Is Obesity a New Risk Factor for Gastritis?

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Obesity · Gastritis · Adiponectin

Abstract
Obesity has become a major concern among gastroenterologists due to its large influence on gastrointestinal and hepatic diseases: reflux esophagitis, pancreatitis, gallstone disease, liver fibrosis, and neoplastic tumors of the esophagus, pancreas, and colon. Studies of morbid obese subjects undergoing bariatric surgery have revealed that obesity is related with an increased prevalence of endoscopic and histologic gastritis. A recent study of health check-up subjects demonstrated an association of obesity with endoscopic gastritis and gastric ulcers. We recently investigated the underlying mechanisms of the effects of obesity on endoscopic gastritis in subjects undergoing health check-up examination, and demonstrated that adiponectin, a bioactive molecule released from visceral fat, could be a protective factor of endoscopic gastritis. We would like to propose a new category of gastritis, obesity-related gastritis, which could become dominant in the near future.

Introduction

Obesity is a major public health concern in developed countries as it increases the risk of cardiovascular disease, diabetes, and dyslipidemia [1]. In addition to these well-known diseases, obesity is associated with common gastrointestinal diseases: gastroesophageal reflux disease, gallstone disease, and neoplastic tumors of the colon, esophagus, and pancreas [2, 3]. An association between obesity and upper gastrointestinal symptoms, such as abdominal pain and vomiting, was recently demonstrated [4, 5]. Moreover, the results of several recent studies, including ours, demonstrate the potential effects of obesity on gastritis [6–9]. Here, we first review recent studies on the relationship between obesity and gastritis. We then discuss how obesity is involved in gastritis by focusing on adiponectin, a bioactive substance secreted from visceral adipose tissue.

Obesity and Histologic Gastritis in Morbid Obesity

The term ‘gastritis’ is used to refer to symptoms, endoscopic findings, and histologic findings. First, we review studies of the relation between obesity and histologic gastritis, because confirming histologically identified gastritis could indicate the presence of definite inflammation of the gastric mucosa as opposed to merely observing symptoms or endoscopic findings. Studies aimed at examining the relationship between obesity and histologic gastritis were performed in patients with morbid obesity [body mass index (BMI) ≥40] who were scheduled to undergo bariatric surgery. Csendes et al. [6] investigated the stomachs of 426 consecutive morbidly obese patients with endoscopic biopsy as a preoperative examination and reported that 27.5% of the patients showed erosions in the stomach, and of 232 patients from whom antral biopsies
were obtained, 62% had histologic chronic superficial gastritis in the gastric antrum. Dutta et al. [7] also investigated 101 preoperative morbidly obese patients and reported that these patients had a significantly increased prevalence of histologically identified gastritis (23.7%) compared to age- and sex-matched control subjects with a normal BMI (11.8%). It is noteworthy that the prevalence of Helicobacter pylori infection in the morbidly obese patients was not different from that in the non-obese control group, suggesting that obesity rather than H. pylori infection accounts for the increased prevalence of histologic gastritis in morbid obesity. Morbid obesity is a suitable model for estimating the effect of obesity on gastritis, because we can expect the maximum effect in severe obesity. Application of these findings to more mildly obese subjects with a BMI <40, however, might be limited.

Obesity and Erosive Gastritis

For this review, erosive gastritis is defined as a flat or minimally depressed white spot surrounded by a reddish area or small elevation with central umbiculations mimicking octopus’ suckers. Kim et al. [8] first reported the relationship between BMI and erosive gastritis in a general population in Korea. They investigated the prevalence of erosive gastritis and gastric or duodenal ulcer in 27,000 subjects by endoscopy and found a significantly increased prevalence in overweight (25 ≤ BMI < 30) and obese (BMI ≥ 30) subjects after adjusting for other clinical factors. Although their study lacks data regarding H. pylori infection and the use of non-steroidal anti-inflammatory drugs, their findings also suggest that obesity is related to erosive gastritis and ulcers.

We focused on erosive gastritis and investigated its relationship with BMI in 2,400 Japanese subjects undergoing a health check-up program [9]. BMI was significantly higher in subjects with erosive gastritis than in those without (23.5 ± 3.1 vs. 22.6 ± 3.1, p < 0.0001), and the prevalence of erosive gastritis gradually increased as BMI increased (table 1). We further analyzed the comorbid endoscopic findings and the location of erosive gastritis to determine the characteristics of erosive gastritis in our study. Subjects with erosive gastritis had significantly more reflux esophagitis and duodenitis than those without. Sixty percent of the erosive gastritis was located in the antrum and considered to be verrucous gastritis, which is related to excess gastric acid. Based on these findings, we speculate that the erosive gastritis in our study was acid-related.

| Table 1. Association of BMI and endoscopic erosive gastritis (EEG) |
|-----------------|-----------------|-----------------|-----------------|
| BMI             | <18.5           | 18.5–25         | 25–30           | >30             |
| Number          | 8               | 175             | 58              | 7               |
| Total           | 177             | 1,727           | 449             | 47              |
| %               | 4.5             | 10.1            | 12.9            | 14.9            |

Adiponectin and Erosive Gastritis

Visceral fat was recently recognized as an endocrine organ that secretes various bioactive substances such as tumor necrosis factor-α, leptin, and adiponectin. Adiponectin exists abundantly in the circulation and exerts anti-atherogenic, anti-diabetic, and anti-inflammatory effects systemically [10]. Serum adiponectin levels are lower in obese subjects compared with normal subjects, and this impaired secretion leads to metabolic disorders [11]. We previously demonstrated that the anti-inflammatory properties of adiponectin have a protective role in several gastrointestinal diseases, such as pancreatitis and gallstone disease [12, 13]. To determine the mechanism underlying the relationship between obesity and erosive gastritis, we examined the serum concentration of adiponectin in the same subjects previously analyzed for the association of obesity with erosive gastritis, and found that the prevalence of erosive gastritis gradually increased as the adiponectin level decreased (table 2). To investigate whether adiponectin is related to erosive gastritis independently of BMI, we conducted a multiple logistic regression analysis in which we included other potential risk factors for gastritis, such as life habits (smoking and drinking), serum metabolic markers (cholesterol, triglyceride, glucose, and insulin levels), and endoscopic findings (reflux esophagitis and duodenitis), in addition to BMI and adiponectin. The results indicated a significant association between adiponectin and erosive gastritis, independently of BMI (for incremental increases of 5 μg/ml of adiponectin; odds ratio 0.82, 95% confidence interval 0.70–0.95). This finding suggests that hypoadiponectinemia increases the risk of endoscopic erosive gastritis. Although we could not clarify the role of adiponectin in the pathogenesis of erosive gastritis in our observational study, we suspect that adiponectin protects the stomach from relatively excessive gastric acid through its anti-inflammatory effects.
**Conclusions and Perspectives**

This review of recent studies on histologic gastritis in morbid obesity as well as endoscopic erosive gastritis reveals a consistent association of obesity with both types of gastritis. The findings indicate the emergence of a new category of gastritis, obesity-related gastritis, in which obesity is thought to be causative in the pathogenesis of gastritis. Based on our observational study, adiponectin is a candidate molecule accounting for the association between obesity and gastritis. Inadequate dietary habits in obese subjects or other hormonal factors such as leptin might also be involved in the mechanism. Further studies to clarify the role of various factors, including hypoadiponectinemia, in the pathogenesis of obesity-related gastritis are needed.

After the discovery of *H. pylori* in 1983, these bacteria have been considered to be the primary cause of gastritis. The prevalence of *H. pylori* infection has decreased, however, in Western countries and in some parts of Asia such as Japan [14, 15]. In contrast, obesity is prevalent around the world and has become a serious social problem [16]. The present findings suggest that obesity-related gastritis could become increasingly dominant in the near future.

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**Disclosure Statement**

The authors have no conflicts of interest to disclose.

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**Table 2. Distribution of endoscopic erosive gastritis (EEG) in each adiponectin quartile**

<table>
<thead>
<tr>
<th>Quartile 1</th>
<th>Quartile 2</th>
<th>Quartile 3</th>
<th>Quartile 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adiponectin, μg/ml</td>
<td>1.6–6.0</td>
<td>6.0–8.5</td>
<td>8.5–12.2</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>4.6 ± 1.0</td>
<td>7.2 ± 0.7</td>
<td>10.2 ± 1.1</td>
</tr>
<tr>
<td>EEG (n = 600), n (%)</td>
<td>84 (33.9)</td>
<td>67 (27.0)</td>
<td>49 (19.8)</td>
</tr>
</tbody>
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