HHS Public Access

Author manuscript

Clin Gastroenterol Hepatol. Author manuscript; available in PMC 2024 January 01.

Published in final edited form as:

Clin Gastroenterol Hepatol. 2023 January ; 21(1): 64–71. doi:10.1016/j.cgh.2022.04.033.

Inverse association between gluteofemoral obesity and risk of non-cardia gastric intestinal metaplasia

Andre G. Jove[1], **Hudson M. Holmes**[1], **Mimi C. Tan**[2], **Hashem B. El-Serag**[2,3], **Aaron P. Thrift**[4,5]

[1]Department of Medicine, Baylor College of Medicine, Houston, Texas, USA

[2]Section of Gastroenterology and Hepatology, Department of Medicine, Baylor College of Medicine, Houston, Texas, USA

[3]Houston VA HSR&D Center for Innovations in Quality, Effectiveness and Safety, Michael E. DeBakey Veterans Affairs Medical Center, Houston, Texas, USA

[4]Section of Epidemiology and Population Sciences, Department of Medicine, Baylor College of Medicine, Houston, Texas, USA

[5]Dan L Duncan Comprehensive Cancer Center, Baylor College of Medicine, Houston, Texas, USA

Abstract

Background & Aims: It is unclear whether obesity confers increased risk of non-cardia gastric adenocarcinoma and its precursor, gastric intestinal metaplasia. Here, we examined whether various dimensions of adiposity independently predispose to the development of non-cardia gastric intestinal metaplasia.

Methods: We compared data from 409 non-cardia gastric intestinal metaplasia cases and 1748 controls without any gastric intestinal metaplasia from a cross-sectional study at the VA Medical Center in Houston, Texas. Participants completed standardized questionnaires, underwent anthropometric measurements, and underwent a study endoscopy with gastric mapping biopsies. Non-cardia gastric intestinal metaplasia cases included participants with intestinal metaplasia on any non-cardia gastric biopsy. We calculated odds ratios (OR) and 95% confidence intervals (95% CI) using logistic regression models.

Results: Increasing body mass index (BMI) was not associated with risk of non-cardia gastric intestinal metaplasia (per unit BMI adjusted OR, 0.98; 95% CI, 0.96–1.00). Similarly, we found no associations with increase in waist circumference (per 10 cm increase adjusted OR, 0.94;

Correspondence: Aaron P. Thrift, Ph.D., Baylor College of Medicine, One Baylor Plaza, MS: BCM307, Room 621D, Houston, TX 77030-3498. aaron.thrift@bcm.edu.

Author contributions: Conception and design: APT. Patient recruitment and acquisition of the data: MCT and HES. Data preparation and analysis: MCT, APT. Interpretation of the data: AGJ, HMH, MCT, HES and APT. Manuscript preparation and review: AGJ, HMH, MCT, HES and APT. All authors read and approved the final version for submission.

Conflicts of interest: The authors report no competing interests for this publication.

95% CI, 0.87–1.03) and waist-to-hip ratio (WHR) (per unit WHR adjusted OR, 2.34; 95% CI, 0.37–14.7). However, there was a significant inverse association with gastric intestinal metaplasia and increasing hip circumference, reflecting gluteofemoral obesity (per 10 cm increase adjusted OR, 0.89; 95% CI, 0.80–0.98). The inverse association was observed for both extensive and focal gastric intestinal metaplasia.

Conclusions: The independent dimensions of adiposity (BMI, waist circumference) are not associated with increased risk of non-cardia gastric intestinal metaplasia. The inverse association between gluteofemoral obesity and risk of gastric intestinal metaplasia warrants additional study.

Keywords

gastric intestinal metaplasia; obesity; gluteofemoral obesity; gastric cancer; risk factors; epidemiology; *Helicobacter pylori*

INTRODUCTION

Gastric cancer is the 5th most common neoplasm and 3rd most common cause of cancer death worldwide[1]. Non-cardia gastric adenocarcinoma generally arises from a continuum from superficial gastritis, chronic atrophic gastritis, gastric intestinal metaplasia to dysplasia (i.e., intraepithelial neoplasia) and cancer[2]. Among the precancerous lesions, gastric intestinal metaplasia appears with a prevalence of 3–19% in Western populations[3–5]. Non-cardia gastric intestinal metaplasia is strongly associated with *H. pylori* infection[6], whereas cardia gastric intestinal metaplasia has been associated with esophageal adenocarcinoma risk factors, such as gastroesophageal reflux[7–9]. However, complete examination, especially in Western populations, of the modifiable risk factors for gastric intestinal metaplasia remains to be achieved.

Obesity has demonstrated heterogeneity among studies in its association with overall risk of gastric cancer[10]. This discrepancy may be accounted for by the differential influence of obesity on tumor location, as well as obesity measurement and distribution (i.e., overall obesity measured by body mass index [BMI] or abdominal obesity). While cardia gastric adenocarcinoma is frequently associated with obesity[11–13], the association between non-cardia gastric adenocarcinoma and obesity remains controversial. Although Levi et al. in a recent cohort study reports a positive association between obesity and non-cardia gastric adenocarcinoma[14], similar studies have found no association[11–13]. Additionally, it remains unclear whether overall obesity (i.e., BMI ≥30 kg/m^2) independently influences the development of gastric adenocarcinoma or whether associations may better be depicted by other adiposity-related dimensions (i.e., waist circumference, hip circumference, and waist-to-hip ratio [WHR]). These anthropometric measures of adiposity have been reported to significantly increase obesity-related outcomes independently of BMI[15]. Therefore, BMI measured overall obesity may not be the most significant indicator of gastric cardia adenocarcinoma risk.

Whether obesity confers increased risk of gastric cancer precursor lesions remains unclear. Kim et al. in their recent retrospective cohort study of 142,832 Korean adults reported a dose-response relationship between BMI and the risk of new-onset gastric

intestinal metaplasia[16]. Associations between BMI defined overall obesity and increased risk of atrophic gastritis[16] and gastric dysplasia[17,18] have also been reported from Asian populations. However, data are largely absent for United States populations, and few studies, regardless of geographic region, have comprehensively assessed the independent contributions of each obesity-related dimension to determine which, if any, are associated with gastric intestinal metaplasia risk.

We therefore explored the relationship of multiple dimensions of adiposity (BMI, waist circumference, hip circumference, and WHR) on the risk of non-cardia gastric intestinal metaplasia. Specifically, we sought to quantify the independent associations between dimensions of obesity and dose-response patterns and the risk of non-cardia gastric intestinal metaplasia and to examine potential effect modifiers of these associations.

METHODS

Study Population

Data for the current analysis are from a cross-sectional study conducted at the Michael E. DeBakey Veterans Affairs Medical Center (MEDVAMC) in Houston, Texas, the details of which have been reported in full elsewhere[19]. Study participants were recruited from two sources: (1) among consecutive eligible patients undergoing an elective esophagogastroduodenoscopy (EGD) for any indication; and (2) among consecutive patients attending one of seven selected primary care clinics. The primary care patients were eligible for a routine (i.e., average risk) colon cancer screening colonoscopy and invited to participate in our study, which required them to undergo the study EGD at the same time as their colonoscopy. None of the primary care patients were primarily referred for EGD and none were approached during a time of a pre-scheduled colonoscopy. These two groups represent the source population for gastric intestinal metaplasia cases at the MEDVAMC. The eligibility criteria were: (1) age 50–80 years (40–80 years for the elective EGD group); (2) no previous gastroesophageal surgery; (3) no previous gastroesophageal cancer; (4) no active lung, liver, colon, breast or stomach cancer; (5) no current anticoagulants; (6) no significant liver disease indicated by platelet count below 70,000, ascites, or known gastroesophageal varices; and (7) no history of major stroke or mental condition. The study obtained approval from the Institutional Review Boards for MEDVAMC and Baylor College of Medicine.

A study EGD was performed on all participants with at least 10 biopsies taken (2 biopsies each from 5–7 biopsy sites according to adoption of the Sydney System at the time of study EGD) from the antrum (both greater and lesser curvature), corpus (proximal greater curvature, proximal lesser curvature, with optional additional biopsies at distal greater curvature and distal lesser curvature), and cardia. Endoscopic findings from the upper endoscopy were systematically recorded. Biopsy specimens were embedded in paraffin, oriented on edge, sectioned in 5-sections, and stained with hematoxylin and eosin, alcian blue at pH 2.5; and in case of negative staining for *H. pylori*, a modified silver stain; and alcian blue–periodic acid Schiff stain. Two gastrointestinal pathologists, blinded to endoscopic findings and patient survey data, independently assessed presence and severity of gastric intestinal metaplasia on each specimen. Disagreements were resolved by a third

pathologist. We defined cases as those with evidence of intestinal metaplasia on ≥1 *non-cardia* gastric biopsy, and compared cases to controls without gastric intestinal metaplasia on any of their gastric biopsies. We also stratified the gastric intestinal metaplasia cases according to severity as focal (limited to either antrum or corpus) or extensive (involving both antrum and corpus) using the Operative Link for Gastric Intestinal Metaplasia Assessment criteria and, in a secondary analysis, compared these 2 subgroups of cases separately to controls without gastric intestinal metaplasia. Overall, 70% of patients in the EGD group and 43% of eligible patients in the primary care group underwent the study EGD and completed the survey.

Patients were considered to *have H. pylori* infection if *H. pylori* organisms were found on histopathology of ≥1 gastric biopsy site (using hematoxylin and eosin, alcian blue at pH 2.5, a modified silver stain, or alcian blue–periodic acid Schiff stain) or isolated on gastric tissue culture. To process cultures for *H. pylori*, frozen tissue specimens were thawed, homogenized, and inoculated onto two types of selective media: (1) Brain Heart Infusion (nutrient rich agar ideal for culturing fastidious microorganisms) and (2) *H. pylori* Special Peptone Agar plates with 7% horse blood. The plates were incubated at 37°C under micro-aerophilic conditions (5% O2, 10% CO2, and 85% N2) in an Anoxomat jar for up to two weeks. Positive growth was transferred to a fresh, nonselective Brain Heart Infusion blood agar plate and incubated for 48–72 hours. *H. pylori* status was identified when the oxidase, catalase, and urease reactions were positive with a compatible Gram stain.

Data Collection

Surveys—Prior to the study EGD, participants were asked to complete the study survey with assistance from trained research assistants. The survey acquired information about age, sex, race/ethnicity, use of alcohol and smoking, medical history, and use of medications.

Anthropometric measurements—We measured participant body weight in bare feet using a digital upright scale (Health o meter® Professional) designated for our study. Height in inches was also obtained using a study designated stadiometer, and was entered directly into the scale for calculation of BMI using the Quetlet index formula weight in pounds × 703/squared height in inches. A flexible tape measure was used to obtain waist circumference rounded down to nearest half inch at umbilicus level at the narrowest part of the waist. Hip circumference was measured over the participant's right side at greatest buttock protrusion. WHR was calculated as the ratio of waist circumference divided by hip circumference. All research staff was trained to systematically perform and record anthropometric measurements. BMI was categorized as normal (<25), overweight (25-<30), and obese (≥30) according to the World Health Organization. The high WHR cutoff was considered ≥0.9 for males and ≥0.85 for females. Waist circumference and hip circumference were categorized using the quartiles among the controls.

Statistical Analysis

The characteristics of cases with intestinal metaplasia and controls were compared using chi-square tests for categorical variables and t-tests for continuous variables. We estimated odds ratios (OR) and 95% confidence intervals (95% CI) for associations of anthropometric

measures with risk of gastric intestinal metaplasia using unconditional logistic regression. Terms for potential confounders were retained in the final models if they changed the risk estimate or improved the fit of the models. We first examined associations with anthropometric measures adjusted for confounders, including age (years), sex, race/ethnicity, smoking status, and *H. pylori* infection. To more precisely measure the effect of visceral and gluteofemoral (subcutaneous) adipose tissue, and to estimate whether abdominal obesity is associated with gastric intestinal metaplasia beyond the association with general obesity, we fit multivariable models with mutual adjustment. That is, we present results for BMI adjusted for WHR, waist circumference adjusted for BMI, waist circumference adjusted for hip circumference, hip circumference adjusted for waist circumference, and WHR adjusted for BMI.

All analyses were conducted using Stata 13.0 (StataCorp LP, College Station, TX) and all tests for statistical significance two-sided at $\alpha = 0.05$.

RESULTS

This study used data from 409 cases with non-cardia gastric intestinal metaplasia and 1748 controls without gastric intestinal metaplasia. The distributions of study participant characteristics are displayed in Table 1. Of the participants, 92.1% were male; however, cases were more likely than controls to be male (97.3% vs 90.9%). Cases were older on average than controls but had a lower proportion of Whites (40.6% vs. 61.1%). As expected, non-cardia gastric intestinal metaplasia cases were more likely than controls to have a positive *H. pylori* infection status (52.7% vs. 22.3%). Cases were also more likely to be a current or former smoker than controls (80.5% vs. 70.9%).

Table 2 shows the associations between dimensions of obesity and risk of non-cardia gastric intestinal metaplasia both unadjusted and adjusted for other known risk factors (i.e., age, sex, race/ethnicity, smoking, and *H. pylori*). In the multivariate model, we found no association between increasing BMI, waist circumference or WHR with risk of gastric intestinal metaplasia. Conversely, an increasing hip circumference was associated with lower risk for gastric intestinal metaplasia. For every 10cm increase in hip circumference, risk for gastric intestinal metaplasia decreased by 11% (adjusted OR, 0.89; 95% CI, 0.80–0.98). When examined as quartiles, there was a trend among those in the highest quartile of hip circumference to have 23% lower risk of gastric intestinal metaplasia compared to those in the lowest quartile (Q4 vs. Q1 adjusted OR, 0.77; 95% CI, 0.55–1.07).

Table 3 shows the independent associations of non-cardia gastric intestinal metaplasia and obesity-related variables while mutually adjusting for other obesity-related variables. The significant inverse association of hip circumference with risk of gastric intestinal metaplasia persisted following adjustment for waist circumference. For every 10cm increase in hip circumference, there was a 21% decrease in gastric intestinal metaplasia risk (adjusted OR, 0.79; 95% CI, 0.65–0.97).

Among the 409 gastric intestinal metaplasia cases, we classified 299 as having focal disease and 110 as having extensive disease. In secondary analyses, we observed similar findings

to the overall cases vs. controls analysis such that increasing BMI, waist circumference and WHR were not associated with increased risks for extensive or focal gastric intestinal metaplasia. The point estimate for the inverse association with increasing hip circumference was no different for risk of extensive gastric intestinal metaplasia and risk of focal gastric intestinal metaplasia (Table 4).

DISCUSSION

In the present large cross-sectional study, neither overall BMI measured obesity nor abdominal obesity measured by waist circumference were associated with risk of non-cardia gastric intestinal metaplasia. Interestingly, we report new evidence of an inverse relationship between increasing hip circumference and risk of gastric intestinal metaplasia.

Non-cardia gastric intestinal metaplasia is an established precursor state in the stepwise pathogenesis of gastric non-cardia adenocarcinoma[2]. Additionally, *H. pylori* infection is a significant predisposing risk factor in the development of this subtype of gastric cancer, which has also been associated with an elevated consumption of alcohol and tobacco products[20,21]. These main risk factors have been associated, although less consistently, with an increased risk of non-cardia gastric intestinal metaplasia and have demonstrated a high correlation with malnourishment[10,22]. Therefore, since obesity has not been consistently identified as a risk factor in the development of gastric non-cardia adenocarcinoma, it may be perceived that true risk factors align with lower BMI categories. We offer a similar explanation for the lack of risk modification in the context of non-cardia gastric intestinal metaplasia.

While BMI-associated categorizations are commonly employed as the primary measure of adiposity, they do not accurately discern body composition and, thus, cannot discriminate between adiposity and elevated muscle or skeletal mass. Additionally, BMI-based categorizations have demonstrated unreliability or biased predictions of adiposity in certain populations[23–26]. Accurate measures of abdominal obesity are associated with higher prevalence and detection of disease (i.e., cardiovascular disease)[27]. WHR has performed similarly to BMI as anthropometric measure of abdominal obesity and is a less consistent predictor of abdominal obesity[28]. Conversely, waist circumference as an independent anthropometric measure that has been most correlated with abdominal adiposity[28]. Nevertheless, similar to BMI, we did not find independent associations between waist circumference and WHR with risk of non-cardia gastric intestinal metaplasia.

Our study presents a significant inverse association between gluteofemoral obesity as measured by hip circumference and non-cardia gastric intestinal metaplasia. Gluteofemoral obesity refers to adiposity localized to the hips and thighs and may be recorded as an anthropometric dimension of body composition[29]. While abdominal obesity has been linked to a diversity of negative health outcomes including cardiovascular disease[30], diabetes mellitus[30], and cancer[15], gluteofemoral obesity has been reported to have an inverse association with cardiovascular disease[31] and diabetes mellitus[31] upon adjustments for abdominal obesity. Comparably, gluteofemoral obesity has been reported to have an inverse association with Barrett's esophagus and erosive esophagitis after adjustment for

abdominal obesity[32,33]. The mechanism of the conferred protection against non-cardia gastric intestinal metaplasia is unclear and may result from differential serum quantities of proinflammatory cytokines[31,32]. Adipose tissue localized to the gluteofemoral region secretes less inflammatory adipokines than visceral adiposity, and as an adipose storage compartment, may avoid the inflammatory and various humoral effects derived from abdominal adiposity[31]. Furthermore, gluteofemoral obesity demonstrates a positive or favorable association with insulin sensitivity and elevated adiponectin levels, which reduce morbidity, whereas abdominal obesity predisposes to insulin resistance and reduced adiponectin levels[34,35].

Our study demonstrates a number of notable strengths in the analysis, including a large sample size, well-delineated groups of cases and controls, the extensive systemic sampling of the gastric mucosa, the collection of information on a broad spectrum of potential confounders and the systematic set of detailed measures of obesity-related dimensions. We used common and comprehensive measures of abdominal and gluteofemoral obesity to ensure adequate coverage of obesity as an exposure. Finally, it is unlikely for our results to be clarified by differential reporting as we collected the questionnaire data prior to the study EGD (prior to defining case and control status) to minimize the probability of biased recall.

The present study has a few important limitations. First, considering that most participants in our VA-based study were white men and the general characteristics of VA and non-VA populations may vary, our results may not be accurately generalized to women or the general non-VA population. Second, the cross-sectional design of the study precludes any formation of causal inferences from the results. However, the study design should not minimize the significance of the observed association or absence of associations. Third, we were incapable of acquiring information from invited patients who refused participation in the study since they did not consent to participation in a research study. Nevertheless, the sex and racial distribution in our cohort was illustrative of the racial distribution overall in the MEDVAMC, which conveys minimal selection bias. Fourth, our results were limited by only selecting histological samples of non-cardia gastric intestinal metaplasia as being positives. Lastly the focus of this study on non-cardia gastric intestinal metaplasia and therefore we did not employ stratification and analysis of data (gastric cardia versus gastric non-cardia). Adding cardia intestinal metaplasia would have required an addition effort of distinguishing the cardia site from gastroesophageal junction and short segments of Barrett’s esophagus; these are outside the scope of this analysis.

In summary, we revealed that differential distribution of obesity may significantly influence the predisposition for non-cardia gastric intestinal metaplasia. While parameters of abdominal obesity demonstrated an absence of an association with non-cardia gastric intestinal metaplasia, we found increasing gluteofemoral obesity to confer protection against non-cardia gastric intestinal metaplasia. Although obesity has been reported to be associated with an elevated risk of gastric cancer, commonly used clinical anthropometric measures (i.e., BMI and WHR) should not be used to risk stratify patients for their risk of gastric intestinal metaplasia and hence for gastric cancer screening. On the other hand, the novel finding of an inverse association with hip circumference (gluteofemoral obesity) should be further examined for incorporation into clinically applicable risk stratification scores.

However, additional studies are needed to confirm this observation of an inverse association and then, if needed, to elucidate the protective mechanism of gluteofemoral obesity on non-cardia gastric intestinal metaplasia.

Grant support:

This work was supported in part by National Institutes of Health grant P30 DK056338 (Study Design and Clinical Research Core), which supports the Texas Medical Center Digestive Diseases Center. This research was supported in part with resources at the VA HSR&D Center for Innovations in Quality, Effectiveness and Safety (#CIN 13-413), at the Michael E. DeBakey VA Medical Center, Houston, TX. The opinions expressed reflect those of the authors and not necessarily those of the Department of Veterans Affairs, the U.S. government or Baylor College of Medicine.

REFERENCES

1. Bray F et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA. Cancer J. Clin (2018) doi:10.3322/caac.21492.
2. Correa P et al. Gastric Precancerous Process in a High Risk Population: Cross-sectional Studies. Cancer Res. (1990).
3. Sonnenberg A, Lash RH & Genta RM A national study of helicobactor pylori infection in gastric biopsy specimens. Gastroenterology (2010) doi:10.1053/j.gastro.2010.08.018.
4. Simko V, Anand N & Ginter E Gastric intestinal metaplasia - age, ethnicity and surveillance for gastric cancer. Bratislava Med. J (2015) doi:10.4149/BLL_2015_001.
5. Eriksson NK, Kärkkäinen PA, Färkkilä MA & Arkkila PET Prevalence and distribution of gastric intestinal metaplasia and its subtypes. Dig. Liver Dis (2008) doi:10.1016/j.dld.2007.12.012.
6. Kumar S, Metz DC, Kaplan DE & Goldberg DS Seroprevalence of H. pylori Infection in a National Cohort of Veterans With Non-Cardia Gastric Adenocarcinoma. Clin. Gastroenterol. Hepatol (2019) doi:10.1016/j.cgh.2019.07.026.
7. Correa P, Piazuelo MB & Wilson KT Pathology of gastric intestinal metaplasia: Clinical implications. American Journal of Gastroenterology (2010) doi:10.1038/ajg.2009.728.
8. Hackelsberger A et al. Intestinal metaplasia at the gastro-oesophageal junction: Helicobacter pylori gastritis or gastro-oesophageal reflux disease? Gut (1998) doi:10.1136/gut.43.1.17.
9. Öberg S et al. Inflammation and specialized intestinal metaplasia of cardiac mucosa is a manifestation of gastroesophageal reflux disease. Ann. Surg (1997) doi:10.1097/00000658-199710000-00013.
10. Chen Y et al. Body mass index and risk of gastric cancer:ameta-analysis of a population with more than ten million from 24 prospective studies. Cancer Epidemiol. Biomarkers Prev (2013) doi:10.1158/1055-9965.EPI-13-0042.
11. Chow WH et al. Body mass index and risk of adenocarcinomas of the esophagus and gastric cardia. J. Natl. Cancer Inst (1998) doi:10.1093/jnci/90.2.150.
12. MacInnis RJ, English DR, Hopper JL & Giles GG Body size and composition and the risk of gastric and oesophageal adenocarcinoma. Int. J. Cancer (2006) doi:10.1002/ijc.21638.
13. Lindblad M, Rodríguez LAG & Lagergren J Body mass, tobacco and alcohol and risk of esophageal, gastric cardia, and gastric non-cardia adenocarcinoma among men and women in a nested case-control study. Cancer Causes Control (2005) doi:10.1007/s10552-004-3485-7.
14. Levi Z et al. Body mass index at adolescence and risk of noncardia gastric cancer in a cohort of 1.79 million men and women. Cancer (2018) doi:10.1002/cncr.31049.
15. Zhang C, Rexrode KM, Van Dam RM, Li TY & Hu FB Abdominal obesity and the risk of all-cause, cardiovascular, and cancer mortality: Sixteen years of follow-up in US women. Circulation (2008) doi:10.1161/CIRCULATIONAHA.107.739714.
16. Kim K et al. Body mass index and risk of intestinal metaplasia: A cohort study. Cancer Epidemiol. Biomarkers Prev 28, 789–797 (2019). [PubMed: 30700447]
17. Kim HY Metabolic syndrome is associated with gastric dysplasia. Eur. J. Gastroenterol. Hepatol (2011) doi:10.1097/MEG.0b013e328349aa18.

18. Kim HJ et al. Relationship between body mass index and the risk of early gastric cancer and dysplasia regardless of Helicobacter pylori infection. Gastric Cancer (2015) doi:10.1007/s10120-014-0429-0.
19. Fischbach LA et al. Association between Helicobacter pylori and Barrett's Esophagus: A case-control study. Am. J. Gastroenterol (2014) doi:10.1038/ajg.2013.443.
20. Tramacere I et al. A meta-analysis on alcohol drinking and gastric cancer risk. Annals of Oncology (2012) doi:10.1093/annonc/mdr135.
21. Trédaniel J, Boffetta P, Buiatti E, Saracci R & Hirsch A Tobacco smoking and gastric cancer: Review and meta-analysis. Int. J. Cancer (1997) doi:10.1002/(SICI)1097-0215(19970807)72:4<565::AID-IJC3>3.0.CO;2-O.
22. Wu MS, Lee WJ, Wang HH, Huang SP & Lin JT A case-control study of association of Helicobacter pylori infection with morbid obesity in Taiwan. Arch. Intern. Med (2005) doi:10.1001/archinte.165.13.1552.
23. Frankenfield DC, Rowe WA, Cooney RN, Smith JS & Becker D Limits of body mass index to detect obesity and predict body composition. Nutrition (2001) doi:10.1016/S0899-9007(00)00471-8.
24. Romero-Corral A et al. Accuracy of body mass index in diagnosing obesity in the adult general population. Int. J. Obes (2008) doi:10.1038/ijo.2008.11.
25. Jackson AS, Ellis KJ, McFarlin BK, Sailors MH & Bray MS Body mass index bias in defining obesity of diverse young adults: The Training Intervention and Genetics of Exercise Response (TIGER) Study. Br. J. Nutr (2009) doi:10.1017/S0007114509325738.
26. Nevill AM, Stewart AD, Olds T & Holder R Relationship between adiposity and body size reveals limitations of BMI. Am. J. Phys. Anthropol (2006) doi:10.1002/ajpa.20262.
27. Recio-Rodriguez JI et al. Abdominal obesity vs general obesity for identifying arterial stiffness, subclinical atherosclerosis and wave reflection in healthy, diabetics and hypertensive. BMC Cardiovasc. Disord (2012) doi:10.1186/1471-2261-12-3.
28. Chan DC, Watts GF, Barrett PHR & Burke V Waist circumference, waist-to-hip ratio and body mass index as predictors of adipose tissue compartments in men. QJM - Mon. J. Assoc. Physicians (2003) doi:10.1093/qjmed/hcg069.
29. Heitmann BL & Lissner L Hip Hip Hurrah! Hip size inversely related to heart disease and total mortality. Obes. Rev (2011) doi:10.1111/j.1467-789X.2010.00794.x.
30. Casanueva FF et al. Relationship of abdominal obesity with cardiovascular disease, diabetes and hyperlipidaemia in Spain. Clin. Endocrinol. (Oxf) (2010) doi:10.1111/j.1365-2265.2009.03727.x.
31. Manolopoulos KN, Karpe F & Frayn KN Gluteofemoral body fat as a determinant of metabolic health. International Journal of Obesity (2010) doi:10.1038/ijo.2009.286.
32. Rubenstein JH et al. Protective role of gluteofemoral obesity in erosive oesophagitis and Barrett's oesophagus. Gut (2014) doi:10.1136/gutjnl-2012-304103.
33. Kendall BJ et al. Inverse Association Between Gluteofemoral Obesity and Risk of Barrett's Esophagus in a Pooled Analysis. Clin. Gastroenterol. Hepatol (2016) doi:10.1016/j.cgh.2016.05.032.
34. Snijder MB et al. Trunk Fat and Leg Fat Have Independent and Opposite Associations with Fasting and Postload Glucose Levels: The Hoorn Study. Diabetes Care (2004) doi:10.2337/diacare.27.2.372.
35. Buemann B et al. Lower-body fat mass as an independent marker of insulin sensitivity - The role of adiponectin. Int. J. Obes (2005) doi:10.1038/sj.ijo.0802929.

What You Need to Know

Background:

The relationship of multiple dimensions of adiposity (body mass index, waist circumference, hip circumference, and waist-to-hip ratio) on the risk of non-cardia gastric intestinal metaplasia are poorly described.

Findings:

We found that, while parameters of overall and abdominal obesity were not associated with the risk of non-cardia gastric intestinal metaplasia, increasing gluteofemoral obesity, measured by hip circumference, confers lower risk of non-cardia gastric intestinal metaplasia.

Implications for patient care:

The novel finding of an inverse association with hip circumference (gluteofemoral obesity) should be further examined for incorporation into clinically applicable risk stratification scores for gastric cancer prevention.

Table 1.

Characteristics of controls and non-cardia gastric intestinal metaplasia cases

		Controls N=1,748	Cases N=409	
		N (%)	N (%)	P
Age group, years				0.001
	<60	738 (42.2)	136 (33.2)	
	60–69	821 (47.0)	208 (50.9)	
	≥70	189 (10.8)	65 (15.9)	
Sex				<0.001
	Male	1588 (90.9)	398 (97.3)	
	Female	160 (9.1)	11 (2.7)	
Race/Ethnicity				<0.001
	White	1068 (61.1)	166 (40.6)	
	Black	506 (29.0)	173 (42.3)	
	Other	174 (9.9)	70 (17.1)	
Smoking status				<0.001
	Never smoker	450 (29.1)	73 (19.5)	
	Ex-smoker	623 (40.3)	161 (42.9)	
	Current smoker	472 (30.6)	141 (37.6)	
	Missing	203	34	
Alcohol use				0.15
	Non-drinker	149 (9.1)	25 (6.4)	
	Ex-drinker	621 (37.8)	162 (41.3)	
	Current drinker	874 (53.2)	205 (52.3)	
	Missing	104	17	
H. pylori infection				<0.001
	No	1339 (77.7)	191 (47.3)	
	Yes	384 (22.3)	213 (52.7)	
	Missing	25	5	
BMI, kg/m^2				0.07
	<25	313 (17.9)	86 (21.0)	
	25–29.9	621 (35.5)	158 (38.6)	
	≥30	814 (46.6)	165 (40.3)	
	Mean (SD)	30.3 (6.1)	29.3 (5.7)	0.002
Waist circumference, cm				0.26
	≤99.5	439 (25.1)	119 (29.1)	
	99.6–108.2	435 (24.9)	102 (24.9)	
	108.3–117.7	441 (25.2)	102 (24.9)	
	≥118	433 (24.8)	86 (21.0)	
	Mean (SD)	108.7 (14.1)	107.4 (14.6)	0.08

		Controls N=1,748	Cases N=409	
		N (%)	N (%)	P
Hip circumference, cm				0.11
	≤105.1	440 (25.2)	119 (29.1)	
	105.2–112.6	436 (24.9)	112 (27.4)	
	112.7–120.5	435 (24.9)	94 (23.0)	
	≥121	437 (25.0)	84 (20.5)	
	Mean (SD)	113.7 (12.2)	111.7 (11.9)	0.003
WHR				0.80
	Low	248 (14.2)	60 (14.7)	
	High	1500 (85.8)	349 (85.3)	
	Mean (SD)	0.96 (0.07)	0.96 (0.07)	0.30

BMI, body mass index; WHR, waist-to-hip ratio.

WHR was categorized as high if it was ≥0.9 for males or ≥0.85 for females.

Missing category was excluded from statistical tests for differences between controls and cases.

Table 2.

Unadjusted and adjusted odds ratios for associations between obesity-related variables and risk of gastric intestinal metaplasia

		Unadjusted OR (95% CI)	Adjusted OR[a] (95% CI)
BMI, kg/m^2			
	<25	1.00 (ref)	1.00 (ref)
	25–29.9	0.93 (0.69–1.24)	0.97 (0.70–1.33)
	≥30	0.74 (0.55–0.99)	0.86 (0.62–1.18)
	Per unit BMI	0.97 (0.95–0.99)	0.98 (0.96–1.00)
Waist circumference, cm			
	≤99.5	1.00 (ref)	1.00 (ref)
	99.6–108.2	0.87 (0.64–1.16)	0.88 (0.64–1.21)
	108.3–117.7	0.85 (0.63–1.15)	0.83 (0.60–1.15)
	≥118	0.73 (0.54–1.00)	0.79 (0.57–1.11)
	Per 10 cm	0.93 (0.87–1.01)	0.94 (0.87–1.03)
Hip circumference, cm			
	≤105.1	1.00 (ref)	1.00 (ref)
	105.2–112.6	0.95 (0.71–1.27)	0.95 (0.69–1.29)
	112.7–120.5	0.80 (0.59–1.08)	0.84 (0.61–1.16)
	≥121	0.71 (0.52–0.97)	0.77 (0.55–1.07)
	Per 10 cm	0.87 (0.79–0.95)	0.89 (0.80–0.98)
WHR			
	Low	1.00 (ref)	1.00 (ref)
	High	0.96 (0.71–1.30)	1.00 (0.71–1.40)
	Per unit WHR	2.30 (0.47–11.3)	2.34 (0.37–14.7)

CI, confidence interval; OR, odds ratio.

[a]Adjusted for age, sex, race/ethnicity, smoking status, and *H. pylori* infection.

Table 3.

Odds ratios for associations of mutually adjusted obesity-related variables and risk of gastric intestinal metaplasia

		OR[a] (95% CI)
BMI (kg/m^2) adjusted for WHR		
	<25	1.00 (ref)
	25–29.9	0.96 (0.69–1.33)
	≥30	0.85 (0.60–1.18)
	Per unit BMI	0.98 (0.96–1.00)
Waist circumference (cm) adjusted for BMI		
	≤99.5	1.00 (ref)
	99.6–108.2	0.85 (0.59–1.24)
	108.3–117.7	0.82 (0.53–1.26)
	≥118	0.79 (0.48–1.30)
	Per 10 cm	0.95 (0.84–1.08)
Waist circumference (cm) adjusted for hip circumference		
	≤99.5	1.00 (ref)
	99.6–108.2	0.91 (0.64–1.30)
	108.3–117.7	0.93 (0.61–1.44)
	≥118	0.98 (0.57–1.67)
	Per 10 cm	1.12 (0.95–1.32)
Hip circumference (cm) adjusted for waist circumference		
	≤105.1	1.00 (ref)
	105.2–112.6	0.98 (0.69–1.39)
	112.7–120.5	0.87 (0.56–1.35)
	≥121	0.78 (0.46–1.32)
	Per 10 cm	0.79 (0.65–0.97)
WHR adjusted for BMI		
	Low	1.00 (ref)
	High	1.05 (0.74–1.49)
	Per unit WHR	3.86 (0.54–27.5)

CI, confidence interval; OR, odds ratio.

[a]Adjusted for age, sex, race/ethnicity, smoking status, *H. pylori* infection, in addition to the variable noted above.

Table 4.

Adjusted odds ratios for associations between obesity-related variables and risk of extensive and focal gastric intestinal metaplasia

		Extensive GIM (110 cases vs. 1,748 controls)	Focal GIM (299 cases vs. 1,748 controls)
		Adjusted OR[a] (95% CI)	Adjusted OR[a] (95% CI)
BMI, kg/m^2			
	<25	1.00 (ref)	1.00 (ref)
	25–29.9	1.05 (0.62–1.79)	0.95 (0.66–1.37)
	≥30	0.72 (0.41–1.27)	0.92 (0.64–1.33)
	Per unit BMI	0.98 (0.94–1.01)	0.98 (0.96–1.00)
Waist circumference, cm			
	≤99.5	1.00 (ref)	1.00 (ref)
	99.6–108.2	1.56 (0.91–2.68)	0.71 (0.49–1.02)
	108.3–117.7	0.91 (0.51–1.64)	0.82 (0.57–1.16)
	≥118	0.72 (0.37–1.40)	0.81 (0.56–1.17)
	Per 10 cm	0.96 (0.82–1.12)	0.94 (0.86–1.04)
Hip circumference, cm			
	≤105.1	1.00 (ref)	1.00 (ref)
	105.2–112.6	1.08 (0.63–1.86)	0.90 (0.63–1.27)
	112.7–120.5	0.89 (0.49–1.59)	0.83 (0.58–1.19)
	≥121	0.80 (0.43–1.48)	0.77 (0.53–1.11)
	Per 10 cm	0.90 (0.75–1.08)	0.89 (0.80–1.00)
WHR			
	Low	1.00 (ref)	1.00 (ref)
	High	0.91 (0.52–1.59)	1.00 (0.68–1.46)
	Per unit WHR	2.75 (0.11–66.6)	2.10 (0.26–16.9)

CI, confidence interval; OR, odds ratio.

[a]Adjusted for age, sex, race/ethnicity, smoking status, and *H. pylori* infection