Original Article

Obesity, peptic ulcer disease and metabolic status in the Wuwei Cohort of northwest China: A cross-sectional study

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Background and Objectives: Peptic ulcer disease is a common digestive system disease. However, whether peptic ulcer disease and obesity are related is unclear. We assessed the associations of obesity and metabolic status with peptic ulcer disease. **Methods and Study Design:** We conducted a cross-sectional study of 3561 individuals from the Wuwei cohort. We evaluated the associations of general and abdominal adiposity, as defined by different anthropometric indices, with peptic ulcer disease. Odds ratios and 95% confidence intervals were determined through binary logistic regression. **Results:** The odds ratio for peptic ulcer disease was 2.37 (1.46–3.84) for women with obesity, compared with the normal group. The association remained significant in Models 2 and 3, with odds ratios of 2.23 (1.35–3.69) and 2.03 (1.19–3.49), respectively. In Model 1, women with obesity had an odds ratio for duodenal ulcer of 2.76 (1.41–5.42) compared with the control group; this result remained significant in Models 2 and 3, with odds ratios of 2.52 (1.24–5.13) and 2.44 (1.13–5.28), respectively. In Model 1, women with metabolically healthy and unhealthy obesity had odds ratios for peptic ulcer disease of 2.26 (1.19–4.28) and 2.15 (1.12–4.15), respectively, compared with the control group. After adjustments for major covariates and *H. pylori* status, these respective odds ratios became 2.27 (1.20–4.30) and 2.17 (1.12–4.20) in Model 2 and 2.2 (1.15–4.20) and 2.16 (1.11–4.19) in Model 3. **Conclusions:** General adiposity defined by body mass index is associated with peptic ulcer disease in women.

Key Words: peptic ulcer disease, gastric ulcer, duodenal ulcer, obesity, metabolic status

INTRODUCTION

Peptic ulcer disease (PUD), including that involving gastric ulcer (GU) or duodenal ulcer (DU), is a common digestive system disease. The prevalence and incidence of PUD have rapidly declined because of the use of antisecretory drugs and the eradication of *Helicobacter pylori*.[1,2] In the Asia–Pacific region, the prevalence of PUD has paralleled a decline in *H. pylori* infection in Malay, Indian, and Chinese populations;[3] however, PUD continues to be one of the most common gastrointestinal diseases worldwide. Therefore, evaluating its risk factors is crucial to improving its management.

Several studies have reported risk factors for PUD. *H. pylori* infection and the use of nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin are widely accepted as major risk factors for PUD.[4-6] Obesity has also been reported to be a risk factor, but the association between the risk of PUD and adiposity is controversial.[7-9] For example, the multivariate-adjusted hazard ratio for GU was 1.83 (95% CI, 1.20–2.78) for obese men compared with normal BMI participants in Boylan's study,[9] and the multivariate-adjusted OR for PUD was 3.6 (95% CI, 1.5–8.7) in Wang's study.[7] Nevertheless, other studies have demonstrated no relationship between obesity and PUD.[10-12] Obesity is a chronic metabolic disease and a risk factor for metabolic syndrome, which, in turn, increases the risk of type 2 diabetes mellitus, nonalcoholic fatty liver disease, dyslipidemia, hypertension, and cardiovascular and cerebrovascular diseases. A subtype of obesity that meets the diagnostic criteria for obesity without causing metabolic abnormalities such as diabetes or

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hyperlipidemia has been observed in recent years.[13,14] This subtype of obesity has been termed metabolically healthy obesity (MHO), but few studies have evaluated the role of MHO in PUD.

We assessed the cross-sectional relationships between PUD and obesity by using anthropometric indices, including BMI, waist-to-height ratio (WHtR), waist-to-hip ratio (WHR), and waist circumference (WC). In addition, we investigated the role of metabolic status in PUD.

METHODS

Study population

This cross-sectional study was based on the Wuwei cohort,[15] which is a population-based gastric cancer cohort from the Wuwei Municipality of Gansu Province, China, where the incidence and mortality rates of gastric cancer are among the highest in the country.

As is shown in Figure 1, A total of 23,346 participants aged 35–70 years were selected through a cluster sampling method between March 2013 and April 2016; 21,345 of them underwent gastroscopies. From this co-

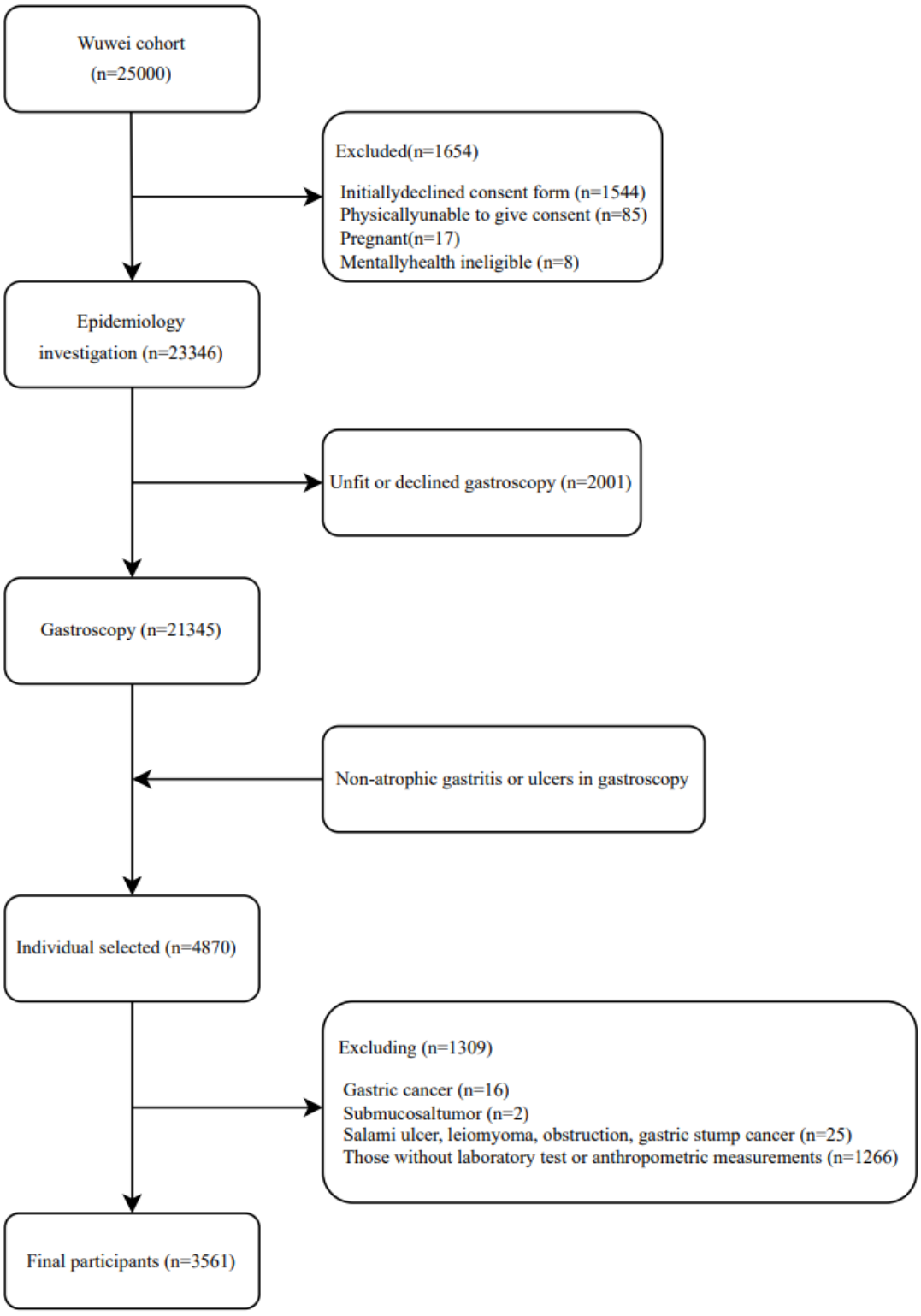

Figure 1. Flowchart of this study.

hort, we selected 1003 and 3867 individuals with and without peptic ulcers, respectively. After excluding individuals with gastric cancer, salami ulcer, leiomyoma, obstruction, or gastric stump cancer and those without anthropometric measurements or serum biochemical parameters, we included 2886 individuals without and 675 individuals with peptic ulcers. We did not exclude patients with ulcers or bleeding of unclear etiology. All of the participants in the Wuwei cohort provided written informed consent and underwent general physical and epidemiological examinations prior to enrollment. In addition, every individual in our sample underwent a gastroscopy. The study was approved by the ethics committee of The First Hospital of Lanzhou University (approval number: LDYYLL2012001), and written informed consent was obtained from all participants prior to enrollment, in accordance with the Declaration of Helsinki.

Assessment of obesity and metabolic status

We defined general adiposity by BMI according the guidelines for prevention and control of overweight and obesity in Chinese adults.[16,17] The participants were classified into four groups on the basis of BMI: underweight (<18.5 kg/m^2), normal (≥18.5 and <24.0 kg/m^2), overweight (≥24.0 and <28.0 kg/m^2), and obese (≥28.0 kg/m^2). Abdominal adiposity defined by WC, WHR, and WHtR. The cutoffs adopted from previous studies.[16,18-20] Metabolically unhealthy status was defined in accordance with the Chinese Guidelines for the Prevention and Treatment of Dyslipidemia in Adults (2016 revision) as the simultaneous presence of three or more of the following risk factors:[21,22] (1) a WC of ≥90 cm for men or ≥85 cm for women; (2) a fasting plasma glucose concentration of ≥6.1 mmol/L or current antidiabetic prescription; (3) systolic blood pressure of ≥130 mmHg, diastolic blood pressure of ≥85 mmHg, or current antihypertensive prescription; (4) triglyceride concentration of ≥1.70 mmol/L; and (5) HDL cholesterol concentration of <1.04 mmol/L.

Assessment of covariates

All participants responded to a questionnaire regarding their basic information, namely, their sex, race, address, marital status, education, and family income; personal medical history of hypertension; family medical history of gastric cancer; and behavioral factors, namely, their diet, smoking status, and alcohol intake.

Trained staff members collected anthropometric measurements and serum biochemical parameters in accordance with standard procedures. The participants were asked to remove their shoes for height measurement to the nearest 0.1 cm. Weight was measured to the nearest 0.1 kg with the participants in clothing; the weight of their clothing, which was estimated on the basis of the season in which their measurements were collected, was deducted. WC and hip circumference were measured to the nearest 0.1 cm with a soft measuring tape. Blood chemistry tests were performed after the participants had fasted overnight.

Assessment of PUD and H. pylori status

Trained hospital staff members conducted esophagogastroduodenoscopy (EGD) to confirm PUD after the participants had fasted overnight. A peptic ulcer was defined as a mucosal break ≥3 mm in diameter.[23] *H. pylori* status was determined through 14C-Urea breath tests (Urea-14C Breath Test, Shenzhen Zhonghe Headway BIO-SCI & TECH, China)

Statistical analysis

Statistical analysis was performed in Stata (version 14.0, StataCorp, College Station, TX, USA). To compare the baseline characteristics of our study sample, we assessed categorical variables as proportions (%) and continuous variables as means ± standard deviations (SD) or as medians (interquartile ranges). We compared the continuous variables were through two-sample Student's t tests or Wilcoxon rank sum tests, and we compared the categorical variables through chi-square tests.

We employed binary logistic regression to analyze the associations between anthropometric indices and PUD in a crude analysis and ORs (with 95% CIs). We performed further analyses after adjusting for confounding factors, including age, sex, education, income, smoking habits, and alcohol intake. Moreover, we assessed metabolic status in a separate analysis using the same method.

RESULTS

Our study sample comprised 3561 individuals. The adiposity measures and metabolic characteristics of the sample are listed in Table 1. In total, 422 (62.5%) of the individuals with PUD and 1026 (35.6%) of those without PUD were men. The mean ages for the individuals with and with PUD were 50.4±8.0 and 47.3±6.7 years, respectively. The overall prevalence of obesity was 18.9%. Individuals in the overweight and obese subgroups were more likely to have PUD. In total, 61.3% of men and 65.9% of women had abdominal obesity (WC of ≥85 or ≥80 cm, respectively). Age, sex, education, smoking habits, consumption of spicy food, *H. pylori* status, BMI, WC (in women), systolic blood pressure, diastolic blood pressure, fasting blood glucose, hypertension history, and HDL cholesterol differed significantly (p<0.05) between normal and PUD groups, the remaining covariates did not differ significantly (Table 1).

General adiposity and PUD

We assessed general adiposity on the basis of BMI (Table 2). In men, BMI was not associated with PUD, GU, or DU. This relationship did not change after adjustment for covariates in Model 2 or Model 3. Women with obesity had an OR (95% CI) of 2.37 (1.46–3.84) for PUD, compared with women with normal BMI. This finding remained statistically significant in Models 2 and 3, which yielded ORs (95% CI) of 2.23 (1.35–3.69) and 2.03 (1.19–3.49), respectively. For GU, women with obesity had an OR (95% CI) of 2.26 (1.18–4.31) as compared with women with normal BMI, and this finding remained significant in Model 2, which yielded an OR of 2.28 (1.16–4.47); after additional adjustment for WC in Model 3, the significance disappeared. For DU, women with obesity and overweight had ORs (95% CI) of 1.54 (1.01–2.36) and 2.76 (1.41–5.42), respectively, compared with normal BMIs. No association was observed between overweight and DU after adjustment for covariates, but

Table 1. Baseline characteristics of the study subjects

	Normal (n=2886)	PUD (n=675)	*p*
Age (year)	47.3±6.7	50.4±8.0	<0.001
Sex (male, %)	1026 (35.6%)	422 (62.5%)	<0.001
Education (n, %)			0.002
Uneducated	467 (16.2%)	106 (15.7%)	
Primary school	1115 (38.6%)	213 (31.6%)	
Middle/high school	1293 (44.8%)	354 (52.4%)	
University	11 (0.4%)	2 (0.3%)	
Married	2794 (96.8%)	648 (96.0%)	0.285
Occupation			1.000
Farmer	2717 (94.1%)	636 (94.2%)	
Non-farmer	169 (5.9%)	39 (5.8%)	
Income	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	0.254
Smoking	735 (25.5%)	328 (48.7%)	<0.001
Drinking	132 (4.6%)	36 (5.3%)	0..420
Hot food	1885 (65.3%)	413 (61.2%)	0.044
Diet fast	708 (24.5%)	156 (23.1%)	0.455
BMI (kg/m^2)			0.008
<18.5	69 (2.4%)	10 (1.5%)	
18.5 to <24.0	1573 (54.5%)	342 (50.7%)	
24.0 to <28.0	1057 (36.6%)	257 (38.1%)	
≥28.0	187 (6.5%)	66 (9.8%)	
WC (cm, male)			0.461
<70	6 (0.6%)	3 (0.7%)	
70 to <85	385 (37.5%)	166 (39.3%)	
85 to <90	241 (23.5%)	112 (26.5%)	
90 to <95	182 (17.7%)	66 (15.6%)	
≥95	212 (20.7%)	75 (17.8%)	
WC (cm, female)			0.008
<65	16 (0.8%)	0 (0.0%)	
65 to <80	632 (34.0%)	72 (28.5%)	
80 to <85	474 (25.5%)	74 (29.2%)	
85 to <90	452 (24.3%)	50 (19.8%)	
≥90	286 (15.4%)	57 (22.5%)	
WHR (male)			0.876
<0.9	461 (44.9%)	192 (45.5%)	
0.9 to <0.95	383 (37.3%)	152 (36.0%)	
≥0.95	182 (17.7%)	78 (18.5%)	
WHR (female)			0.301
<0.8	96 (5.2%)	18 (7.1%)	
0.8 to <0.85	302 (16.2%)	35 (13.8%)	
≥0.85	1462 (78.6%)	200 (79.1%)	
WHtR			0.930
<0.5	1101 (38.1%)	256 (37.9%)	
≥0.5	1785 (61.9%)	419 (62.1%)	
Systolic BP (mmHg)	121±14.4	123±14.6	<0.001
Diastolic BP (mmHg)	76.4±9.9	77.5±9.8	0.011
Fasting blood glucose	4.8±1.1	4.9±1.2	0.183
HDL-cholesterol	1.2±0.3	1.1±0.3	0.010
LDL- cholesterol	2.7±0.8	2.8±0.7	0.227
Triglycerides	1.6±0.9	1.7±0.9	0.099
Hypertension (%)	891 (30.9%)	253 (37.5%)	0.001
Gastric cancer family history	12 (0.4%)	3 (0.4%)	1.000
Helicobacter pylori status (%)	1391 (48.3%)	446 (66.2%)	<0.001

BP: blood pressure; LDL: low-density lipoprotein; HDL: high-density lipoprotein; BMI: body mass index; WHR: waist to hip ratio; WHtR: waist to height ratio; WC: waist circumference; PUD: peptic ulcer disease.

the association between obesity and DU among women remained statistically significant in Models 2 and 3, with ORs (95% CI) of 2.52 (1.24–5.13) and 2.44 (1.13–5.28), respectively.

Abdominal adiposity and PUD

Among men, WC was not associated with PUD, GU, or DU; these findings did not change after adjustment for covariates and BMI in Model 2 or Model 3 (Table 3). The OR (95% CI) for PUD of women with a WC of ≥90 cm in Model 1 was 1.59 (1.08–2.33), compared with women with a WC of 65–80 cm. After adjustment for additional covariates and BMI in Models 2 and 3, the ORs (95% CI) for PUD of these women were 1.55 (1.04–2.30) and 1.30 (0.85–1.98), respectively, but the statistical significance disappeared in Model 3 (p<0.05). GU and WC consistently exhibited no significant association. The association between WC and DU was similar to that between WC

Table 2. The association between body mass index and peptic ulcer disease

	BMI							
	Male				Female			
	<18.5	18.5 to <24.0	24.0 to <28.0	≥28.0	<18.5	18.5 to <24.0	24.0 to <28.0	≥28.0
PUD								
Model 1	0.81 (0.31-2.1)	1.00	0.78 (0.61-1.01)	0.97 (0.64-1.47)	0.41 (0.13-1.36)	1.00	1.33 (1.00-1.77)	2.37 (1.46-3.84)
Model 2	0.78 (0.28-2.1)	1.00	0.83 (0.64-1.08)	1.07 (0.28-2.13)	0.36 (0.11-1.18)	1.00	1.32 (0.98-1.77)	2.23 (1.35-3.69)
Model 3	0.77 (0.28-2.1)	1.00	0.84 (0.64-1.11)	1.08 (0.67-1.75)	0.37 (0.11-1.23)	1.00	1.27 (0.94-1.72)	2.03 (1.19-3.49)
GU								
Model 1	0.73 (0.22-2.3)	1.00	0.75 (0.55-1.02)	1.14 (0.70-1.85)	0.5 (0.12-2.13)	1.00	1.22 (0.83-1.79)	2.26 (1.18-4.31)
Model 2	0.60 (0.17-2.1)	1.00	0.79 (0.57-1.10)	1.27 (0.75-2.15)	0.43 (0.10-1.85)	1.00	1.23 (0.83-1.83)	2.28 (1.16-4.47)
Model 3	0.58 (0.16-2.0)	1.00	0.84 (0.59-1.18)	1.43 (0.81-2.55)	0.47 (0.11-2.02)	1.00	1.15 (0.76-1.73)	1.93 (0.94-3.98)
DU								
Model 1	0.65 (0.14-3.0)	1.00	0.85 (0.60-1.23)	0.73 (0.37-1.43)	0.35 (0.05-2.62)	1.00	1.54 (1.01-2.36)	2.76 (1.41-5.42)
Model 2	0.68 (0.14-3.2)	1.00	0.89 (0.61-1.29)	0.77 (0.38-1.55)	0.30 (0.04-2.25)	1.00	1.50 (0.97-2.32)	2.52 (1.24-5.13)
Model 3	0.72 (0.15-3.5)	1.00	0.83 (0.56-1.24)	0.67 (0.31-1.43)	0.30 (0.04-2.29)	1.00	1.48 (0.94-2.33)	2.44 (1.13-5.28)

LDL: low-density lipoprotein; HDL: high-density; PUD: peptic ulcer disease; GU: gastric ulcer; DU: duodenal ulcers; BMI body mass index.
Model 1: adjusted age, education, marriage, occupation income
Model 2: adjusted for variables in model 1, plus smoking, drinking, hot food diet, diet fast, H. pylori status, blood pressure, fasting blood glucose, HDL-cholesterol, LDL-cholesterol, triglyceride, family history of gastric cancer
Model 3: adjusted for variables in model 2, plus waist circumference.

Table 3. The association between waist circumference and peptic ulcer disease in men

	WC				
	<70	70 to <85	85 to <90	90 to <95	≥95
PUD					
Model 1	1.11 (0.26-4.64)	1.00	1.10 (0.82-1.47)	0.84 (0.60-1.18)	0.81 (0.58-1.12)
Model 2	1.19 (0.27-5.37)	1.00	1.04 (0.76-1.42)	0.87 (0.61-1.25)	0.85 (0.60-1.21)
Model 3	1.21 (0.27-5.45)	1.00	1.05 (0.77-1.44)	0.89 (0.61-1.30)	0.88 (0.59-1.29)
GU					
Model 1	1.30 (0.25-6.86)	1.00	0.96 (0.67-1.38)	0.67 (0.43-1.04)	0.72 (0.48-1.09)
Model 2	1.50 (0.26-8.82)	1.00	0.86 (0.59-1.26)	0.66 (0.41-1.04)	0.71 (0.46-1.11)
Model 3	1.47 (0.25-8.67)	1.00	0.84 (0.57-1.25)	0.64 (0.39-1.03)	0.68 (0.42-1.11)
DU					
Model 1	-	1.00	1.34 (0.86-2.07)	1.14 (0.70-1.86)	0.99 (0.61-1.61)
Model 2	-	1.00	1.27 (0.81-1.98)	1.20 (0.72-2.00)	1.02 (0.61-1.71)
Model 3	-	1.00	1.32 (0.84-2.07)	1.30 (0.76-2.21)	1.15 (0.65-2.02)

LDL: low-density lipoprotein; HDL: high-density; PUD: peptic ulcer disease; GU: gastric ulcer; DU: duodenal ulcers; WC: waist circumference.
Model 1: adjusted age, education, marriage, occupation income
Model 2: adjusted for variables in model 1, plus smoking, drinking, hot food diet, diet fast, H. pylori status, blood pressure, fasting blood glucose, HDL-cholesterol, LDL-cholesterol, triglyceride, family history of gastric cancer
Model 3: adjusted for variables in model 2, plus body mass index.

and PUD; the ORs (95% CI) for DU of women with a WC of ≥90 cm in Models 1 and 2 were significant, at 2.01 (1.13–3.57) and 1.83 (1.01–3.31), respectively, but this association disappeared in Model 3 (Table 4). However, WHR and WHtR were not associated with PUD, GU, or DU in any of the three models (Tables 5 and 6).

Metabolic status, obesity, and PUD

We conducted subgroup analysis to investigate the relationships among healthy metabolic status, obesity defined by BMI, and PUD. In Model 1, men with MHO had an OR (95% CI) for GU of 0.65 (0.42–0.99), compared with men with normal BMI; after adjustment for major covariates and H. pylori status, their ORs (95% CI) were 0.64 (0.41–0.91) and 0.66 (0.42–1.02) in Models 2 and 3, respectively (Table 7). In Model 1, women with MHO and metabolically unhealthy obesity had ORs (95% CI) for PUD of 2.26 (1.19–4.28) and 2.15 (1.12–4.15), respectively, as compared with the control group. After adjustment for major covariates and H. pylori status, these ORs (95% CI) became 2.27 (1.20–4.30) and 2.17 (1.12–4.20), respectively, in Model 2 and 2.2 (1.15–4.20) and 2.16 (1.11–4.19), respectively, in Model 3. However, none of the models revealed any statistical significance relating to GU. The OR (95%) of women for DU was significant only in Model 1, at 2.45 (1.01–5.93; Table 8).

DISCUSSION

As shown in Figure 2, We evaluated the relationship between obesity and PUD in the Wuwei cohort by using anthropometric measures, including BMI, WHR, WC, and WHtR. Women with general adiposity as defined by BMI had higher ORs of PUD, particularly of DU, and their OR increased with BMI. However, the association between general adiposity and DU was not statistically significant in men. The association between general adiposity and GU was not statistically significant in either men or women. Individuals with abdominal adiposity as defined by WC did not differ ORs significantly from those with a normal WC (≥70 and <85 cm for men; ≥65 and <80 cm for women) after adjustment for covariates. The other anthropometric measures of abdominal adiposity, including WHR and WHtR, exhibited no significant associations with PUD. Furthermore, women with MHO or metabolically unhealthy obesity had increased odds only for PUD and not for GU or DU specifically.

The association between obesity and PUD is uncertain. We used different anthropometric measures to assess general and abdominal adiposity; general adiposity defined by BMI was relevant to PUD, whereas abdominal adiposity defined by WC was not, but even this finding was significant only in women. This result is in disagreement with those of previous studies;[10-12] however, such studies[11,12] have used questionnaires to diagnose PUD, leading potentially to limitations and biases. H. pylori infection is recognized as a major risk factor for PUD;[1,2] previous studies have found a positive correlation between BMI and *H. pylori* infection prevalence.[24-26] The pathogenic mechanism of PUD is likely to involve mucosal inflammation and breakdown due to bacterial virulence and drug toxicity;[27,28] therefore *H. pylori* infection may play an important role in PUD development. PUD outcomes depend on both individual susceptibility and risk factors,[29] but individuals who have no *H. pylori* infection and are not taking NSAIDs rarely develop PUD or other types of bleeding ulcer. Studies have reported diet-induced obesity to be associated with low-grade intestinal inflammation,[30,31] metabolic disorders, and insulin resistance, implicating changes in immune homeostasis or mucosal barriers in intestinal impairment. Adipose tissue is not only involved in glucose and lipid energy metabolism as an energy storage tissue, but also an endocrine organ, which is involved in the occurrence and development of inflammation by secreting adipokines.[32,33] Adipose tissue and inflammatory cells further maintain the dysfunction caused by adipocyte hypertrophy and promotes inflammation and insulin resistance, leading to the expression of adhesion molecules and pro-inflammatory cytokines.[34] These factors together induce chronic low-grade inflammation of the body and can promote PUD. Studies on the relationship between autophagy and metabolic diseases such as obesity had reported a lot. It may

Table 4. The association between waist circumference and peptic ulcer disease in women

	WC				
	<65	65 to <80	80 to <85	85 to <90	≥90
PUD					
Model 1	-	1.00	1.31 (0.92-1.86)	0.94 (0.64-1.38)	1.59 (1.08-2.33)
Model 2	-	1.00	1.26 (0.88-1.80)	0.88 (0.59-1.31)	1.55 (1.04-2.30)
Model 3	-	1.00	1.20 (0.83-1.72)	0.80 (0.53-1.20)	1.30 (0.85-1.98)
GU					
Model 1	-	1.00	0.82 (0.50-1.35)	0.99 (0.61-1.61)	1.45 (0.88-2.37)
Model 2	-	1.00	0.81 (0.49-1.35)	0.98 (0.60-1.62)	1.49 (0.89-2.48)
Model 3	-	1.00	0.78 (0.47-1.30)	0.92 (0.55-1.53)	1.29 (0.75-2.24)
DU					
Model 1	-	1.00	2.01 (1.21-3.36)	0.74 (0.38-1.44)	2.01 (1.13-3.57)
Model 2	-	1.00	1.88 (1.12-3.17)	0.66 (0.34-1.31)	1.83 (1.01-3.31)
Model 3	-	1.00	1.76 (1.04-2.97)	0.59 (0.30-1.17)	1.43 (0.76-2.70)

LDL: low-density lipoprotein; HDL: high-density; PUD: peptic ulcer disease; GU: gastric ulcer; DU: duodenal ulcers; WC: waist circumference.

Model 1: adjusted age, education, marriage, occupation income

Model 2: adjusted for variables in model 1, plus smoking, drinking, hot food diet, diet fast, H. pylori status, blood pressure, fasting blood glucose, HDL-cholesterol, LDL-cholesterol, triglyceride, family history of gastric cancer

Model 3: adjusted for variables in model 2, plus body mass index.

Table 5. The association between waist-to-hip ration and peptic ulcer disease

	WHR					
	Male			Female		
	<0.9	0.9 to <0.95	≥0.95	<0.8	0.8 to <0.85	≥0.85
PUD						
Model 1	1.00	1.05 (0.82-1.36)	1.07 (0.77-1.50)	1.00	1.80 (0.97-3.37)	1.20 (0.82-1.77)
Model 2	1.00	1.02 (0.78-1.34)	1.04 (0.74-1.47)	1.00	1.76 (0.93-3.33)	1.18 (0.80-1.75)
Model 3	1.00	1.01 (0.77-1.32)	1.05 (0.74-1.48)	1.00	1.82 (0.96-3.45)	1.16 (0.78-1.72)
GU						
Model 1	1.00	1.04 (0.76-1.43)	1.05 (0.69-1.58)	1.00	2.17 (0.98-4.83)	1.20 (0.72-2.02)
Model 2	1.00	1.02 (0.73-1.42)	1.00 (0.65-1.53)	1.00	2.08 (0.93-4.68)	1.19 (0.71-2.02)
Model 3	1.00	1.01 (0.72-1.41)	1.00 (0.65-1.54)	1.00	2.14 (0.95-4.81)	1.17 (0.69-1.99)
DU						
Model 1	1.00	1.08 (0.74-1.57)	0.98 (0.60-1.62)	1.00	1.40 (0.52-3.77)	1.24 (0.70-2.22)
Model 2	1.00	1.08 (0.73-1.59)	0.96 (0.58-1.60)	1.00	1.53 (0.56-4.18)	1.25 (0.69-2.24)
Model 3	1.00	1.06 (0.72-1.56)	0.97 (0.58-1.61)	1.00	1.61 (0.59-4.39)	1.22 (0.68-2.20)

LDL: low-density lipoprotein; HDL: high-density; PUD: peptic ulcer disease; GU: gastric ulcer; DU: duodenal ulcers; WHR: waist-to-hip ratio.
Model 1: adjusted age, education, marriage, occupation income. Model 2: adjusted for variables in model 1, plus smoking, drinking, hot food diet, diet fast, H. pylori status, blood pressure, fasting blood glucose, HDL-cholesterol, LDL-cholesterol, triglyceride, family history of gastric cancer. Model 3: adjusted for variables in model 2, plus body mass index.

Table 6. The association between waist-to-height ratio and peptic ulcer disease

	WHtR			
	Male		Female	
	<0.5	≥0.5	<0.5	≥0.5
PUD				
Model 1	1.00	1.00 (0.79-1.27)	1.00	1.03 (0.78-1.36)
Model 2	1.00	1.07 (0.83-1.38)	1.00	0.97 (0.73-1.29)
Model 3	1.00	1.13 (0.86-1.48)	1.00	0.84 (0.61-1.14)
GU				
Model 1	1.00	0.90 (0.68-1.21)	1.00	0.96 (0.66-1.39)
Model 2	1.00	0.94 (0.69-1.28)	1.00	0.93 (0.63-1.36)
Model 3	1.00	0.96 (0.69-1.34)	1.00	0.81 (0.54-1.22)
DU				
Model 1	1.00	1.27 (0.88-1.81)	1.00	1.20 (0.78-1.83)
Model 2	1.00	1.32 (0.91-1.92)	1.00	1.10 (0.71-1.70)
Model 3	1.00	1.46 (0.98-2.17)	1.00	0.91 (0.57-1.44)

LDL: low-density lipoprotein; HDL: high-density; PUD: peptic ulcer disease; GU: gastric ulcer; DU: duodenal ulcers; WHtR: waist-to-height ratio.
Model 1: adjusted age, education, marriage, occupation income. Model 2: adjusted for variables in model 1, plus smoking, drinking, hot food diet, diet fast, H. pylori status, blood pressure, fasting blood glucose, HDL-cholesterol, LDL-cholesterol, triglyceride, family history of gastric cancer. Model 3: adjusted for variables in model 2, plus body mass index.

Table 7. The association between metabolic health, obesity, and peptic ulcer disease in men

	Model 1		Model 2		Model 3	
	OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*
PUD						
Metabolically healthy, non-obese	1.00		1.00		1.00	
Metabolically unhealthy, non-obese	0.85 (0.62-1.17)	0.32	0.85 (0.62-1.16)	0.304	0.89 (0.64-1.24)	0.502
Metabolically healthy, obese	1.29 (0.72-2.32)	0.393	1.37 (0.76-2.47)	0.303	1.48 (0.81-2.70)	0.205
Metabolically unhealthy, obese	0.91 (0.54-1.53)	0.723	0.90 (0.53-1.52)	0.689	0.90 (0.53-1.55)	0.709
GU						
Metabolically healthy, non-obese	1.00		1.00		1.00	
Metabolically unhealthy, non-obese	0.65 (0.42-0.99)	0.043	0.64 (0.41-0.97)	0.037	0.66 (0.42-1.02)	0.059
Metabolically healthy, obese	1.48 (0.74-2.96)	0.263	1.54 (0.77-3.09)	0.223	1.70 (0.83-3.47)	0.147
Metabolically unhealthy, obese	1.04 (0.56-1.93)	0.895	1.01 (0.55-1.88)	0.969	1.04 (0.55-1.96)	0.907
DU						
Metabolically healthy, non-obese	1.00		1.00		1.00	
Metabolically unhealthy, non-obese	1.22 (0.80-1.86)	0.345	1.2 (0.78-1.84)	0.4	1.23 (0.80-1.89)	0.351
Metabolically healthy, obese	0.93 (0.35-2.45)	0.885	0.97 (0.37-2.57)	0.951	1.08 (0.40-2.88)	0.879
Metabolically unhealthy, obese	0.75 (0.31-1.79)	0.517	0.72 (0.30-1.73)	0.468	0.72 (0.30-1.73)	0.462

LDL: low-density lipoprotein; HDL: high-density; PUD: peptic ulcer disease; GU: gastric ulcer; DU: duodenal ulcers; WHtR: waist-to-height ratio.
Model 1: adjusted age, education, marriage, occupation income. Model 2: adjusted for variables in model 1, plus smoking, drinking, hot food diet, diet fast, family history of gastric cancer. Model 3: adjusted for variables in model 2, plus *H. pylori* status.

Table 8. The association between metabolic health, obesity, and peptic ulcer disease in women

	Model 1		Model 2		Model 3	
	OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*
PUD						
Metabolically healthy, non-obese	1.00		1.00		1.00	
Metabolically unhealthy, non-obese	1.12 (0.77-1.63)	0.563	1.12 (0.76-1.63)	0.574	1.13 (0.77-1.66)	0.54
Metabolically healthy, obese	2.26 (1.19-4.28)	0.012	2.27 (1.20-4.30)	0.012	2.2 (1.15-4.20)	0.017
Metabolically unhealthy, obese	2.15 (1.12-4.15)	0.022	2.17 (1.12-4.20)	0.021	2.16 (1.11-4.19)	0.023
GU						
Metabolically healthy, non-obese	1.00		1.00		1.00	
Metabolically unhealthy, non-obese	1.05 (0.63-1.74)	0.848	1.06 (0.64-1.75)	0.835	1.05 (0.63-1.75)	0.855
Metabolically healthy, obese	2.05 (0.85-4.99)	0.112	2.08 (0.86-5.08)	0.106	2.02 (0.83-4.94)	0.123
Metabolically unhealthy, obese	2.24 (0.96-5.27)	0.063	2.28 (0.96-5.42)	0.062	2.28 (0.95-5.46)	0.064
DU						
Metabolically healthy, non-obese	1.00		1.00		1.00	
Metabolically unhealthy, non-obese	1.21 (0.69-2.12)	0.489	1.19 (0.68-2.10)	0.538	1.21 (0.69-2.14)	0.507
Metabolically healthy, obese	2.45 (1.01-5.93)	0.047	2.3 (0.94-5.64)	0.068	2.27 (0.92-5.55)	0.074
Metabolically unhealthy, obese	2.44 (1.00-5.97)	0.051	2.43 (0.99-5.98)	0.054	2.44 (0.98-6.05)	0.055

LDL: low-density lipoprotein; HDL: high-density; PUD: peptic ulcer disease; GU: gastric ulcer; DU: duodenal ulcers; WHtR: waist-to-height ratio.
Model 1: adjusted age, education, marriage, occupation income. Model 2: adjusted for variables in model 1, plus smoking, drinking, hot food diet, diet fast, family history of gastric cancer. Model 3: adjusted for variables in model 2, plus *H. pylori* status.

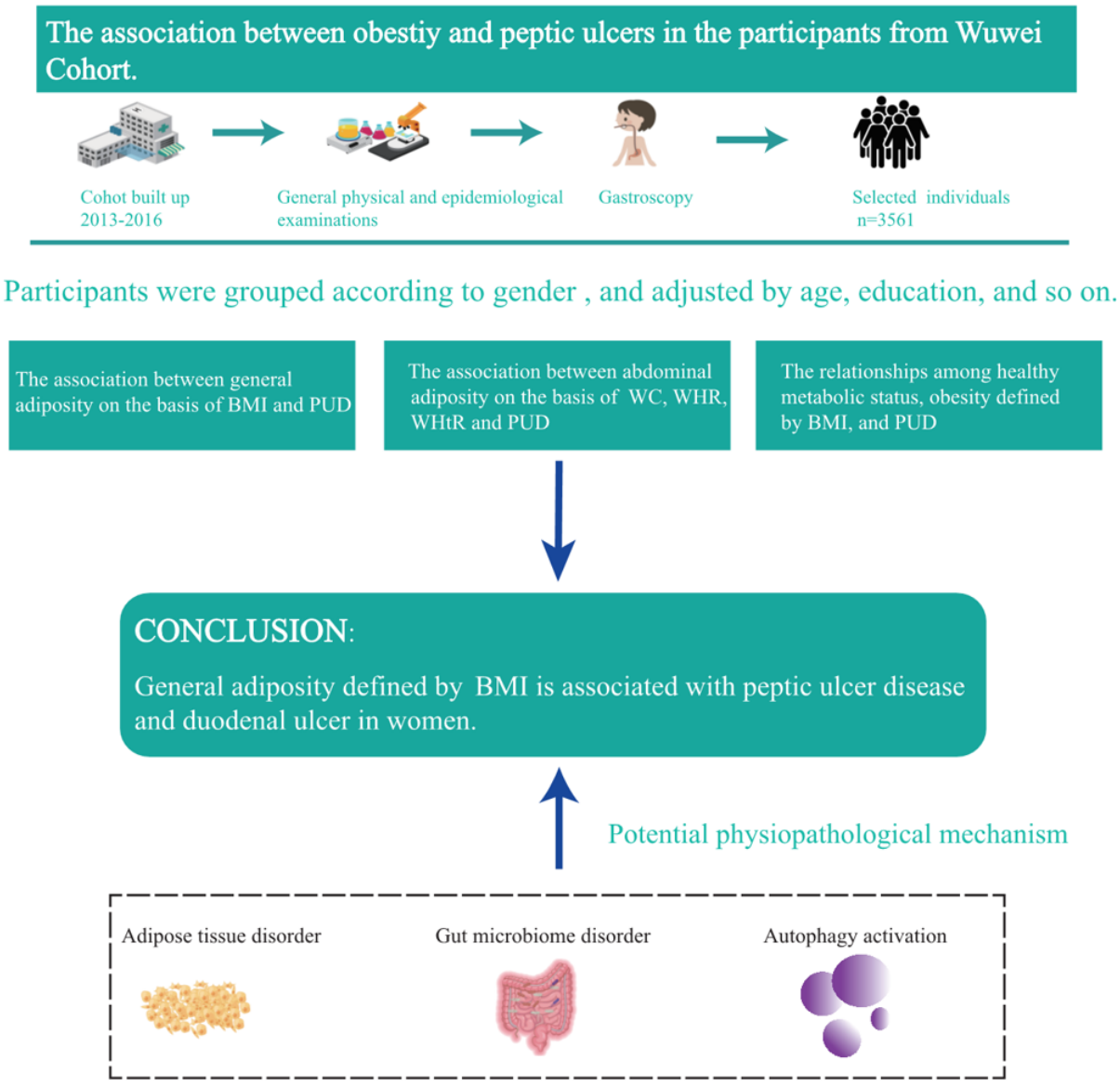

Figure 2. Graphical abstract of this study.

exert its influence by regulating adipocyte differentiation and inflammatory state in adipose tissue. The occurrence and development of obesity is accompanied by changes in autophagy activity. Autophagy also plays an important role in regulating inflammatory response.[35] It may be a factor to accelerate the inflammatory process and progress of PUD. Evidence has increasingly indicated that obesity is associated with gut microbiota disorder,[36,37] which may respond to diet changes, antibiotics, and other interventions. Inflammation-induced changes in the gut microbiome and increases of epithelial permeability disturb the homeostasis of the humoral and neural pathways that control food intake and body weight.[38] Because of technological and methodological limitations, the causality of the complex relationship between obesity and the gut microbiome has not been determined, despite studies reporting a strong association between them. Obesity is a chronic metabolic disease, but a subtype of obesity without metabolic abnormalities has attracted attention. Compared with individuals with metabolically unhealthy obesity, individuals with MHO have lower concentrations of C-reactive protein, tumor necrosis factor-α, interleukin 6 and lower blood leukocyte counts, indicating less inflammation.[39] The difference between MHO and metabolically unhealthy obesity in the prevalence of PUD remains debatable. In a Korean study,[10] participants with MHO did not have an increased risk of PUD, and PUD was not associated with MHO or typical obesity. By contrast, we observed MHO and metabolically unhealthy obesity to be associated with PUD in women. However, the Korean study included only individuals who visited a health center and did not examine *H. pylori* status in all participants, both of which may account for the different results. We discovered an association between general obesity and PUD in women and not in men, after adjusting for major covariates, including *H. pylori* status. Women faced gender inequality during China's transition to a more market-based economy in the last century. Marriage and childbearing[40] can negatively affect the chances of workplace promotions of women and increase their likelihood of withdrawing from the labor force.

A strength of our study is that all of our participants underwent EGD, unlike those in other studies that have diagnosed PUD on the basis of questionnaires or self-reports. We also distinguished general and abdominal adiposity by assessing them in terms of different anthro-

pometric indices. Because obesity, especially abdominal adiposity, and metabolic status are often related, we conducted a subgroup analysis to evaluate the relationships among obesity, metabolic status, and PUD.

Our study also has some limitations. First, because this was a cross-sectional study, we could not ascertain the causal relationship between PUD and obesity. Second, we did not analyze the use of NSAIDs (including aspirin), which is a risk factor for PUD. Third, our study was based on a gastric cancer cohort from a single center in Wuwei Municipality, Gansu Province, where the incidence and mortality rates of gastric cancer are among the highest in China. Our results may thus not be representative of other populations. Finally, our small sample size and potential recall, sampling, and confounding biases are additional limitations.

In conclusion, we report that general adiposity (defined by BMI) is associated with PUD and DU in women. In addition, both MHO and metabolically unhealthy obesity are associated with greater odds of PUD in women. Maintaining a healthy BMI may help to prevent PUD in women if this association is confirmed to be causal. Although our data provide a reference for PUD prevention, further prospective studies are warranted to validate our findings.

AUTHOR DISCLOSURES

The authors declare no conflict of interest.

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