±3.04	22.23±3.14	2.14	0.043	0.98±0.06	0.96±0.07	1.15	0.326	0.96±0.08	0.89±0.07	5.90	0.001
50–	26.83±3.31	23.73±3.50	2.77	0.016	0.99±0.03	0.88±0.01	7.36	0.001	0.94±0.02	0.89±0.09	2.26	0.042
55–	25.41±4.03	24.82±3.86	1.63	0.631	0.97±0.05	0.89±0.02	5.72	0.001	0.97±0.08	0.94±0.04	1.71	0.080
60–	23.42±3.24	22.69±3.52	1.15	0.347	0.92±0.06	0.92±0.05	0.24	0.863	0.96±0.03	0.94±0.06	1.23	0.231
65–	24.01±3.70	22.32±3.03	2.24	0.039	0.98±0.07	0.91±0.05	3.14	0.004	0.95±0.07	0.94±0.05	2.59	0.025
70–	23.52±2.65	22.68±3.38	1.41	0.166	0.96±0.03	0.93±0.06	2.07	0.045	0.92±0.05	0.91±0.07	0.25	0.866
76	22.18±3.10	20.64±2.01	2.32	0.034	0.92±0.05	0.91±0.04	0.56	0.622	0.93±0.06	0.85±0.03	3.83	0.003
	24.43±3.40	22.79±3.30	3.52	0.002	0.96±0.05	0.91±0.05	4.68	0.001	0.95±0.05	0.90±0.07	4.47	0.002

Table 3. Association of BMI and WHR with the risk for esophageal cancer

	Case group		Control group		Single factor analysis		Multi-factor analysis	
	n	%	*n*	%	OR value	95% CI	OR value	95% CI
BMI (kg/m^2)								
18.50–23.99	108	38.30	144	51.06	1.000		1.000	
<18.50	27	9.57	20	7.09	1.815	0.891–3.381	1.293	0.753–1.884
24.00–27.99	76	26.95	67	23.76	1.526	1.032–2.524	1.594	1.058–2.587
≥28.00	71	25.18	51	18.09	1.817	1.163–2.857	1.782	1.101–2.786
WHR								
Lowest quartile (Q1)	49	17.38	68	24.11	1.000		1.000	
Second highest quartile (Q2)	69	24.47	80	28.37	1.183	0.662–1.934	1.048	1.012–1.532
Third highest quartile (Q3)	78	27.66	69	24.47	1.568	0.916–2.533	1.326	1.023–1.741
Highest quartile (Q4)	86	30.49	65	23.05	1.854	1.165–2.941	1.365	1.148–1.865

*Age, gender, occupation, educational background, family income, cigarette smoking, alcohol consumption, diabetes, hypertension, and other potential confounding factors have been adjusted.

OR=1.58 and 95% CI, 1.14–2.18; male, OR=1.41 and 95% CI, 1.07–1.86). Thus, the presence of diabetes was associated with esophageal cancer, and might be an independent risk factor for esophageal cancer.

The current study showed that the mean BMI in the case group during each age group was significantly higher than the control group, and there was a significant difference between the two groups during the 45–, 50–, 65–, and 76-year age groups ($P<0.05$). In addition, the mean WHR of the males in the case group was significantly higher than the control group ($P<0.01$), and the mean WHR of the females in the case group was also higher than the control group ($P<0.01$). Similarly, for males, there was a very significant difference between the two groups during the 50– and 55–59-year age groups; middle-aged (42–49 years) women had the most significant difference ($P=0.001$). Single-factor logistic regression analysis revealed that the risk for esophageal cancer in groups of overweight and obese patients was 1.53 and 1.82 times the normoweight patients in the control group, while the risk for patients within the highest WHR quartile was

1.85 times the control group patients within the lowest WHR quartile. After various confounding factors, such as gender and age, were adjusted, multiple-factor logistic regression analysis indicated that the risk for esophageal cancer in the overweight and obese patients in the case group increased by 59.4% (OR=1.594) and 78.2% (OR=1.782), respectively, when compared with normoweight patients. When compared with patients within the lowest WHR quartile, the risk for esophageal cancer in patients within the second highest, third highest, and highest WHR quartiles increased by 4.8%, 32.6%, and 36.5%, respectively

Steffen et al. [8] conducted a prospective study involving 346,554 subjects participating in the European Cancer and Nutrition Survey. During the 8.9-year follow-up, there were 198 newly-diagnosed cases of esophageal cancer. The results of the survey showed that BMI, WC, and WHR were positively related with the risk for esophageal cancer (when the highest and lowest quintiles were compared, the RR=2.60 and 95% CI=1.23–5.51; $P<0.01$) [8].

At present, it is thought that fat metabolism is active in overweight and obese patients. Metabolism of fats can produce a variety of compounds which circulate throughout the body, and the metabolism of intra-abdominal fat is different than that of surrounding fat [18]. Some metabolites, such as insulin-like growth factor (IGF) and leptin, have been shown to be associated with malignant tumors. The fat metabolites may reduce cellular death by promoting growth changes during the cell cycle, and producing similar tumor-promoting changes at the cellular level [19, 20], and these compounds can directly affect the occurrence and development of tumor.

In summary, an increase in BMI and WHR is associated with the risk for esophageal cancer, and is an important risk factor for esophageal cancer, which is basically consistent with the international study reports. Overweight and obese patients have a significantly increased risk of esophageal cancer. Maintaining a normal body weight, following a reasonable diet, and participating in appropriate physical activities can lower the risk for esophageal cancer. Therefore, a change in bad dietary habits is recommended and measures, such as a reasonable diet, balanced nutrition, adequate intake of protein, reduced intake of high energy foods, and keeping a healthy lifestyle, such as participating in more physical activities or sports, can help maintain a normal BMI and WHR, and effectively prevent the occurrence of esophageal carcinoma.

Conflict of interest

The authors declare no conflict of interest.

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