Obesity Facts

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High Obesity Indices Are Associated with Gastroesophageal Reflux Disease, but Low Obesity Indices Are Associated with Peptic Ulcer Disease in a Large Taiwanese Population Study

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Keywords
Obesity indices · Gastroesophageal reflux disease · Peptic ulcer disease · Taiwan biobank

Abstract
Introduction: Gastroesophageal reflux disease (GERD) and peptic ulcer disease (PUD) are prevalent in Taiwan. Few studies have investigated the associations between obesity indices with GERD and PUD simultaneously. This study aimed to investigate the correlations among obesity indices with GERD and PUD in a large cohort of participants, around 120,000, in the Taiwan Biobank (TWB). ***Methods:*** A total of 121,583 participants (male: 43,698; female: 77,885; mean age 49.9 ± 11.0 years) were included to analyze the associations among obesity indices, including body mass index (BMI), waist-hip ratio (WHR), waist-to-height ratio (WHtR), body roundness index (BRI), abdominal volume index (AVI), lipid accumulation product (LAP), visceral adiposity index (VAI), and triglyceride-glucose index (TyG index), with GERD and PUD. Self-reported GERD and PUD were obtained by questionnaires. Multivariate logistic regression analysis was employed to analyze the relationship between obesity indices with GERD and PUD. ***Results:*** The prevalence of GERD and PUD was 13.7% and 14.6%, respectively. After multivariable analysis, high WHR (odds ratio [OR] = 1.009, $p < 0.001$), WHtR (OR = 1.005, $p = 0.003$), BRI (OR = 1.022, $p = 0.005$), AVI (OR = 1.013, $p < 0.001$), LAP (OR = 1.001, $p < 0.001$), TyG index (OR = 1.068, $p < 0.001$), and VAI (OR = 1.013, $p = 0.002$) were significantly associated with GERD, except BMI ($p = 0.384$). On the other hand, low BMI (OR = 0.984; $p < 0.001$) and AVI (OR = 0.994; $p = 0.036$) were significantly associated with PUD. However, the values of WHR ($p = 0.151$), WHtR ($p = 0.304$), BRI ($p = 0.452$), LAP

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(p = 0.799), VAI (p = 0.347), and TyG index (p = 0.642) were not. ***Conclusion:*** This study found that high obesity indices are associated with GERD, but low obesity indices are associated with PUD in a large Taiwanese population study. Our findings may alert physicians to notice that different obesity index may be associated with different gastrointestinal disorder.

Introduction

Gastroesophageal reflux disease (GERD) is a condition in which symptoms and/or complications are caused by the reflux of stomach contents into the esophagus [1]. Based on the presence or lack of visible breaks in the distal esophageal mucosa on endoscopy, GERD is classified as erosive esophagitis or nonerosive reflux disease. Peptic ulcer disease (PUD) is defined as a mucosal defect larger than 3–5 mm extending through the muscularis mucosa over the gastrointestinal tract, although it usually occurs in the stomach and proximal duodenum [2]. Both GERD and PUD are common digestive diseases in Taiwan, with prevalence rates of around 25% and 9.4%, respectively [3, 4]. The global prevalence of GERD increased from 1990 to 2019 [5], resulting in a significant health burden and adversely affecting the quality of life of patients. GERD can lead to Barrett's esophagus, which has malignant potential and has also been linked to other diseases such as asthma [6], depression, and anxiety [7]. PUD has also been associated with serious complications such as bleeding and even perforation, with a mortality rate of up to 30% [8]. Other complications such as obstruction of the gastric outlet or duodenum, although relatively rare, can necessitate endoscopic balloon dilatation or even surgical interventions in severe cases [9]. The known risk factors for GERD include hiatal hernia [10], obesity [11], and specific foods such as fat, caffeine, and chocolate [12]. In addition, medications such as calcium channel blockers, theophylline, and anticholinergics can induce lower esophageal sphincter hypotension [13]. Regarding PUD, the most common etiologies are *Helicobacter pylori* (*H. pylori*) infection and the use of nonsteroidal anti-inflammatory drugs [14]. In addition, lifestyle factors and stress have also been associated with the onset and course of PUD [15].

Anthropometric indices such as body mass index (BMI) have been shown to be useful predictors of metabolic syndrome [16] and to be correlated with cardiovascular factors [17]. BMI along with abdominal volume index (AVI), body roundness index (BRI), waist-to-hip ratio (WHR), and waist-to-height ratio (WHtR) can be calculated using body height/weight (BH/BW) and hip/waist circumference (HC/WC). In addition, other indices such as lipid accumulation product (LAP), visceral adiposity index (VAI), and triglyceride-glucose index (TyG index) can be calculated using triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), and fasting blood glucose levels.

Previous studies have investigated the association of GERD with anthropometric indices such as BMI and muscle mass [18, 19]. In addition, several studies have investigated the relationships among anthropometric indices, obesity, and PUD; however, the results have been inconclusive. Some studies have not identified an association between PUD with BMI and/or WHR [20–22], whereas others have shown such an association [23, 24]. Interestingly, most of the studies that identified an association between PUD and BMI found that high BMI was an independent indicator [4, 25–28], and only a few studies have reported the occurrence of PUD in patients with a low BMI [29, 30]. However, few studies have investigated the associations between obesity indices with GERD and PUD simultaneously. Therefore, this study aimed to investigate correlations among the aforementioned obesity indices with GERD and PUD in a large Taiwanese cohort derived from the Taiwan Biobank (TWB).

Materials and Methods

The TWB

The TWB is a large research initiative established in 2008 to record health-related data on Taiwanese individuals living in the community. The TWB enrolls cancer-free members of the community aged 30–70 years and includes data on medical, genetic, and lifestyle factors [31, 32]. All enrollees are interviewed before undergoing a physical examination and the collection of biological samples.

Ethics Statement

All enrollees in the TWB are asked to sign informed consent forms. Ethical approval for the TWB was granted by the Institutional Review Board on Biomedical Science Research, Academia Sinica, Taiwan, and the Ethics and Governance Council of the TWB. The Institutional Review Board of Kaohsiung Medical University Hospital approved this study (KMUHIRB-E(I)-20210058). All participants provide written informed consent before they are enrolled. This research was performed in compliance with the ethical standards set forth in the Helsinki Declaration.

Study Participants

We identified a total of 121,675 individuals in the TWB, excluded those without complete anthropometric data (n = 92), and included the remaining 121,583. The mean age of the included participants was 49.9 ± 11.0 years, 43,698 were male, and 77,885 were female (Fig. 1).

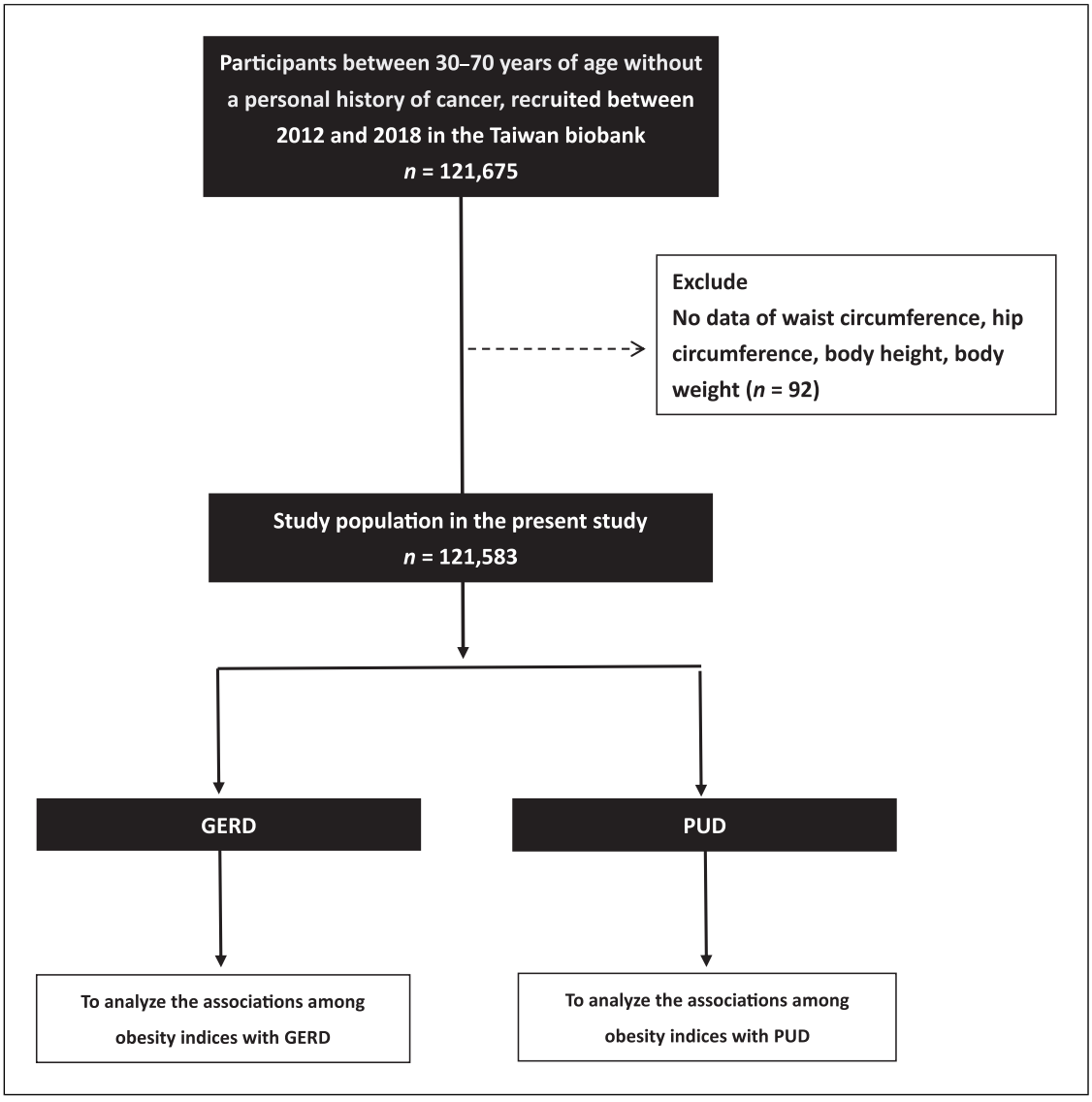

Fig. 1. Flowchart of study population.

Collection of Study Variables

Data obtained from the TWB included systolic and diastolic blood pressure (BP; average of 3 readings), WC/HC and BH/BW, the presence of hypertension and diabetes mellitus (DM), use of tobacco products, alcohol, and betel nut, age, and sex. Other data including HDL-C, low-density lipoprotein cholesterol (LDL-C), total cholesterol, TGs, hemoglobin, fasting glucose, uric acid, and estimated glomerular filtration rate (eGFR; calculated as described previously [33]) were also obtained.

Calculation of Obesity Indices

1. BMI was calculated as:

$$\text{BMI} = \text{BW (kg)}/\text{BH}^2\ \text{(m)}$$

2. WHR was calculated as:

$$\text{WHR} = \text{WC (cm)}/\text{HC (cm)}$$

3. WHtR was calculated as:

$$\text{WHtR} = \text{WC (cm)}/\text{BH (cm)}$$

4. BRI was calculated as:

$$\text{BRI} = 364.2 - 365.5 \times \sqrt{1 - \left(\frac{\frac{\text{WC}_{(\text{m})}}{2\pi}}{0.5 \times \text{BH}_{(\text{m})}}\right)^2}$$ [34].

5. AVI was calculated as: AVI = $\frac{2 \times \left(\text{WC}_{(\text{cm})}\right)^2 + 0.7 \times \left(\text{WC}_{(\text{cm})} - \text{HC}_{(\text{cm})}\right)^2}{1{,}000}$ [35].

6. LAP was calculated as:

$$\text{LAP} = \left(\text{WC}_{(\text{cm})} - 65\right) \times \text{TG}_{(\text{mmol/L})} \text{ in males, and}$$

$$\text{LAP} = \left(\text{WC}_{(\text{cm})} - 58\right) \times \text{TG}_{(\text{mmol/L})} \text{ in females [36].}$$

7. VAI was calculated as described previously [37] using the following sex-specific equations:

$$\text{VAI} = \left(\frac{\text{WC}_{(\text{cm})}}{39.68 + (1.88 \times \text{BMI})}\right) \times \left(\frac{\text{TG}_{(\text{mmol/L})}}{1.03}\right) \times \left(\frac{1.31}{\text{HDL} - \text{C}_{(\text{mmol/L})}}\right) \text{ in males, and}$$

$$\text{VAI} = \left(\frac{\text{WC}_{(\text{cm})}}{36.58 + (1.89 \times \text{BMI})}\right) \times \left(\frac{\text{TG}_{(\text{mmol/L})}}{0.81}\right) \times \left(\frac{1.52}{\text{HDL} - \text{C}_{(\text{mmol/L})}}\right) \text{ in females.}$$

8. The TyG index was calculated as ln fasting triglycerides mg/dL × fasting glucose mg/dL/2 [38].

Definitions of GERD and PUD

The participants were classified into the GERD or PUD group according to whether or not they reported a history of either condition.

Statistical Analysis

Data are shown as number (%) or mean (±SD). Continuous and categorical variables were compared using the independent *t*-test and χ^2 test, respectively. Three multivariable logistic regression models were used to examine associations among the obesity indices with GERD and PUD. BMI, WHR, WHtR, BRI, and AVI were entered into model 1. For GERD, model 1 was adjusted for age, sex, DM, hypertension, smoking, and alcohol history, regular exercise, fasting glucose, TGs, total cholesterol, LDL cholesterol, eGFR, and uric acid. For PUD, model 1 was adjusted for the same variables with the addition of systolic BP and hemoglobin. For both GERD and PUD, LAP and VAI were entered into model 2, which included the same adjustments as for model 1 without TGs. The TyG index was entered into model 3, which included the same adjustments as for model 1 without TGs and fasting glucose. Using the propensity score matching method, scores were derived for each GERD or PUD patient based on recruitment age and sex. These scores were calculated using a multiple logistic regression model. A 1:4 or 1:3 Greedy nearest neighbor-matching algorithm with a caliper of 0.25 was employed to match each eligible patient based on these scores, creating a matched cohort. This facilitated the conduct of baseline statistical analyses. We used SPSS for the analysis (v19, IBM Inc., Armonk, NY, USA), and a two-tailed p value <0.05 was considered statistically significant.

Results

Of the 121,583 participants included in the analysis, 16,664 had GERD (13.7%) and 104,919 (86.3%) did not. In addition, 17,696 (14.6%) had PUD and 103,887 (85.4%) did not.

Comparison of Clinical Characteristics between Those with and without GERD

The participants with GERD were older, predominantly female, and had higher prevalence rates of DM, hypertension, smoking and alcohol history, and regular exercise than those without GERD. In addition, they had lower BH/BW and HC, and higher WC, as well as higher fasting glucose, TGs, total cholesterol, and LDL-C, and lower eGFR and uric acid than those without GERD. Regarding obesity indices, the participants with GERD had higher values of all the studied obesity indices except for BMI (Table 1).

Associations among the Obesity-Related Indices with GERD

The results of multivariable logistic regression analysis for the associations among the obesity indices with GERD are shown in Table 2. High values of WHR (per 1%; odds ratio [OR] = 1.009; 95% confidence interval [CI] = 1.006–1.012; $p < 0.001$), WHtR (per 1%; OR = 1.005; 95% CI = 1.002–1.008; $p = 0.003$), BRI (per 1; OR = 1.022; 95% CI = 1.007–1.038; $p = 0.005$), AVI (per 1; OR = 1.013; 95% CI = 1.008–1.019; $p < 0.001$), LAP (per 1; OR = 1.001; 95% CI = 1.001–1.002; $p < 0.001$), VAI (per 1; OR = 1.013; 95% CI = 1.005–1.022; $p = 0.002$), and TyG index (per 1; OR = 1.068; 95% CI = 1.036–1.102; $p < 0.001$) were significantly associated with GERD. However, BMI ($p = 0.384$) was not associated with GERD (Table 2).

Because the percentage of female is higher in each subgroup, which may lead some bias. Therefore, we use the propensity score matching method, a 1:4 Greedy nearest neighbor matching algorithm with a caliper of 0.25 was employed to match each eligible patient based on these scores, creating a matched cohort. This facilitated the conduct of baseline statistical analyses (online suppl. Tables 1, 2; for all online suppl. material, see https://doi.org/10.1159/000540281). We found the similar findings, except BMI and albumin, high values of WHR, WHtR, BRI, AVI, LAP, VAI, and TyG index were significantly associated with GERD.

Comparison of Clinical Characteristics between Those with and without PUD

The participants with PUD were older, predominantly female, and had higher prevalence rates of DM, hypertension, smoking and alcohol history, and regular exercise. In addition, they had higher systolic BP and WC, and lower BW/BH and HC, as well as lower fasting glucose and eGFR, and higher hemoglobin, TGs, total cholesterol, LDL-C, and uric acid. Regarding obesity indices, the participants with PUD had lower BMI and higher WHR, WHtR, BRI, AVI, and TyG index (Table 3).

Table 1. Clinical characteristics of the study participants classified by the presence of GERD

Characteristics	GERD (n = 121,583)		p value
	GERD (–) (n = 104,919)	GERD (+) (n = 16,664)	
Age, years	49.6±11.0	51.9±10.4	<0.001
Male sex, %	36.2	34.2	<0.001
DM, %	5.0	6.3	<0.001
Hypertension, %	11.7	15.3	<0.001
Smoking history, %	26.9	29.3	<0.001
Alcohol history, %	8.3	9.8	<0.001
Regular exercise habits, %	40.2	43.0	<0.001
Systolic BP, mm Hg	120.4±18.8	120.7±17.8	0.102
Diastolic BP, mm Hg	73.8±11.5	73.8±10.9	0.562
Body height, cm	162.0±8.3	161.5±8.2	<0.001
Body weight, Kg	63.8±12.7	63.5±12.7	0.010
Waist circumference, cm	83.2±10.2	83.7±10.3	<0.001
Hip circumference, cm	96.0±7.1	95.9±7.2	0.011
Laboratory parameters			
Fasting glucose, mg/dL	95.9±20.9	96.4±19.7	0.002
Hemoglobin, g/dL	13.8±1.6	13.8±1.5	0.083
Triglycerides, mg/dL	115.1±94.3	119.0±92.3	<0.001
Total cholesterol, mg/dL	195.4±35.9	197.4±35.2	<0.001
HDL-C, mg/dL	54.6±13.4	54.6±13.6	0.668
LDL-C, mg/d	120.8±31.8	121.8±31.3	<0.001
eGFR, mL/min/1.73 m^2	103.5±23.9	102.1±23.7	<0.001
Uric acid, mg/dL	5.4±1.4	5.4±1.4	0.002
Obesity-related indices			
BMI, kg/m^2	24.2±3.8	24.2±3.8	0.277
WHR, %	86.5±6.9	87.2±6.9	<0.001
WHtR, %	51.4±6.1	51.9±6.1	<0.001
BRI	3.7±1.2	3.8±1.2	<0.001
AVI	14.2±3.5	14.4±3.5	<0.001
LAP	32.1±34.5	34.0±35.2	<0.001
VAI	1.7±1.9	1.8±2.0	<0.001
TyG index	8.4±0.6	8.5±0.6	<0.001

GERD, gastroesophageal reflux disease; PUD, peptic ulcer disease; DM, diabetes mellitus; BP, blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate; BMI, body mass index; WHR, waist-hip ratio; WHtR, waist-to-height ratio; BRI, body roundness index; AVI, abdominal volume index; ABSI, a body shape index; LAP, lipid accumulation product; TyG index, triglyceride-glucose index; VAI, visceral adiposity index.

Associations among the Obesity Indices with PUD

The results of multivariable logistic regression analysis for the associations among the obesity indices with PUD are shown in Table 4. Low values of BMI (per 1%; OR = 0.984; 95% CI = 0.978–0.989; $p < 0.001$) and AVI (per 1; OR = 0.994; 95% CI = 0.988–1.000; $p = 0.036$) were significantly associated with PUD. However, WHR ($p = 0.151$), WHtR ($p = 0.304$), BRI ($p = 0.452$), LAP ($p = 0.799$), VAI ($p = 0.347$), and TyG index ($p = 0.642$) were not associated with PUD.

Because the percentage of female is higher in each subgroup, which may lead some bias. Therefore, we use the propensity score matching method, and a 1:3 Greedy nearest neighbor matching algorithm with a caliper of 0.25 was employed to match each eligible patient based on these scores, creating a matched cohort. This facilitated the conduct of baseline statistical analyses (online suppl. Tables 3, 4). Low values of BMI and AVI were significantly associated with PUD, whereas high BRI was significantly associated with PUD.

Discussion

In this large Taiwanese population-based study, we examined associations among various obesity indices with GERD and PUD. Our results showed that high

Table 2. Association of obesity-related indices with GERD using multivariable logistic regression analysis

Variables	Multivariable (GERD)	
	OR (95% CI)	*p* value
BMI, per 1 kg/m^{2}[a]	1.002 (0.997–1.007)	0.384
WHR, per 1%[a]	1.009 (1.006–1.012)	<0.001
WHtR, per 1%[a]	1.005 (1.002–1.008)	0.003
BRI (per 1)[a]	1.022 (1.007–1.038)	0.005
AVI (per 1)[a]	1.013 (1.008–1.019)	<0.001
LAP (per 1)[b]	1.001 (1.001–1.002)	<0.001
VAI (per 1)[b]	1.013 (1.005–1.022)	0.002
TyG index (per 1)[c]	1.068 (1.036–1.102)	<0.001

Values expressed as odds ratio and 95% confidence interval (CI). [a]Covariates in the multivariable model included age, sex, DM and hypertension, smoking and alcohol history, regular exercise habit, fasting glucose, triglycerides, total cholesterol, LDL cholesterol, eGFR, and uric acid. [b]Covariates included in [a], except for triglycerides. [c]Covariates included in [a], except for fasting glucose and triglycerides.

values of WHR, WHtR, BRI, AVI, LAP, VAI, and TyG index were associated with GERD, whereas low values of BMI and AVI were associated with PUD.

Our results showed associations among high values of all of the studied obesity indices (WHR, WHtR, BRI, AVI, LAP, VAI, and TyG index) with GERD, but not BMI. Obesity is generally considered to be a risk factor for GERD, and most previous studies have reported a strong association between BMI and GERD. A meta-analysis of 8 studies identified a trend toward a dose-response relationship with an increase in the pooled adjusted OR for GERD symptoms of 1.43 (95% CI, 1.158–1.774) for a BMI of 25 kg/m^{2} to 30 kg/m^{2} and 1.94 (95% CI, 1.468–2.566) for a BMI greater than 30 kg/m^{2} [39]. In addition, Jacobsen and colleagues used questionnaire data of 10,545 women to determine the symptoms and severity of GERD among randomly selected women in the Nurses' Health Study and reported a dose-dependent relationship between higher BMI with reflux symptoms (p for trend <0.001) in both normal weight and overweight women [40]. A recent study in Korea investigated associations among anthropometric indices with endoscopic erosive esophagitis in individuals over 40 years of age during health checkups and found that high muscle mass, but not BMI, was an independent risk factor for erosive esophagitis [19]. Although the mechanisms for the associations between obesity and GERD may be multifocal and are still under debate, a leading hypothesis is that increased visceral and subcutaneous fat causes increased intra-abdominal pressure, which further facilitates reflux of gastric contents back into the esophagus [41]. Other possible mechanisms include a higher prevalence of hiatal hernia in obese patients, which is a known risk factor for GERD [10]. Hormones including adiponectin and estrogen have also been discussed. Adiponectin is a peptide mostly secreted from visceral adipocytes and has both anti-inflammatory and antiapoptotic properties [42], and serum levels of adiponectin have been inversely correlated with BMI [43]. Rafat et al. [44] reported that a low serum adiponectin level appeared to be associated with an increased risk of erosive esophagitis, although the actual pathogenesis still needs to be clarified. Regarding estrogen, Nilsson et al. [45] evaluated the relationship between BMI and endoscopy-confirmed reflux esophagitis among men and women and showed a strong and dose-dependent association between BMI and reflux esophagitis in women but not in men. A possible reason may be increased estrogen activity in obese women. A previous study reported lower esophageal sphincter pressure in women using oral contraceptives [46]. Estrogen has also been associated with increased nitric oxide synthesis and consequently lower smooth muscle tone or prolonged transient relaxation of the lower esophageal sphincter [47], further resulting in GERD. In our study, all of the obesity indices were associated with GERD, except BMI. It is widely recognized that general obesity defined by BMI does not accurately reflect body fat distribution, and a high prevalence of central obesity among people with normal BMI has also recently been reported [48]. Therefore, we hypothesize that central obesity (or abdominal obesity) as an indicator of excess body fat accumulation more specifically related to the abdomen may be a more important causative factor for GERD than general obesity, which is defined by BMI. A systematic review also showed that GERD-related complications including Barrett's esophagus, esophageal inflammation, and esophageal adenocarcinoma were all associated with central adiposity but independent of BMI [49]. Moreover, another study also showed that compared to general obesity, central obesity was a more reliable predictor of other diseases such as major adverse cardiac events [50]. A possible explanation is that visceral adiposity has been linked to impaired suppression of adipocyte lipolysis and systemic inflammation with endothelial dysfunction [51]. In addition, complex inflammatory mediators have recently been demonstrated to participate in the inflammatory processes of GERD [52], and another study also showed an association between obesity markers and esophageal inflammation on fluorodeoxyglucose positron emission tomography/computed tomography [53]. Therefore, it is

Table 3. Clinical characteristics of the study participants classified by the presence of PUD

Characteristics	PUD (n = 121,583)		
	PUD (–) (n = 103,887)	PUD (+) (n = 17,696)	p value
Age, years	49.3±11.0	53.2±1.01	<0.001
Male sex, %	35.1	40.7	<0.001
DM, %	4.9	6.7	<0.001
Hypertension, %	11.7	15.6	<0.001
Smoking history, %	26.4	32.6	<0.001
Alcohol history, %	8.2	10.3	<0.001
Regular exercise habits, %	39.9	44.5	<0.001
Systolic BP, mm Hg	120.3±18.7	121.1±18.3	<0.001
Diastolic BP, mm Hg	73.8±11.4	73.9±11.1	0.076
Body height, cm	161.9±8.3	161.7±8.2	0.002
Body weight, Kg	63.9±12.8	63.3±12.2	<0.001
Waist circumference, cm	83.2±10.3	83.6±10.1	<0.001
Hip circumference, cm	96.1±7.1	95.5±7.0	<0.001
Laboratory parameters			
Fasting glucose, mg/dL	95.8±20.8	86.8±19.9	<0.001
Hemoglobin, g/dL	13.7±1.6	13.9±1.6	<0.001
Triglyceride, mg/dL	115.2±94.8	117.8±89.0	0.001
Total cholesterol, mg/dL	195.5±35.9	196.6±35.6	<0.001
HDL-C, mg/dL	54.6±13.4	54.4±13.7	0.111
LDL-C, mg/dL	120.8±31.8	121.5±31.6	0.007
eGFR, mL/min/1.73 m^2	103.8±23.9	100.4±23.6	<0.001
Uric acid, mg/dL	5.4±1.4	5.5±1.4	<0.001
Obesity-related indices			
BMI, kg/m^2	24.2±3.8	24.1±3.7	<0.001
WHR, %	86.5±6.9	87.4±6.9	<0.001
WHtR, %	51.4±6.1	51.7±6.1	<0.001
BRI	3.7±1.2	3.8±1.2	<0.001
AVI	14.2±3.5	14.3±3.4	<0.001
LAP	32.3±34.9	32.7±33.0	0.118
VAI	1.7±1.9	1.7±2.0	0.122
TyG index	8.4±0.6	8.5±0.6	<0.001

possible that the visceral adiposity-related systemic inflammation in central obesity also plays a causal role in GERD, although evidence is still insufficient to draw definitive conclusions. On the other hand, diet and lifestyle habits in obese patients may also be related to GERD since GERD has been linked to high dietary fat intake [12], which is a cause of obesity. In addition, lifestyle and eating habits such as fast food and irregular meals have also been associated with both GERD [54] and obesity [55]. The possibility of a bidirectional association between GERD and obesity is another possible but difficult to clarify issue. In our study, high values of WHR, WHtR, BRI, AVI, LAP, and VAI were associated with GERD. All of these indices are calculated using WC, which is usually used to define central obesity; therefore, these indices are believed to be more specifically related to central obesity. In addition, the accuracy of the TyG index, which is calculated using fasting plasma glucose and TGs, has been shown in screening for metabolic syndrome [56]. A novel finding of the current study is the positive association between the TyG index and GERD, which has not been reported previously.

A second key finding of this study is that low BMI and AVI values were associated with PUD. Previous studies on the associations among anthropometric indices, obesity, and PUD are heterogeneous and difficult to compare, and the results are also controversial. Cheng and colleagues did not find evidence of a relationship between BMI and PUD [21], which is compatible with another single center study from Taiwan [22]. However, a recent study in southern Taiwan found that central obesity was associated with PUD in a middle-aged healthy population [27], and the result of an association between high BMI and PUD is similar to a previous study conducted in America [25]. In addition, a study conducted in China also reported an

Table 4. Association of obesity-related indices with PUD using multivariable logistic regression analysis

Variables	Multivariable (PUD)	
	Odds ratio (95% CI)	*p* value
BMI, per 1 kg/m^2[a]	0.984 (0.978–0.989)	<0.001
WHR, per 1%[a]	1.002 (0.999–1.005)	0.151
WHtR, per 1%[a]	0.998 (0.995–1.002)	0.304
BRI (per 1)[a]	0.994 (0.979–1.010)	0.452
AVI (per 1)[a]	0.994 (0.988–1.000)	0.036
LAP (per 1)[b]	1.000 (0.999–1.000)	0.799
VAI (per 1)[b]	1.004 (0.995–1.014)	0.347
TyG index (per 1)[c]	1.008 (0.976–1.040)	0.642

Values expressed as odds ratio and 95% confidence interval (CI). [a]Covariates in the multivariable model included age, sex, DM and hypertension, smoking and alcohol history, regular exercise habit, systolic BP, fasting glucose, hemoglobin, triglycerides, total cholesterol, LDL cholesterol, eGFR, and uric acid. [b]Covariates included in [a], except for triglycerides. [c]Covariates included in [a], except for fasting glucose and triglycerides.

association between high BMI and PUD, but specifically in women only [28]. Interestingly, another recent study in Korea showed that decreased BW, BMI, and HC values were associated with an elevated risk of PUD in Korean women [30]. Reports from different areas have been inconsistent, which may be due to differences in the ethnicity and sex of the studied populations, diagnostic tools, and study design. In our study, low BMI was related to PUD, which is compatible with the study by Kim and colleagues in Korea [30]. In addition, we also found that low AVI was associated with PUD, which has not been reported before. Although the prevalence of idiopathic peptic ulcer, defined as gastric or duodenal ulcers without obvious risk factors, continues to increase [57], *H. pylori* infection is still the most important cause of PUD worldwide [58]. The associations among BMI, obesity, and *H. pylori* infection are also still unclear and controversial. Xu et al. [59] found that *H. pylori* infection was positively associated with obesity in a Chinese population, and another recent study in China reported that although no significant differences were found between *H. pylori* infection and obesity/weight gain, a trend toward weight loss was linked to *H. pylori* infection [60]. Another study showed that *H. pylori* eradication was significantly related to increased BMI and BW [61]. Possible reasons include that the eradication of *H. pylori* may be related to increased gastric secretion of ghrelin and decreased gastric leptin expression [62, 63], which may then further increase appetite and weight gain. Another possible explanation is improvement in symptoms such as dyspepsia after *H. pylori* eradication [64]. Considering that the major cause of PUD is still *H. pylori* infection, and that *H. pylori* infection is possibly related to weight loss, we hypothesize that there may also be relationship between PUD and weight loss. However, further evidence is needed to confirm this hypothesis, and it may not explain the occurrence of PUD in patients without *H. pylori* infection. Another possible explanation is that some PUD patients who present with complications or symptoms such as bleeding, perforation, or severe gastrointestinal discomfort may also be related to poor dietary intake and nutritional status. We tried to analyze the link between the PUD and malnutrition; however, albumin was not significantly associated with PUD because the participants in Taiwan biobank are relatively healthy, which may result in no significant finding. Further evidence is needed to confirm this hypothesis.

The main strengths of this research are the inclusion of a large study cohort, along with the comprehensive analysis of associations among obesity indices with GERD and PUD. The limitations of this study include that this was a cross-sectional study and we did not evaluate how long the patients had GERD or PUD, thereby precluding the ability to evaluate causal relationships between the obesity indices with GERD and PUD. Further longitudinal studies are warranted to investigate the risk of incident GERD and PUD. In addition, the occurrence of GERD and PUD was confirmed using questionnaires without verification, and we did not have information of *H. pylori* infection and the type or severity of GERD and PUD. Nevertheless, Wu et al. [65] reported fair consistency between self-reported diseases with claims records in Taiwan. Another limitation is that we did not have information on other important and possible causes of PUD and GERD such as hiatal hernia and use of nonsteroidal anti-inflammatory drugs. Finally, the Chinese ethnicity of our participants may limit the findings to other groups.

In conclusion, high levels of the obesity indices WHR, WHtR, BRI, AVI, LAP, VAI, and TyG index were associated with GERD, and low values of BMI and AVI were associated with PUD. Our findings may suggest that different obesity indices are associated with different gastrointestinal disorders.

Statement of Ethics

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of Kaohsiung Medical University Hospital (protocol code KMU-HIRB-E(I)-20210058 and 2021/4/8 approval). All participants provide written informed consent before they are enrolled.

Conflict of Interest Statement

The authors declare no conflicts of interest.

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Author Contributions

Conceptualization, methodology, validation, formal analysis, writing – review and editing, and supervision: Szu-Chia Chen and Chao-Hung Kuo. Software and investigation: Chien-Cheng Chen, Jiun-Hung Geng, Szu-Chia Chen, and Chao-Hung Kuo. Resources, project administration, and visualization: Szu-Chia Chen. Data curation: Chien-Cheng Chen, Jiun-Hung Geng, Pei-Yu Wu, Jiun-Chi Huang, Huang-Ming Hu, Szu-Chia Chen, and Chao-Hung Kuo. Writing – original draft preparation: Chien-Cheng Chen and Szu-Chia Chen. All authors have read and agreed to the published version of the manuscript.

Data Availability Statement

The data underlying this study are from the Taiwan Biobank. Due to restrictions placed on the data by the Personal Information Protection Act of Taiwan, the minimal dataset cannot be made publicly available. Data may be available upon request to interested researchers. Please send data requests to Szu-Chia Chen, Division of Nephrology, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University.

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