Korean J Gastroenterol Vol. 83 No. 3, 81-86
https://doi.org/10.4166/kjg.2024.015
pISSN 1598-9992 eISSN 2233-6869

REVIEW ARTICLE

비만과 상부 위장관 질환

최영희
가톨릭대학교 의과대학 내과학교실

Obesity and Upper Gastrointestinal Diseases

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Obesity increases gastroesophageal reflux disease through several factors. As a result, Barrett's esophagus, esophageal adenocarcinoma, and gastroesophageal junctional gastric cancer are increasing. Existing studies usually defined obesity by body mass index and analyzed the correlation. Recently, more studies have shown that central obesity is a more important variable in upper gastrointestinal diseases related to gastroesophageal reflux. Studies have reported that weight loss is effective in reducing gastroesophageal reflux symptoms. Obesity also affects functional gastrointestinal diseases. A significant correlation was shown in upper abdominal pain, reflux, vomiting, and diarrhea rather than lower abdominal diseases. **(Korean J Gastroenterol 2024;83:81-86)**

Key Words: Adenocarcinoma of esophagus; Barrett esophagus; Body mass index; Gastroesophageal reflux disease; Obesity

INTRODUCTION

As the obese population increases, related diseases are also increasing. In the United States, about 65% of adults are said to have been overweight or obese since 2000.[1,2] In Korea, the number of obese people is also steadily increasing due to Western eating habits and sedentary lifestyle patterns. In Korea, the prevalence of adult obesity and abdominal obesity has also continued to increase over the past 10 years. In 2021, the prevalence of obesity in Korea was 38.4% and the prevalence of abdominal obesity was 24.5%.[3] It is already known that obesity is closely related to metabolic syndrome, which is a combination of high blood pressure, diabetes, and hyperlipidemia.[4] It is also closely related to gastrointestinal diseases, especially upper gastrointestinal diseases. This has been reported in several studies.[5]

Peptides such as leptin and ghrelin secreted by adipocytes are associated with inflammation, carcinogenesis, and gastrointestinal motility. This review will examine each of the upper gastrointestinal diseases associated with obesity.

DEFINITION OF OBESITY

Obesity is usually defined in three ways. Body mass index (BMI) is the most commonly used unit, and it is calculated by dividing weight (kg) by the square of height (m^2). A BMI of 23–24.9 kg/m^2 is considered overweight, and a BMI of 25 kg/m^2 or more is considered obese. Additionally, the defi-

Received February 4, 2024. **Revised** March 19, 2024. **Accepted** March 19, 2024.

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Financial support: None. Conflict of interest: None.

nition of obesity through waist circumference is 90 cm or more for men and 85 cm or more for women. Lastly, men are considered obese if their waist-to-hip ratio is over 0.9 and women are over 0.85. This method is more accurate in identifying central obesity. Because obesity promotes or causes gastroesophageal reflux, symptoms such as heartburn, soreness, and reflux occur, and various diseases that develop due to this are also increasing.[6]

PATHOPHYSIOLOGY OF OBESITY

Several factors play a role in the pathophysiology of obesity. Several physiological synthetic substances are excessively produced in visceral fat, including free fatty acids, leptin, adiponectin, and inflammatory cytokines.[7,8] When leptin levels increase, mitogenic and angiogenic mechanisms are activated. Through this, carcinogenesis can be promoted.[9] It acts as a pro-inflammatory cytokine in addition to these metabolic properties.[10] Adioponectin is a substance that shows anti-inflammatory effects, and its concentration was found to be reduced in overweight people. It can help suppress the production of tumor necrosis factor-alpha by macrophages, bind to mitogenic growth factors, and regulate multiple signaling pathways related to angiogenesis and proliferation.[11,12] Additionally, a wide range of pro-inflammatory cytokines and receptors, such as interleukin-6 and tumor necrosis factor, are produced in significant amounts in adipocytes, especially in the intestines.[13]

Ghrelin promotes gastric motility, gastric emptying, and acid secretion. Therefore, as ghrelin levels rise, gastric motility and emptying increase, which can improve symptoms of functional gastrointestinal diseases. Conversely, if serum ghrelin levels drop, symptoms such as indigestion may be more likely to occur.[14]

OBESITY AND GASTROESOPHAGEAL REFLUX

Gastroesophageal reflux is reported to be highly correlated with obesity. It is known that relaxation of the lower esophageal sphincter, high rate of esophageal hiatal hernia, accompanying esophageal motor and sensory dysfunction, and hormonal changes can work together to produce symptoms.[5,15] Studies have also reported that the extensive metabolic activity of adipocytes promotes Barrett's esophagus and esophageal adenocarcinoma.[16]

There are several studies on BMI and reflux symptoms (Table 1).[17-24] Obese people have a higher prevalence of gastroesophageal reflux symptoms, such as heartburn or regurgitation, than non-obese people, and a significant correlation has been reported.[15] An extensive public study involving approximately 65,000 people in Norway Health surveys have shown that the risk of reflux symptoms increases as BMI increases and that the association is stronger in women, where estrogen may play an important role. Reflux symptoms significantly increased at BMI ≥35 kg/m^2, especially in women (odds ratio [OR] 6.3, 95% confidence interval [CI] 4.9–8.0 for women vs. OR 3.3, 95% CI 2.4–4.7 for men).[25]

In a meta-analysis on obesity and reflux, the adjusted odds ratio for the association with symptoms at BMI ≥25 kg/m^2 was 1.4 (95% CI, 1.2–1.8), and the adjusted odds ratio for the association with erosive esophagitis was 1.8 (95% CI, 1.2–2.7).

Additionally, the adjusted odds ratio for reflux symptoms

Table 1. Studies on the Risk of Gastroesophageal Reflux Symptoms according to Body Mass Index

Studies	Country	Number of subjects	Adjusted ORs (95% CIs) according to BMI		
			<25 kg/m^2	25–30 kg/m^2	≥30 kg/m^2
Cremonini et al.[17], 2009	USA	4,096	1	2.0 (1.4–2.9)	3.4 (2.4–4.9)
Diaz-Rubio et al.[18], 2004	Spain	2,500	1	1.5 (1.2–1.9)	1.7 (1.3-2.3)
El-Serag et al.[19], 2005	USA	129	1	1.7 (0.7–4.2)	4.0 (1.4–11.1)
Kang et al.[20], 2007	Korea	2,281	1	0.7 (0.4–1.1)	0.9 (0.4–2.4)
Murray et al.[21], 2003	UK	10,537	1	1.5 (1.1–2.0)	2.2 (1.4–3.5)
Nocon et al.[22], 2006	Germany	7,124	1	1.8 (1.5–2.2)	2.6 (2.2–3.2)
Rey et al.[23], 2006	USA	2,500	1	1.8 (1.2–2.7)	1.9 (1.2–3.0)
Stanghellini[24], 1999	USA	2,590	1	1.8 (1.5–2.3)	2.9 (2.2–3.8)

BMI, body mass index; CIs, confidence intervals; ORs, odds ratios.

at BMI ≥30 kg/m^2 was 1.9 (95% CI, 1.5–2.6).[26] In a questionnaire administered to 6,226 people in the United States, based on people with a BMI of 20–22.4 kg/m^2, the odds ratio for the occurrence of gastroesophageal reflux symptoms in BMI <20 kg/m^2 was 0.7 (95% CI, 0.5–0.9), and the odds ratio increased to 2.9 (95% CI, 2.2–3.9) for BMI ≥35 kg/m^2.[27] In a population-based study of 7,124 people in the general population in Germany, obesity was reported to increase the risk of reflux symptoms (OR 2.6, 95% CI, 2.2–3.2).[22]

Obesity has been reported to cause symptoms and affect the severity and frequency of gastroesophageal reflux.[27,28] Reflux symptoms are more closely related to obesity than heartburn. It is said that the severity of reflux symptoms in obese people is approximately 2.1 times higher than in normal people. Additionally, a Spanish study found that the risk of developing reflux symptoms increased 1.5 times for weight gain of less than 5 kg and approximately three times for weight gain of more than 5 kg.[23]

CENTRAL OBESITY AND WEIGHT LOSS

According to several studies, central obesity appears to be more important in the occurrence of reflux symptoms than simple BMI. A United States study performed 24-hour ambulatory pH monitoring on 206 patients showed a relationship between waist circumference, esophageal acid exposure, and obesity.[29] In a domestic study, the odds ratio of erosive esophagitis was 0.7 (95% CI, 0.4–1.1) at a BMI of 25–30 kg/m^2 and 0.9 (95% CI, 0.4–2.4) at a BMI ≥30 kg/m^2, which did not increase the risk.[20] On the other hand, for central obesity, the odds ratio rose to 2.4 (95% CI, 1.4–3.9). Additionally, hiatal hernia was an independent risk factor with an odds ratio of 9.0 (95% CI, 4.9–16.4). There are also studies comparing obesity and gastroesophageal reflux by race. Both BMI and waist circumference showed a more pronounced correlation with gastroesophageal reflux symptoms in white men.[30]

There are several studies examining whether losing weight improves reflux symptoms in gastroesophageal reflux. The European HUNT study published in 2013 showed that the more weight loss in the general population, the greater the reduction in gastroesophageal reflux symptoms.[31] Also, in a United States study, structured weight loss showed complete resolution of gastroesophageal reflux symptoms. It was even said that it was possible.[32] However, on the contrary, there were reports that reflux symptoms did not improve even after weight loss and that medication had to be taken every day as before.[33,34] A study conducted on the general population in Sweden showed no correlation between the degree of obesity and symptoms.[35] A Korean study including 15,295 people reported that erosive esophagitis significantly improved after weight loss.[36] 2020 Seoul Consensus recommend weight reduction as important.[37]

OBESITY AND BARRETT'S ESOPHAGUS

Barrett's esophagus can be said to result from chronic, repetitive gastric acid reflux. Relaxation of the lower esophageal sphincter, a high rate of esophageal hiatal hernia, esophageal motor and sensory abnormalities, and hormonal changes can all work together to cause symptoms.[16,38] Studies are showing that as obesity increases, the rate of Barrett's esophagus increases.[38] The risk of developing Barrett's esophagus increased in BMI ≥30 kg/m^2 (OR 4.0; 95% CI 1.4–11.1) and high visceral fat area (OR 3.2; 95% CI 1.1–9.3).[19] Although it is not yet a large proportion in Korea, Barrett's esophagus, esophageal adenocarcinoma, or gastroesophageal junction (GEJ) cancer accounts for a very high proportion in the United States.[39] This can also be a long-term complication of obesity. A study looked at the relationship between abdominal fat and Barrett's esophagus.[40] In a case-control study in the United States, visceral abdominal fat was analyzed through abdominal computerized axial tomography images of 173 patients with Barrett's esophagus. Compared with 515 control subjects, Barrett's esophagus patients had a visceral adipose tissue to subcutaneous adipose tissue ratio that was approximately twice as high.

OBESITY AND ESOPHAGEAL/GEJ GASTRIC CANCER

Risk factors for esophageal adenocarcinoma include drinking alcohol and obesity. Although other malignancies have been linked to obesity, esophageal adenocarcinoma is believed to have a stronger association. The mechanism of obesity and esophageal adenocarcinoma can be a step-by-step process, starting from gastroesophageal reflux and passing through Barrett's esophagus to esophageal adenocarcinoma. In various studies, the risk of obese people developing esophageal ad-

Table 2. Studies on the Risk of Esophageal Adenocarcinoma according to Body Mass Index

Studies	Country	Number of subjects	Reference BMI	Cut-off BMI for obesity	Odds ratios (95% CIs)
Abnet et al.[41], 2008	USA	50,000	<25 kg/m^2	≥25 kg/m^2	1.3 (1.1–1.5)
Jansson et al.[42], 2005	Sweden	260,052	<25 kg/m^2	≥25 kg/m^2	1.5 (1.1–2.1)
Lukanova et al.[43], 2006	Sweden	68,786	<25 kg/m^2	≥25 kg/m^2	1.2 (0.7–1.9)
Oh et al.[44], 2005	Korea	781,283	<25 kg/m^2	≥25 kg/m^2	1.1 (1.0–1.2)
Reeves et al.[45], 2007	UK	1,200,000	<25 kg/m^2	≥25 kg/m^2	1.1 (0.9–1.4)
Sjödahl et al.[46], 2008	Sweden	73,133	<25 kg/m^2	≥25 kg/m^2	1.7 (1.3–2.2)
Veugelers et al.[5], 2006	Canada	159	20–25 kg/m^2	≥30 kg/m^2	4.5 (1.5–13.9)

BMI, body mass index; CIs, confidence intervals.

enocarcinoma is usually reported to be 1.3 to 4.5 times higher (Table 2).[5,41-46] In the United States, which has the highest obesity rate, esophageal adenocarcinoma increased approximately six-fold between 30 and 40 years, with a clear increase in non-smokers, not the elderly. In one epidemiological study, the odds ratio for esophageal adenocarcinoma and GEJ cancer was 2.4 (95% CI, 1.8–3.2) for a BMI of 35–40 kg/m^2. At BMI ≥40 kg/m^2, the odds ratios for esophageal adenocarcinoma and GEJ cancer, respectively, were 4.8 (95% CI, 3.0–7.7) and 3.1 (1.9–5.0).[47]

Additionally, in a meta-analysis on the occurrence of obesity and esophageal adenocarcinoma, the odds ratios of esophageal adenocarcinoma and GEJ gastric cancer in obese people were 2.4 (95% CI, 2.0–2.8) and 1.5 (95% CI, 1.2–1.9), respectively.[48] There was also a study showing that GEJ gastric cancer, unlike non-GEJ gastric cancer, showed an association with obesity. At BMI ≥25 kg/m^2, the risk of overall stomach cancer did not increase, but the risk of GEJ gastric cancer increased.[49] In a 2006 Canadian case-control study, obese people compared to normal weight people. The odds ratio for developing esophageal adenocarcinoma was 4.5 (95% CI, 1.5–13.9).[5]

OBESITY AND FUNCTIONAL GASTROINTESTINAL DISEASES

The relationship between obesity and gastroesophageal reflux disease or esophageal adenocarcinoma has been reported relatively frequently, but there has not yet been much research on functional dyspepsia. Although functional dyspepsia may overlap with other diseases, there may also be ambiguous reasons for the patient's symptoms. However, studies related to related symptoms report a stronger relationship between diseases of the upper abdomen and obesity than the lower part.

In a meta-analysis that included data from over 77,000 people in 21 studies, obesity increased the risk of other functional gastrointestinal diseases in addition to gastroesophageal reflux symptoms. Upper abdominal pain (OR, 2.7; 95% CI, 1.2–5.3), gastroesophageal reflux (OR, 1.9; 95% CI, 1.7–2.1), vomiting (OR, 1.8; 95% CI, 1.3–2.4), retching (OR, 1.8; 95% CI, 1.3–2.4), chest pain/heartburn (OR, 1.7; 95% CI, 1.5–2.0), diarrhea (OR, 1.5; 95% CI, 1.3–1.6), incomplete evacuation (OR, 1.3; 95% CI, 1.0–1.7).[50] On the other hand, lower abdominal pain, nausea, bloating, constipation, fecal incontinence, and anal blockage were not related to obesity.

In a study using postal questionnaires randomly sent to 5,000 Australian adults, abdominal pain (OR, 1.3; 95% CI, 1.0–1.8), esophageal symptoms (OR, 1.4; 95% CI: 1.0–1.8), diarrhea (OR, 1.9; 95% CI, 1.5–2.3) was associated with obesity, but dysmotility symptoms or constipation were not associated with obesity.[51] Another survey study conducted in Norway also found that obesity increased the occurrence of functional gastrointestinal symptoms (OR, 1.6; 95% CI, 1.1–2.5).[17] Many studies have shown that obesity is associated with upper abdominal gastrointestinal diseases or diarrhea rather than lower gastrointestinal diseases.[6]

CONCLUSION

Obesity increases gastroesophageal reflux disease through several factors. As a result, Barrett's esophagus, esophageal adenocarcinoma, and GEJ gastric cancer are increasing. Studies on the treatment of long-term complications of gastroesophageal reflux caused by obesity are actively underway, and existing studies usually define obesity by BMI and analyze

the correlation. Recently, more studies have shown that central obesity is a more important variable in upper gastrointestinal diseases related to gastroesophageal reflux.

In particular, Korea showed a greater association between central obesity and related symptoms than Western countries. Obesity is more clearly associated with upper gastrointestinal disease than lower gastrointestinal disease, and Korea shows different characteristics and behavior patterns from Western countries. Therefore, various studies are expected to be conducted in non-Western countries, including Korea.

REFERENCES

1. Flegal KM, Carroll MD, Ogden CL, Johnson CL. Prevalence and trends in obesity among US adults, 1999-2000. JAMA 2002;288:1723-1727.
2. Ogden CL, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM. Prevalence of overweight and obesity in the United States, 1999-2004. JAMA 2006;295:1549-1555.
3. 2023 Obesity fact sheet. [Internet]. Korean Society for the Study of Obesity; 2023 Dec 27 [cited 2024 Mar 16]. Available from: https://cdn.medsoft.co.kr/kosso/2023_Obesity_Fact_sheet_web_kor.pdf.
4. Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Heath CW Jr. Body-mass index and mortality in a prospective cohort of U.S. adults. N Engl J Med 1999;341:1097-1105.
5. Veugelers PJ, Porter GA, Guernsey DL, Casson AG. Obesity and lifestyle risk factors for gastroesophageal reflux disease, Barrett esophagus and esophageal adenocarcinoma. Dis Esophagus 2006;19:321-328.
6. Delgado-Aros S, Locke GR 3rd, Camilleri M, et al. Obesity is associated with increased risk of gastrointestinal symptoms: a population-based study. Am J Gastroenterol 2004;99:1801-1806.
7. Koerner A, Kratzsch J, Kiess W. Adipocytokines: leptin--the classical, resistin--the controversical, adiponectin--the promising, and more to come. Best Pract Res Clin Endocrinol Metab 2005;19:525-546.
8. Trayhurn P, Bing C, Wood IS. Adipose tissue and adipokines--energy regulation from the human perspective. J Nutr 2006;136(7 Suppl):1935S-1939S.
9. Somasundar P, McFadden DW, Hileman SM, Vona-Davis L. Leptin is a growth factor in cancer. J Surg Res 2004;116:337-349.
10. Considine RV, Sinha MK, Heiman ML, et al. Serum immunoreactive-leptin concentrations in normal-weight and obese humans. N Engl J Med 1996;334:292-295.
11. Zahorska-Markiewicz B, Janowska J, Olszanecka-Glinianowicz M, Zurakowski A. Serum concentrations of TNF-alpha and soluble TNF-alpha receptors in obesity. Int J Obes Relat Metab Disord 2000;24:1392-1395.
12. Kelesidis I, Kelesidis T, Mantzoros CS. Adiponectin and cancer: a systematic review. Br J Cancer 2006;94:1221-1225.
13. Fried SK, Bunkin DA, Greenberg AS. Omental and subcutaneous adipose tissues of obese subjects release interleukin-6: depot difference and regulation by glucocorticoid. J Clin Endocrinol Metab 1998;83:847-850.
14. Lee KJ. [Obesity and functional gastrointestinal disorders]. Korean J Gastroenterol 2012;59:1-7. Korean.
15. El-Serag HB, Graham DY, Satia JA, Rabeneck L. Obesity is an independent risk factor for GERD symptoms and erosive esophagitis. Am J Gastroenterol 2005;100:1243-1250.
16. Edelstein ZR, Farrow DC, Bronner MP, Rosen SN, Vaughan TL. Central adiposity and risk of Barrett's esophagus. Gastroenterology 2007;133:403-411.
17. Cremonini F, Camilleri M, Clark MM, et al. Associations among binge eating behavior patterns and gastrointestinal symptoms: a population-based study. Int J Obes (Lond) 2009;33:342-353.
18. Diaz-Rubio M, Moreno-Elola-Olaso C, Rey E, Locke GR 3rd, Rodriguez-Artalejo F. Symptoms of gastro-oesophageal reflux: prevalence, severity, duration and associated factors in a Spanish population. Aliment Pharmacol Ther 2004;19:95-105.
19. El-Serag HB, Kvapil P, Hacken-Bitar J, Kramer JR. Abdominal obesity and the risk of Barrett's esophagus. Am J Gastroenterol 2005;100:2151-2156.
20. Kang MS, Park DI, Oh SY, et al. Abdominal obesity is an independent risk factor for erosive esophagitis in a Korean population. J Gastroenterol Hepatol 2007;22:1656-1661.
21. Murray L, Johnston B, Lane A, et al. Relationship between body mass and gastro-oesophageal reflux symptoms: The Bristol Helicobacter Project. Int J Epidemiol 2003;32:645-650.
22. Nocon M, Labenz J, Willich SN. Lifestyle factors and symptoms of gastro-oesophageal reflux – a population-based study. Aliment Pharmacol Ther 2006;23:169-174.
23. Rey E, Moreno-Elola-Olaso C, Artalejo FR, Locke GR 3rd, Diaz-Rubio M. Association between weight gain and symptoms of gastroesophageal reflux in the general population. Am J Gastroenterol 2006;101:229-233.
24. Stanghellini V. Three-month prevalence rates of gastrointestinal symptoms and the influence of demographic factors: results from the Domestic/International Gastroenterology Surveillance Study (DIGEST). Scand J Gastroenterol Suppl 1999;231:20-28.
25. Nilsson M, Johnsen R, Ye W, Hveem K, Lagergren J. Obesity and estrogen as risk factors for gastroesophageal reflux symptoms. JAMA 2003;290:66-72.
26. 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.
27. Jacobson BC, Somers SC, Fuchs CS, Kelly CP, Camargo CA Jr. Body-mass index and symptoms of gastroesophageal reflux in women. N Engl J Med 2006;354:2340-2348.
28. Nocon M, Labenz J, Jaspersen D, et al. 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.
29. El-Serag HB, Ergun GA, Pandolfino J, Fitzgerald S, Tran T, Kramer JR. Obesity increases oesophageal acid exposure. Gut 2007;56:749-755.
30. Corley DA, Kubo A, Zhao W. Abdominal obesity, ethnicity and gastro-oesophageal reflux symptoms. Gut 2007;56:756-762.
31. Ness-Jensen E, Lindam A, Lagergren J, Hveem K. Weight loss and

reduction in gastroesophageal reflux. A prospective population-based cohort study: the HUNT study. Am J Gastroenterol 2013;108:376-382.
32. Singh M, Lee J, Gupta N, et al. Weight loss can lead to resolution of gastroesophageal reflux disease symptoms: a prospective intervention trial. Obesity (Silver Spring) 2013;21:284-290.
33. Kjellin A, Ramel S, Rössner S, Thor K. Gastroesophageal reflux in obese patients is not reduced by weight reduction. Scand J Gastroenterol 1996;31:1047-1051.
34. Frederiksen SG, Johansson J, Johnsson F, Hedenbro J. Neither low-calorie diet nor vertical banded gastroplasty influence gastro-oesophageal reflux in morbidly obese patients. Eur J Surg 2000;166:296-300.
35. 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.
36. Park SK, Lee T, Yang HJ, et al. Weight loss and waist reduction is associated with improvement in gastroesophageal disease reflux symptoms: A longitudinal study of 15 295 subjects undergoing health checkups. Neurogastroenterol Motil 2017 May. doi: 10.1111/nmo.13009.
37. Jung HK, Tae CH, Song KH, et al. 2020 Seoul consensus on the diagnosis and management of gastroesophageal reflux disease. J Neurogastroenterol Motil 2021;27:453-481.
38. Stein DJ, El-Serag HB, Kuczynski J, Kramer JR, Sampliner RE. The association of body mass index with Barrett's oesophagus. Aliment Pharmacol Ther 2005;22:1005-1010.
39. Jacobson BC, Chan AT, Giovannucci EL, Fuchs CS. Body mass index and Barrett's oesophagus in women. Gut 2009;58:1460-1466.
40. El-Serag HB, Hashmi A, Garcia J, et al. Visceral abdominal obesity measured by CT scan is associated with an increased risk of Barrett's oesophagus: a case-control study. Gut 2014;63:220-229.
41. Abnet CC, Freedman ND, Hollenbeck AR, Fraumeni JF Jr, Leitzmann M, Schatzkin A. A prospective study of BMI and risk of oesophageal and gastric adenocarcinoma. Eur J Cancer 2008;44:465-471.
42. Jansson C, Johansson AL, Bergdahl IA, et al. Occupational exposures and risk of esophageal and gastric cardia cancers among male Swedish construction workers. Cancer Causes Control 2005;16:755-764.
43. Lukanova A, Björ O, Kaaks R, et al. Body mass index and cancer: results from the Northern Sweden Health and Disease Cohort. Int J Cancer 2006;118:458-466.
44. Oh SW, Yoon YS, Shin SA. Effects of excess weight on cancer incidences depending on cancer sites and histologic findings among men: Korea National Health Insurance Corporation Study. J Clin Oncol 2005;23:4742-4754.
45. Reeves GK, Pirie K, Beral V, Green J, Spencer E, Bull D. Cancer incidence and mortality in relation to body mass index in the Million Women Study: cohort study. BMJ 2007;335:1134.
46. Sjödahl K, Jia C, Vatten L, Nilsen T, Hveem K, Lagergren J. Body mass and physical activity and risk of gastric cancer in a population-based cohort study in Norway. Cancer Epidemiol Biomarkers Prev 2008;17:135-140.
47. Hoyo C, Cook MB, Kamangar F, et al. Body mass index in relation to oesophageal and oesophagogastric junction adenocarcinomas: a pooled analysis from the International BEACON Consortium. Int J Epidemiol 2012;41:1706-1718.
48. Kubo A, Corley DA. Body mass index and adenocarcinomas of the esophagus or gastric cardia: a systematic review and meta-analysis. Cancer Epidemiol Biomarkers Prev 2006;15:872-878.
49. Yang P, Zhou Y, Chen B, et al. Overweight, obesity and gastric cancer risk: results from a meta-analysis of cohort studies. Eur J Cancer 2009;45:2867-2873.
50. Eslick GD. Gastrointestinal symptoms and obesity: a meta-analysis. Obes Rev 2012;13:469-479.
51. Eslick GD, Talley NJ. Prevalence and relationship between gastrointestinal symptoms among individuals of different body mass index: A population-based study. Obes Res Clin Pract 2016;10:143-150.