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BRIEF ARTICLE

Association between body mass index and erosive esophagitis: A meta-analysis

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Abstract

AIM: To conduct a meta-analysis to estimate the determinants of the association between erosive esophagitis (EE) and body mass index (BMI).

METHODS: We identified the studies using PubMed. Studies were selected for analysis based on certain inclusion and exclusion criteria. Data were extracted from each study on the basis of predefined items. Meta-analyses were performed to verify the risk factors, such as obesity and gender.

RESULTS: Twenty-one studies were included in this systematic review. These studies demonstrated an association between increasing BMI and the presence of EE [95% confidence interval (CI): 1.35-1.88, overweight, odds ratio (OR) = 1.60, *P* value homogeneity = 0.003, 95% CI: 1.65-2.55, obese, OR = 2.05, *P* < 0.01]. The heterogeneity disappeared by stratifying for gender. No publication bias was observed in this meta-analysis by the Egger method.

CONCLUSION: This analysis demonstrates a positive association between BMI and the presence of EE, especially in males. The risk seems to progressively increase with increasing weight.

Key words: Erosive esophagitis; Gastroesophageal reflux disease; Obesity; Body mass index; Meta-analysis

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INTRODUCTION

The symptoms of gastroesophageal reflux disease (GERD) are common health problems in industrialized societies. It is a highly prevalent gastrointestinal disorder encountered in clinical practice[1,2]. Erosive esophagitis (EE) is one of the most common forms of GERD. It occurs when excessive reflux of acid and pepsin results in necrosis of surface layers of the esophageal mucosa, thus causing erosions and

ulcers[3]. The etiology of EE may be multifactorial. Esophageal mucosal resistance, gastroesophageal reflux, volume and composition of the gastric contents, contact time for the refluxed material, the degree of incompetence of the intrinsic lower esophageal sphincter, and the presence of a sliding hiatus hernia are likely important determinants[4]. It is a chronic disease that exhausts socioeconomic and medical resources and its symptoms may lower the quality of life of the patients. Additionally, patients with EE are at increasing risk of developing Barrett's esophagus and esophageal adenocarcinoma[5].

During the past several decades, obesity has emerged as a major health concern in the Western world[6]. Several studies have found an increased risk of esophagitis in overweight patients[7-9]. Excess adiposity is a known risk factor for morbidity, including several cancers[10]. Recently, a relationship between obesity and GERD has been reported[11]. One recent population-based case control study reported a strong association between body mass index (BMI) and esophagitis in females, but not in males[12]. Given these associations, it would seem logical that increasing BMI is associated with EE. However, studies on the association between BMI and reflux esophagitis have yielded inconsistent results[13-16], though a few have found a strong relationship between obesity and EE[17,18].

The aim of this study was to investigate the effect of BMI on risk for EE by performing a meta-analysis of all available literature published in PubMed up to April 2011. By performing a meta-analysis of the studies that met our selection criteria, we hoped to better characterize the association between increased BMI and EE.

MATERIALS AND METHODS

Search strategy

Two investigators independently performed a systematic search of all existing English-language literatures published up to April 2011 using PubMed, an electronic search engine for published manuscripts. Search terms included "obesity", "BMI", "overweight" or "BMI", combined with "reflux or EE". A total of 268 articles were identified after the preliminary search was reviewed in further details.

Study selection

Studies were included if they met all the following inclusion criteria: (1) Cross-sectional, case control, or cohort studies that permitted assessment of a causal relationship between BMI and EE; (2) Studies with documented and clearly-defined BMI in kg/m^2 for all participants; (3) Studies that reported a relative risk or odds ratio (OR) with confidence intervals or provided sufficient data to permit their calculation; and (4) Studies with EE diagnosed by upper endoscopy. The inclusion criteria were not otherwise restricted by study size or publication type. The followings were chosen as the exclusion criteria: (1) Studies not limited to humans or not written in English; (2) Studies that did not report risk estimates or raw data to allow independent calculation of these estimates; and (3) Case reports, case series or studies that lacked a control group.

Data abstraction

The abstracted data included information on the source of the study population, study design (case control, cohort, or cross-sectional), length of the study period, primary aim of the study, exposure definitions (BMI definitions of normal, overweight or obese), exposure measurement method (self-reported *vs* measured BMI), outcome definitions (diagnosis of EE with endoscopy), total number of subjects with EE, case and control criteria, ORs or risk ratios with and without adjustment for potential confounders and potential confounders used for adjustment.

Exposure definition

We defined body mass categories using the following BMI [weight (in kilograms)/height (in meters)^2]: "normal" (BMI between 18.5 and 25 kg/m^2), "overweight" (BMI between 25 and 28 kg/m^2), and "obese" (BMI $\geqslant$ 28 kg/m^2). These groupings represented the divisions or quartiles most frequently reported in the literature even though they differed somewhat from BMI categories in common use (overweight, BMI 25-29.9 kg/m^2; obese, BMI $\geqslant$ 30 kg/m^2)[11]. We also created a category that included both overweight and obese (BMI $\geqslant$ 25 kg/m^2). For each study, we selected the BMI classification that most closely approximated each of these categories. We included more than one estimate from the studies (e.g., if a study reported an OR for persons with a BMI 25-28 kg/m^2 and an OR for persons with a BMI $\geqslant$ 28 kg/m^2, both ORs were included in the summary estimate as BMI $\geqslant$ 25 kg/m^2)[11]. We then compared the risk of EE among the BMI categories.

We used estimates adjusted for potential confounders whenever they were available; if no adjusted estimates were provided, unadjusted estimates were used or calculated from the data[11].

Outcome definition

An outcome was defined as EE diagnosed with endoscopy. The severity of EE was graded from A to D according to the LA classification[19] or modified Savary-Miller classification (grade Ⅰ, single or multiple non-confluent erosions; grade Ⅱ, confluent non-circumferential multiple erosion; grade Ⅲ, circumferential erosions; and grade Ⅳ, ulcer and/or stricture)[20].

Statistical analysis

The BMI data were extracted from each study and analyzed with STATA 11.0 (StataCorp, College Station, TX, United States, www.stata.com). Summary OR estimates were calculated using either relative risks (for cohort stud-

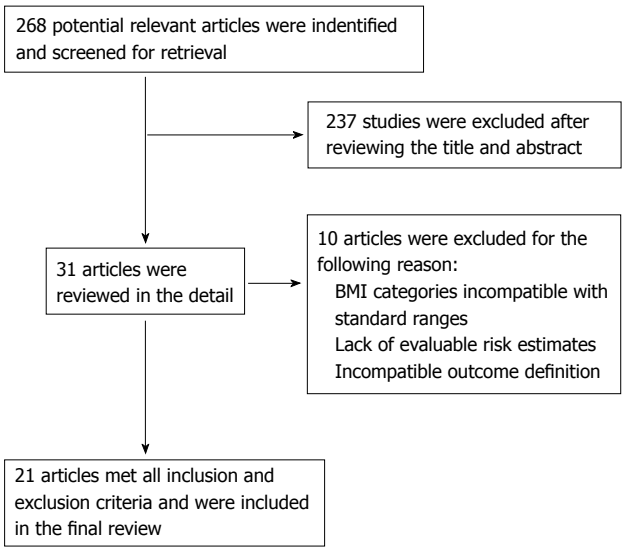

Figure 1 Flow diagram. BMI: Body mass index.

ies) or OR (for case control studies). Summary OR estimates were calculated based on the assumption of fixed effects and heterogeneity was tested using the Mantel-Haenszel method[21]. We evaluated heterogeneity by comparing the results between the fixed effects model and a random effects model[21]. Heterogeneity among the studies was analyzed using χ^2 test and considered present if $P \leqslant 0.05$ or if there was more than a 20% difference in the summary estimates between the two models. To enhance the confidence of the results of the statistics when the number of combined studies was deficient, we used the I^2 metric, which describes the proportion of variability across studies that is due to score heterogeneity. If $I^2 = 0$, there is no heterogeneity. $I^2 > 50\%$ is considered to be indicative of heterogeneity. Larger values indicate greater heterogeneity. If these tests indicated heterogeneity, we explored possible causes[21-24]. Then, to exclude the excessive influence of any single study, we assessed whether exclusion of any single study substantially altered the magnitude or heterogeneity of the summary estimate. We also stratified analyses by several factors[25-31]. Funnel plots were produced and Egger's test[32] was conducted to examine publication bias.

RESULTS

We identified 268 published articles or abstracts (Figure 1). After review of titles and abstracts, 31 articles appeared to meet the initial inclusion criteria. The excluded studies were review articles, animal experiments, case series that lacked appropriate control groups and studies that did not report the subject of interest. These 31 studies underwent a complete data abstraction. Ten additional studies were excluded after data abstraction for the following reasons: BMI categories that were inconsistent with the proposed reference ranges[7,33-36], inconsistent outcome definition[37], lack of proper control group[38], and lack of evaluable risk estimates within the proposed categories[39-41].

The remaining 21 studies[4,8,12,42-59] (i.e., four cross-sectional, three cohort, 14 case control studies) were included in the primary analysis (Tables 1 and 2). Twelve studies were conducted for the primary purpose of evaluating the relationship between BMI and EE[4,44,45,49-52,54,55,57-59], eight studies were conducted to identify the variety of risk factors for EE, including BMI[8,12,42,46-48,53,56], and one study described the clinical characteristics of EE and non-erosive reflux disease, including BMI[43]. In Table 1, controls and normal groups were composed of general population and healthy volunteers. Eighteen studies were included in Table 3 because of their stratification by gender.

The pooled OR of EE related to BMI of 25 kg/m^2 or higher was 1.64-fold greater than that of EE related to BMI less than 25 kg/m^2 (OR, 1.64, 95% CI: 1.45-1.85, test for homogeneity, $P = 0.000$, $I^2 = 65.7\%$) (Figure 2, Table 3).

Stratification by gender and BMI category showed a homogeneous positive association between increased BMI and EE, and the strength of the association with increased BMI (Table 3). The risk for overweight males (OR, 1.40, 95% CI: 1.11-1.75, $P = 0.285$) increased further for obese males (OR, 1.75, 95% CI: 1.02-2.96, $P = 0.099$) (Figure 3). The pooled OR in females and males for BMI greater than 25 kg/m^2 were 1.45 (95% CI: 1.26-1.66) and 1.52 (95% CI: 1.24-1.87), respectively. Therefore, we considered there was a strong positive association between increasing BMI and EE in males, but not in females.

Evaluation of heterogeneity

The initial summary estimates for EE were heterogeneous, as described above. Stratification by BMI category did not substantially resolve the heterogeneity; however, additional stratification by gender provided more homogeneity. Stratification of the entire population by exposure measurement (e.g., self-report *vs* measured), or study design (case control *vs* cohort) did not substantially influence the initial heterogeneity (Table 3).

Publication bias

The rank correlation test did not suggest the presence of publication bias for the main summary estimates for either the overweight ($P = 0.656$) or the obese and overweight ($P = 0.804$). A review of funnel plots did not demonstrate patterns strongly suggestive of publication bias (Figure 4).

DISCUSSION

Our pooled results of observational studies demonstrated a positive association between increased BMI and the risk of EE. The strength of the association increased with increasing BMI and there was a trend towards a stronger association in males than in females. Unlike other non-modifiable risk factors such as age, race and gender, BMI is potentially modifiable. Thus, identifying a relationship

Table 1 Study characteristics

Authors	Yr	Design	Region	Population size	Case population	Reference population	Confounders adjusted for
Ha *et al*[43]	2010	Case-control	South Korea	*n* = 292 (EE), *n* = 500 (NERD)	Single hospital	Hospital controls	G, E, T, J, OD, WHR, TG
Nam *et al*[44]	2010	Cohort	South Korea	*n* = 495 (EE), *n* = 3779 (normal)	General population	General population	WC , WHR , VAT , SAT
Wang *et al*[46]	2010	Case-control	China	*n* = 70 (EE), *n* = 502 (non-EE)	General population	General population	A, G, S, B, T, E, C, tea drinking, spicy food consumption, betel nut use
Koo *et al*[45]	2009	Case-control	South Korea	*n* = 42 (EE), *n* = 987 (control)	General population	General population	G, T, E, TG ,
Koo *et al*[45]	2009	Case-control	South Korea	*n* = 42 (EE), *n* = 1007 (control)	General population	General population	G, T, E, TG ,
Chua *et al*[47]	2009	Case-control	Taiwan, China	*n* = 427 (EE), *n* = 427 (control)	Single hospital	Hospital controls	TG, Glucose intolerance, HDL-C, SBP
Song *et al*[48]	2009	Case-control	South Korea	*n* = 639 (EE), *n* = 5443 (non-EE)	Single hospital	Hospital controls	A, G, T, E, H, TC, HDL-C, LDL-C, TG, BP, fasting glucose
Lien *et al*[49]	2009	Case-control	Taiwan, China	*n* = 102 (EE), *n* = 1942 (non-EE)	Single hospital	Hospital controls	A, G, J
Lien *et al*[49]	2009	Case-control	Taiwan, China	*n* = 240 (EE), *n* = 1662 (non-EE)	Single hospital	Hospital controls	A, G, J
Nam *et al*[50]	2009	Cohort	South Korea	*n* = 552 (EE), *n* = 8019 (non-EE)	General population	General population	A, WC, E, T
Lee *et al*[51]	2009	Case-control	South Korea	*n* = 100 (EE), *n* = 100 (control)	Single hospital	Hospital controls	WHR, T, J, VAT, SAT, VAT/SAT
Chung *et al*[52]	2008	Case-control	South Korea	*n* = 3539 (EE), *n* = 3539 (control)	Single hospital	Hospital controls	E, T, metabolic syndrome
Zagari *et al*[53]	2008	Cross-sectional	Italy	*n* = 122 (EE), *n* = 911 (non-EE)	General population	General population	A, G, E, T, H, J, C, medication use, peptic ulcer
Lee *et al*[54]	2008	Case-control	South Korea	*n* = 292 (EE), *n* = 2896 (control)	Medical center	Medical center	G, TC, TG, WHR, J, T, OD, PBF
Kim *et al*[42]	2008	Case-control	South Korea	*n* = 1810 (EE), *n* = 20154 (normal)	Multiple hospital	Multiple hospital	G, E, J, H, TC, TG, T, medications for liver/heart disease
Moki *et al*[56]	2007	Case-control	Japan	*n* = 191 (EE), *n* = 4968 (non-EE)	General population	General population	A, G, BP, TG, FBG
Kim *et al*[58]	2007	Case-control	South Korea	*n* = 1090 (EE), *n* = 26229 (non-EE)	Single hospital	Hospital controls	A, G, E, T
Nocon *et al*[55]	2007	Cohort	Germany	*n* = 5289 (EE), *n* = 926 (non-EE)	General population	General population	A, T, E,
Kang *et al*[57]	2007	Cross-sectional	South Korea	*n* = 161 (EE), *n* = 2281 (non-EE)	Single hospital	Hospital controls	A, G, J, T, B, hypertensive drugs, lifestyle choices, abdominal obesity
Labenz *et al*[8]	2004	Cross-sectional	Germany	*n* = 2455 (EE), *n* = 2834 (control)	Medical center	Medical center	A, G, R, S, T, E, B, H, concomitant disease, concomitant medicatons
Nilsson *et al*[12]	2002	Case-control	Sweden	*n* = 179 (EE), *n* = 179 (control)	Multiple hospital	Multiple hospital	T, cholecystectomy, I, drugs use
Wilson *et al*[59]	1999	Case-control	United States	*n* = 189 (EE), *n* = 1024 (control)	Single hospital	Single hospital	A, G, J, R
Stene-Larsen *et al*[4]	1988	Cross-sectional	Sweden	*n* = 195 (EE), *n* = 1029 (control)	Single hospital	Single hospital	None

A: Age; B: Aspirin or NSAID intake; C: Coffee; D: Meal size; E: Alcohol/ethanol; F: Family history; G: Gender; H: *Helicobacter pylori* infection; I: Asthma or asthma medication; J: Hiatal hernia; K: Hospital visit or hospitalization; M: Marital status; O: Symptom checklist-90 score; P: Physical activity; Q: Psychosomatic symptoms; R: Race; S: Socioeconomic status, education; T: Tobacco; W: Right handedness; V: Comorbidity; X: Case control status; Y: Birthplace; Z: Hormone replacement therapy; VAT: Visceral adipose tissue; SAT: Subcutaneous adipose tissue; BP: Blood pressure; SBP: Systolic; DBP: Diastolic blood pressure; TC: Total cholesterol; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; TG: Triglyceride; HbAlc: Hemoglobin Alc; OD: Obesity degree; WHR: Waist-to-hip ratio; WC: Waist circumference; PBF: Percentage of body fat; FBG: Fasting blood glucose; EE: Erosive esophagitis; NERD: Non-erosive reflux disease; NSAID: Nonsteroidal antiinflammatory drugs.

between obesity and EE might have significant implications for counseling.

A recent meta-analysis of BMI and GERD complications found heterogeneous results and it was not able to identify strata with homogeneous results[60]. It was possibly due to their methods of stratification, the utilization of estimates with markedly different measures of BMI association, the absence of studies included in the current analysis, and the inclusion of studies that did not set up a non-GERD control group. In contrast, in the cur-

Table 2 Exposure and outcome definitions

Authors	Yr	Exposure (source)	BMI reference (kg/m^2)	Exposure (definitions)			Outcome (source)	Outcome (definitions)
				BMI overweight (kg/m^2)	BMI obese (kg/m^2)	BMI overweight + obese (kg/m^2)		
Ha *et al*[43]	2010	Measured BMI	≤ 25			≥ 25	Endoscopy	Los Angeles classification
Nam *et al*[44]	2010	Measured BMI	< 20	25-29.9	≥ 30	≥ 25	Endoscopy	Los Angeles classification
Wang *et al*[46]	2010	Measured BMI	< 25	25-30	> 30	≥ 25	Endoscopy	Los Angeles classification
Koo *et al*[45]	2009	Measured BMI	< 23	23-24.9	≥ 25	≥ 23	Endoscopy	Los Angeles classification
Koo *et al*[45]	2009	Measured BMI	< 23	23-24.9	≥ 25	≥ 23	Endoscopy	Los Angeles classification
Chua *et al*[47]	2009	Self-report	< 25		≥ 25	≥ 25	Endoscopy	Los Angeles classification
Song *et al*[48]	2009	Measured BMI			≥ 30		Endoscopy	Los Angeles classification
Lien *et al*[49]	2009	Self-report	< 24	24-26.9	≥ 27	≥ 24	Endoscopy	Modified Savary-Miller endoscopic classification
Lien *et al*[49]	2009	Self-report	< 24	24-26.9	≥ 27	≥ 24	Endoscopy	Modified Savary-Miller endoscopic classification
Nam *et al*[50]	2009	Self-report	< 20	25-29.9	≥ 30	≥ 25	Endoscopy	Los Angeles classification
Lee *et al*[51]	2009	Measured BMI	20-25	25-30	≥ 30	≥ 25	Endoscopy	Los Angeles classification
Chung *et al*[52]	2008	Measured BMI	< 23	23-24.9	≥ 25	≥ 23	Endoscopy	Los Angeles classification
Zagari *et al*[53]	2008	Self-report	20-24.9	25-29.9	≥ 30	≥ 25	Endoscopy	Modified Savary-Miller endoscopic classification
Lee *et al*[54]	2008	Measured BMI	< 20	25-30	> 30	≥ 25	Endoscopy	Los Angeles classification
Kim *et al*[42]	2008	Measured BMI	< 23			≥ 25	Endoscopy	Los Angeles classification
Moki *et al*[56]	2007	Measured BMI	< 25		≥ 25		Endoscopy	Los Angeles classification
Kim *et al*[58]	2007	Measured BMI	18.9-24.5	25-29.9	≥ 30	≥ 25	Endoscopy	Los Angeles classification
Nocon *et al*[55]	2007	Measured BMI		25-30	> 30		Endoscopy	Los Angeles classification
Kang *et al*[57]	2006	Measured BMI	< 25	25-30	> 30	≥ 25	Endoscopy	Los Angeles classification
Labenz *et al*[8]	2004	Measured BMI	< 25	25-30	> 30		Endoscopy	Los Angeles classification
Nilsson *et al*[12]	2002	Self-report	< 25	25-30	> 30	≥ 25	Endoscopy	Modified Savary-Miller endoscopic classification
Wilson *et al*[59]	1999	Measured BMI	< 20	25-30	> 30	≥ 25	Endoscopy	NA
Stene-Larsen *et al*[4]	1988	Measured BMI	< 25	25-28	> 28		Endoscopy	NA

BMI: Body mass index; NA: Not available.

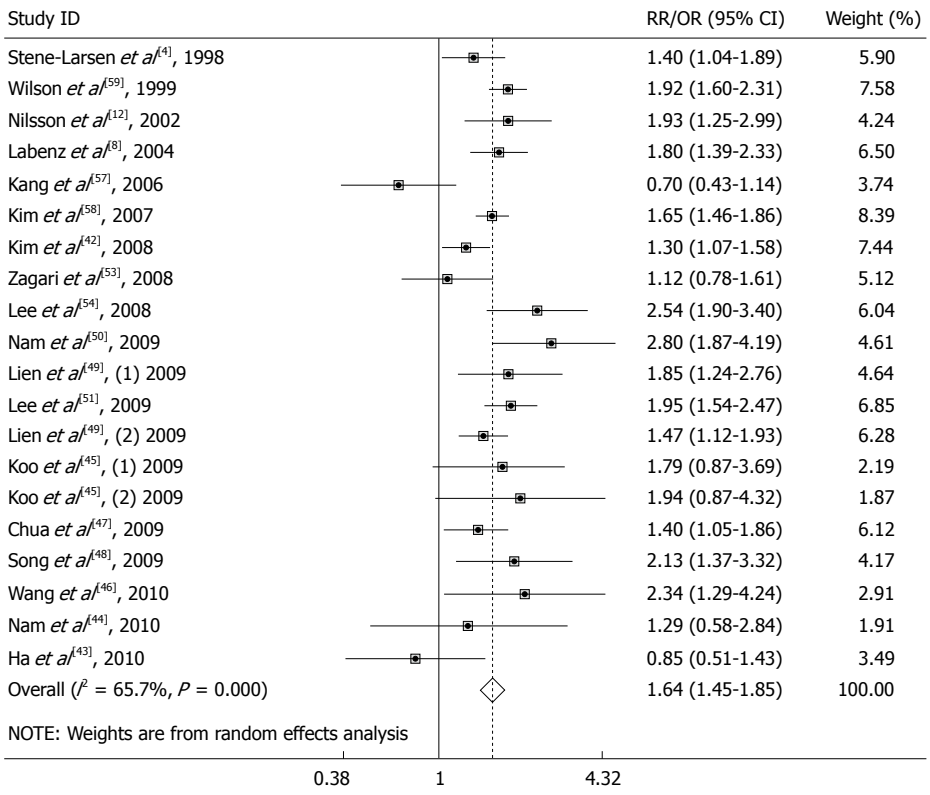

Figure 2 Erosive esophagitis and body mass index (overweight and obese) in males and females. The size of the square represents the weight that the corresponding study exerts in the meta-analysis. RR: Relative risk; OR: Odds ratio.

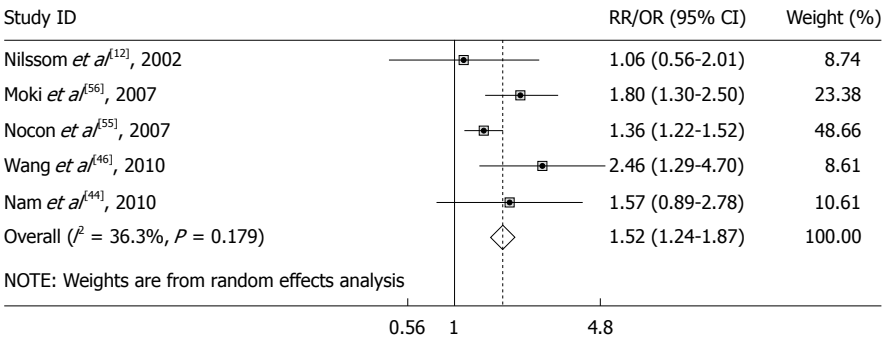

Figure 3 Erosive esophagitis and body mass index (overweight and obese) in males. The size of the square represents the weight that the corresponding study exerts in the meta-analysis. RR: Relative risk; OR: Odds ratio.

Table 3 Meta-analysis results in association between body mass index and erosive esophagitis

BMI category	OR (95% CI)	$P_{homogeneity}$	I^2 (%)	No. of studies
Overall				
Overweight	1.60 (1.35-1.88)	0.003	59.8	12[4,8,12,44,45,50,51,53,54,57-59]
Obese	2.05 (1.65-2.55)	0.000	74.2	15[4,8,12,44-46,50-54,56-59]
Overweight + obese	1.64 (1.45-1.85)	0.000	65.7	18[4,8,12,43-47,49,50-54,56-59]
Females				
Overweight	1.47 (1.15-1.88)	0.011	7.4	3[12,44,55]
Obese	3.76 (0.92-15.28)	0.340	78.0	3[12,44,55]
Overweight + obese	1.45 (1.26-1.66)	0.579	0.0	4[12,44,55,56]
Males				
Overweight	1.40 (1.11-1.75)	0.285	20.8	4[12,44,46,55]
Obese	1.74 (1.02-2.96)	0.099	52.1	4[12,44,46,55]
Overweight + obese	1.52 (1.24-1.87)	0.179	36.3	5[12,44,46,55,56]

BMI: Body mass index; OR: Odds ratio.

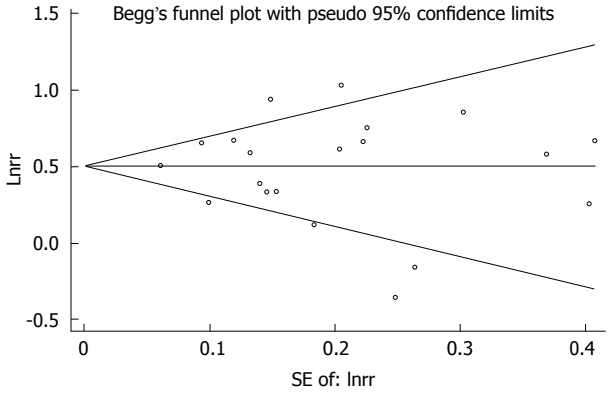

Figure 4 Evaluation of publication bias using a funnel plot. No significant funnel asymmetry was observed which could indicate publication bias. The horizontal line in the funnel plot indicates the random effects summary estimate, while the sloping lines indicate the expected 95% CI for a given standard error, assuming no heterogeneity between studies. Each trial is represented by a circle, the area of which represents the trial's precision. Larger circles represent trials that offer more information.

rent study, after the creation of more categories of BMI among the studies, stratification by gender demonstrated a homogeneous increase in EE with increasing BMI. A study showed a positive correlation between BMI and EE in females, but not in males[12] and a study of reflux patients showed that obese females, but not obese males, had an increased risk of severe esophagitis[55]. The study by Nilsson[12] also found that the association between obesity and EE was further strengthened by the use of oestrogen replacement medication. The prevalence of GERD symptoms as determined in a study investigating a cohort from North America did not differ between males and females[61]. In contrast, in another study, EE was more common in males than in females from Asia[42]. However, in our study, we found a strong positive association between increasing BMI and EE in males, but not in females. This may be because the populations of the included studies were from Asia.

Several hypotheses have been proposed to explain how obesity can cause EE. Abdominal fat may cause reflux through an increase in intrabdominal pressure and subsequent esophageal acid exposure[62,63]. Also, there was a suggestion that hormonal factors related to adiposity are more important than mechanical factors[63]. Obesity is also associated with increased transient lower oesophageal sphincter relaxation[64]. Strengths of this analysis include the use of strict criteria for defining our outcome of interest and the consistency of the BMI-EE association within the males despite different patient populations and different study designs. All the included studies used endoscopy to confirm the diagnosis of EE, which eliminated the possibility of false positive EE cases. Also, we included stratification by study design, location, and source population.

There are potential limitations of this analysis. First, only observational studies were included; study results may be influenced by the presence of measured or unmeasured confounding factors, such as physical activity. Second, bias may also exist in the present study because unpublished data were not included, nor were conference abstracts or articles published in a language other than

English. Third, the exposure definitions (i.e., normal, obese or overweight) differed slightly among the studies. We addressed this, however, by creating more comparable and consistent categories, although few differences still remained. Also, the accuracy of the BMI measurement and its reliability as a measure of adiposity are known to be imperfect.

In summary, based on our extensive review and synthesis of the literature, there appears to be a statistically significant association between elevated BMI and EE. Considering the prevalence of obesity and increasing incidence rates of EE, it is important to pay more attention to further studies that evaluate the influence of gender, ethnicity or age on EE to examine this association. Several studies have found abdominal visceral obesity to be an independent risk factor for EE[44,57]. Nam *et al*[44] demonstrated that association between EE and abdominal visceral adipose tissue volume was consistent among males and females, unlike the association between EE and BMI. However, CT or MRI is needed to test abdominal visceral adipose, which are time consuming and costly. So, measuring BMI may be more feasible. It is also important to determine whether weight loss can decrease the incidence of EE. Further studies are needed to evaluate the relationship between obesity and EE.

COMMENTS

Background

Both obesity and erosive esophagitis (EE) have a high prevalence worldwide. The relationship between them remains controversial.

Research frontiers

Many studies have been performed to evaluate the body mass index (BMI) for gastroesophageal reflux disease risk. It has been found that there was a positive correlation between BMI and EE in females, but not in males.

Innovations and breakthroughs

Findings from this meta-analysis suggested the importance of BMI in EE, especially in males.

Applications

This study provided the potential measurement indicators to identify high-risk groups for EE in obesity population, especially in males.

Terminology

BMI: BMI is a heuristic proxy for human body fat based on an individual's weight and height. It is defined as the individual's body mass divided by the square of his or her height; EE: EE is a term used to indicate any inflammation, swelling, or irritation of the esophagus. The esophagus becomes inflamed (swollen, irritated and red).

Peer review

The meta-analysis presents the data on association between obesity and EE. The topic is interesting and the methodology of the meta-analysis is appropriate.

REFERENCES

1 **Dent J**, El-Serag HB, Wallander MA, Johansson S. Epidemiology of gastro-oesophageal reflux disease: a systematic review. *Gut* 2005; **54**: 710-717
2 **Holtmann G**. Reflux disease: the disorder of the third millennium. *Eur J Gastroenterol Hepatol* 2001; **13** Suppl 1: S5-S11
3 **Kahrilas PJ**. Clinical practice. Gastroesophageal reflux disease. *N Engl J Med* 2008; **359**: 1700-1707
4 **Stene-Larsen G**, Weberg R, Frøyshov Larsen I, Bjørtuft O, Hoel B, Berstad A. Relationship of overweight to hiatus hernia and reflux oesophagitis. *Scand J Gastroenterol* 1988; **23**: 427-432
5 **Pisegna J**, Holtmann G, Howden CW, Katelaris PH, Sharma P, Spechler S, Triadafilopoulos G, Tytgat G. Review article: oesophageal complications and consequences of persistent gastro-oesophageal reflux disease. *Aliment Pharmacol Ther* 2004; **20** Suppl 9: 47-56
6 **Rennie KL**, Jebb SA. Prevalence of obesity in Great Britain. *Obes Rev* 2005; **6**: 11-12
7 **Fujiwara Y**, Higuchi K, Shiba M, Yamamori K, Watanabe Y, Sasaki E, Tominaga K, Watanabe T, Oshitani N, Arakawa T. Differences in clinical characteristics between patients with endoscopy-negative reflux disease and erosive esophagitis in Japan. *Am J Gastroenterol* 2005; **100**: 754-758
8 **Labenz J**, Jaspersen D, Kulig M, Leodolter A, Lind T, Meyer-Sabellek W, Stolte M, Vieth M, Willich S, Malfertheiner P. Risk factors for erosive esophagitis: a multivariate analysis based on the ProGERD study initiative. *Am J Gastroenterol* 2004; **99**: 1652-1656
9 **Butany VJ**, Singh SH, Lal SK. Study of urinary volume and creatinine excretion in women medical students. *Indian J Physiol Pharmacol* 1975; **19**: 193-198
10 **Vainio H**, Bianchini F. Evaluation of cancer-preventive agents and strategies a new program at the International Agency for Research on Cancer. *Ann N Y Acad Sci* 2001; **952**: 177-180
11 **Corley DA**, Kubo A. Body mass index and gastroesophageal reflux disease: a systematic review and meta-analysis. *Am J Gastroenterol* 2006; **101**: 2619-2628
12 **Nilsson M**, Lundegårdh G, Carling L, Ye W, Lagergren J. Body mass and reflux oesophagitis: an oestrogen-dependent association? *Scand J Gastroenterol* 2002; **37**: 626-630
13 **Nandurkar S**, Locke GR, Fett S, Zinsmeister AR, Cameron AJ, Talley NJ. Relationship between body mass index, diet, exercise and gastro-oesophageal reflux symptoms in a community. *Aliment Pharmacol Ther* 2004; **20**: 497-505
14 **Ruigómez A**, García Rodríguez LA, Wallander MA, Johansson S, Graffner H, Dent J. Natural history of gastro-oesophageal reflux disease diagnosed in general practice. *Aliment Pharmacol Ther* 2004; **20**: 751-760
15 **Locke GR**, Talley NJ, Weaver AL, Zinsmeister AR. A new questionnaire for gastroesophageal reflux disease. *Mayo Clin Proc* 1994; **69**: 539-547
16 **Wang JH**, Luo JY, Dong L, Gong J, Tong M. Epidemiology of gastroesophageal reflux disease: a general population-based study in Xi'an of Northwest China. *World J Gastroenterol* 2004; **10**: 1647-1651
17 **Lagergren J**, Bergström R, Nyrén O. No relation between body mass and gastro-oesophageal reflux symptoms in a Swedish population based study. *Gut* 2000; **47**: 26-29
18 **Incarbone R**, Bonavina L, Szachnowicz S, Saino G, Peracchia A. Rising incidence of esophageal adenocarcinoma in Western countries: is it possible to identify a population at risk? *Dis Esophagus* 2000; **13**: 275-278
19 **Inamori M**, Togawa J, Nagase H, Abe Y, Umezawa T, Nakajima A, Saito T, Ueno N, Tanaka K, Sekihara H, Kaifu H, Tsuboi H, Kayama H, Tominaga S, Nagura H. Clinical characteristics of Japanese reflux esophagitis patients as determined by Los Angeles classification. *J Gastroenterol Hepatol* 2003; **18**: 172-176
20 **Savary M**, Miller G. The oesophagus Handbook and atlas of endoscopy. Switzerland: Verlag Gassman AG, 1978
21 **Petitti DB**. Meta-analysis, decision analysis, and cost-effectiveness analysis. 2nd ed. New York: Oxford University Press, 2000
22 **Olkin I**. Re: "A critical look at some popular meta-analytic methods". *Am J Epidemiol* 1994; **140**: 297-299; discussion 300-301

23 **Poole C**, Greenland S. Random-effects meta-analyses are not always conservative. *Am J Epidemiol* 1999; **150**: 469-475
24 **DerSimonian R**, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986; **7**: 177-188
25 **Chalmers TC**, Celano P, Sacks HS, Smith H. Bias in treatment assignment in controlled clinical trials. *N Engl J Med* 1983; **309**: 1358-1361
26 **Jadad AR**, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, McQuay HJ. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Control Clin Trials* 1996; **17**: 1-12
27 **Schulz KF**, Chalmers I, Hayes RJ, Altman DG. Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *JAMA* 1995; **273**: 408-412
28 **Schulz KF**, Chalmers I, Grimes DA, Altman DG. Assessing the quality of randomization from reports of controlled trials published in obstetrics and gynecology journals. *JAMA* 1994; **272**: 125-128
29 **Imperiale TF**. Meta-analysis: when and how. *Hepatology* 1999; **29**: 26S-31S
30 **Gerbarg ZB**, Horwitz RI. Resolving conflicting clinical trials: guidelines for meta-analysis. *J Clin Epidemiol* 1988; **41**: 503-509
31 **Kleinbaum DG**, Kupper LL, Morgenstern H. Epidemiologic research: Principles and quantitative methods. New York: John Wiley and Sons, 1982
32 **Banki F**, Demeester SR, Mason RJ, Campos G, Hagen JA, Peters JH, Bremner CG, Demeester TR. Barrett's esophagus in females: a comparative analysis of risk factors in females and males. *Am J Gastroenterol* 2005; **100**: 560-567
33 **Gunji T**, Sato H, Iijima K, Fujibayashi K, Okumura M, Sasabe N, Urabe A, Matsuhashi N. Risk factors for erosive esophagitis: a cross-sectional study of a large number of Japanese males. *J Gastroenterol* 2011; **46**: 448-455
34 **Patel NR**, Ward MJ, Beneck D, Cunningham-Rundles S, Moon A. The Association between Childhood Overweight and Reflux Esophagitis. *J Obes* 2010; **2010**: 136909
35 **Tai CM**, Lee YC, Tu HP, Huang CK, Wu MT, Chang CY, Lee CT, Wu MS, Lin JT, Wang WM. The relationship between visceral adiposity and the risk of erosive esophagitis in severely obese Chinese patients. *Obesity* (Silver Spring) 2010; **18**: 2165-2169
36 **Yasuhara H**, Miyake Y, Toyokawa T, Matsumoto K, Takahara M, Imada T, Yagi S, Miyatake H, Nakatsu M, Ando M, Hirohata M. Large waist circumference is a risk factor for reflux esophagitis in Japanese males. *Digestion* 2010; **81**: 181-187
37 **Elitsur Y**, Dementieva Y, Elitsur R, Rewalt M. Obesity is not a risk factor in children with reflux esophagitis: a retrospective analysis of 738 children. *Metab Syndr Relat Disord* 2009; **7**: 211-214
38 **Nozu T**, Komiyama H. Clinical characteristics of asymptomatic esophagitis. *J Gastroenterol* 2008; **43**: 27-31
39 **Lee SJ**, Song CW, Jeen YT, Chun HJ, Lee HS, Um SH, Lee SW, Choi JH, Kim CD, Ryu HS, Hyun JH. Prevalence of endoscopic reflux esophagitis among Koreans. *J Gastroenterol Hepatol* 2001; **16**: 373-376
40 **Chang CS**, Poon SK, Lien HC, Chen GH. The incidence of reflux esophagitis among the Chinese. *Am J Gastroenterol* 1997; **92**: 668-671
41 **Furukawa N**, Iwakiri R, Koyama T, Okamoto K, Yoshida T, Kashiwagi Y, Ohyama T, Noda T, Sakata H, Fujimoto K. Proportion of reflux esophagitis in 6010 Japanese adults: prospective evaluation by endoscopy. *J Gastroenterol* 1999; **34**: 441-444
42 **Kim N**, Lee SW, Cho SI, Park CG, Yang CH, Kim HS, Rew JS, Moon JS, Kim S, Park SH, Jung HC, Chung IS. The prevalence of and risk factors for erosive oesophagitis and non-erosive reflux disease: a nationwide multicentre prospective study in Korea. *Aliment Pharmacol Ther* 2008; **27**: 173-185
43 **Ha NR**, Lee HL, Lee OY, Yoon BC, Choi HS, Hahm JS, Ahn YH, Koh DH. Differences in clinical characteristics between patients with non-erosive reflux disease and erosive esophagitis in Korea. *J Korean Med Sci* 2010; **25**: 1318-1322
44 **Nam SY**, Choi IJ, Ryu KH, Park BJ, Kim HB, Nam BH. Abdominal visceral adipose tissue volume is associated with increased risk of erosive esophagitis in men and women. *Gastroenterology* 2010; **139**: 1902-1911.e2
45 **Koo JS**, Lee SW, Park SM, Jung SW, Yim HJ, Park JJ, Chun HJ, Lee HS, Choi JH, Kim CD, Ryu HS. Abdominal obesity as a risk factor for the development of erosive esophagitis in subjects with a normal esophago-gastric junction. *Gut Liver* 2009; **3**: 276-284
46 **Wang FW**, Tu MS, Chuang HY, Yu HC, Cheng LC, Hsu PI. Erosive esophagitis in asymptomatic subjects: risk factors. *Dig Dis Sci* 2010; **55**: 1320-1324
47 **Chua CS**, Lin YM, Yu FC, Hsu YH, Chen JH, Yang KC, Shih CH. Metabolic risk factors associated with erosive esophagitis. *J Gastroenterol Hepatol* 2009; **24**: 1375-1379
48 **Song HJ**, Shim KN, Yoon SJ, Kim SE, Oh HJ, Ryu KH, Ha CY, Yeom HJ, Song JH, Jung SA, Yoo K. The prevalence and clinical characteristics of reflux esophagitis in koreans and its possible relation to metabolic syndrome. *J Korean Med Sci* 2009; **24**: 197-202
49 **Lien HC**, Chang CS, Yeh HZ, Ko CW, Chang HY, Cheng KF, Sung FC. Increasing prevalence of erosive esophagitis among Taiwanese aged 40 years and above: a comparison between two time periods. *J Clin Gastroenterol* 2009; **43**: 926-932
50 **Nam SY**, Choi IJ, Nam BH, Park KW, Kim CG. Obesity and weight gain as risk factors for erosive oesophagitis in men. *Aliment Pharmacol Ther* 2009; **29**: 1042-1052
51 **Lee HL**, Eun CS, Lee OY, Jeon YC, Han DS, Yoon BC, Choi HS, Hahm JS, Ahn YH, Song SY. Association between erosive esophagitis and visceral fat accumulation quantified by abdominal CT scan. *J Clin Gastroenterol* 2009; **43**: 240-243
52 **Chung SJ**, Kim D, Park MJ, Kim YS, Kim JS, Jung HC, Song IS. Metabolic syndrome and visceral obesity as risk factors for reflux oesophagitis: a cross-sectional case-control study of 7078 Koreans undergoing health check-ups. *Gut* 2008; **57**: 1360-1365
53 **Zagari RM**, Fuccio L, Wallander MA, Johansson S, Fiocca R, Casanova S, Farahmand BY, Winchester CC, Roda E, Bazzoli F. Gastro-oesophageal reflux symptoms, oesophagitis and Barrett's oesophagus in the general population: the Loiano-Monghidoro study. *Gut* 2008; **57**: 1354-1359
54 **Lee HL**, Eun CS, Lee OY, Jeon YC, Sohn JH, Han DS, Yoon BC, Choi HS, Hahm JS, Lee MH, Lee DH. Association between GERD-related erosive esophagitis and obesity. *J Clin Gastroenterol* 2008; **42**: 672-675
55 **Nocon M**, Labenz J, Jaspersen D, Meyer-Sabellek W, Stolte M, Lind T, Malfertheiner P, Willich SN. Association of body mass index with heartburn, regurgitation and esophagitis: results of the Progression of Gastroesophageal Reflux Disease study. *J Gastroenterol Hepatol* 2007; **22**: 1728-1731
56 **Moki F**, Kusano M, Mizuide M, Shimoyama Y, Kawamura O, Takagi H, Imai T, Mori M. Association between reflux oesophagitis and features of the metabolic syndrome in Japan. *Aliment Pharmacol Ther* 2007; **26**: 1069-1075
57 **Kang MS**, Park DI, Oh SY, Yoo TW, Ryu SH, Park JH, Kim HJ, Cho YK, Sohn CI, Jeon WK, Kim BI. Abdominal obesity is an independent risk factor for erosive esophagitis in a Korean population. *J Gastroenterol Hepatol* 2007; **22**: 1656-1661
58 **Kim HJ**, Yoo TW, Park DI, Park JH, Cho YK, Sohn CI, Jeon WK, Kim BI. Influence of overweight and obesity on upper endoscopic findings. *J Gastroenterol Hepatol* 2007; **22**: 477-481
59 **Wilson LJ**, Ma W, Hirschowitz BI. Association of obesity

with hiatal hernia and esophagitis. *Am J Gastroenterol* 1999; **94**: 2840-2844
60 **Hampel H**, Abraham NS, El-Serag HB. Meta-analysis: obesity and the risk for gastroesophageal reflux disease and its complications. *Ann Intern Med* 2005; **143**: 199-211
61 **Locke GR**, Talley NJ, Fett SL, Zinsmeister AR, Melton LJ. Prevalence and clinical spectrum of gastroesophageal reflux: a population-based study in Olmsted County, Minnesota. *Gastroenterology* 1997; **112**: 1448-1456
62 **El-Serag HB**, Ergun GA, Pandolfino J, Fitzgerald S, Tran T, Kramer JR. Obesity increases oesophageal acid exposure. *Gut* 2007; **56**: 749-755
63 **El-Serag HB**, Tran T, Richardson P, Ergun G. Anthropometric correlates of intragastric pressure. *Scand J Gastroenterol* 2006; **41**: 887-891
64 **Wu JC**, Mui LM, Cheung CM, Chan Y, Sung JJ. Obesity is associated with increased transient lower esophageal sphincter relaxation. *Gastroenterology* 2007; **132**: 883-889

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