



High Incidence of Reflux Esophagitis Observed by Routine Endoscopic Examination after Gastric Pull-up Esophagectomy

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Abstract. A gastric tube has been widely used for reconstruction of the esophagus after esophagectomy for esophageal cancer. Reflux esophagitis after esophagectomy is frequently observed. Therefore we retrospectively investigated the risk factors for reflux esophagitis after gastric pull-up esophagectomy in 74 outpatients with thoracic esophageal cancer. Reflux esophagitis was diagnosed endoscopically. Esophagitis was classified according to the Los Angeles classification. Reflux symptoms, medications, and the surgical procedure were reviewed. The relation between reflux symptoms and reflux esophagitis and the influence of the anastomotic site were evaluated. Reflux esophagitis was observed in 53 patients. Severe esophagitis (grade C or D) was found in 75.6% of these patients. Although all patients with esophagitis took antacid agents, histamine receptor-2 blocker was effective in only 35% of them. The correlation between reflux symptoms and reflux esophagitis was not significant. Reflux esophagitis was present in 56.4% of patients with neck anastomosis and in 88.6% of patients with intrathoracic anastomosis ($p = 0.0039$). We concluded that routine endoscopic examination is necessary after gastric pull-up esophagectomy because reflux esophagitis is not diagnosed based on reflux symptoms. When a gastric tube is used for reconstruction after esophagectomy, neck anastomosis is recommended to lower the risk of reflux esophagitis.

A gastric tube has been widely used as an esophageal substitute after esophagectomy. There are no structures that prevent gastroesophageal reflux in these patients. Many of them complain of reflux symptoms (acidic regurgitation and cervical heartburn), and they often have esophagitis in the residual esophagus when examined by endoscopy.

Skinner showed that the incidence of esophagitis after esophagectomy was higher than 30% when the stomach was used as a sub-

stitute for the esophagus [1]. Gutshow, Collard, and others showed that 38.5% of patients had reflux esophagitis in the remnant esophagus for 3 years or more after esophagectomy. However, it seemed that the incidence of reflux esophagitis in our hospital was higher than that found in previous studies [1–4]. Therefore the aims of this study were to investigate the occurrence and severity of reflux esophagitis in the remnant esophagus and to evaluate the relation between reflux symptoms and reflux esophagitis in patients who underwent reconstruction using a gastric tube after esophagectomy. Additionally, the risk factors for reflux esophagitis in the remnant esophagus were investigated.

Patients and Methods

We reviewed the clinical records of 74 outpatients [60 men and 14 women whose ages at the time of endoscopy were 47 to 83 years (mean 67.0 years)] who had been subjected to esophagectomy followed by reconstruction using a gastric tube through the posterior mediastinal route as treatment for esophageal cancer in our hospital. To prevent reflux, they were instructed not to lie down after each meal for at least 1 hour and to keep the head-up position at night when they left the hospital after esophagectomy. Informed consent was obtained from each patient.

Postoperative follow-up ranged from 5 to 217 months (mean 36.8 months). All gastric tubes were trimmed along the greater curvature of the stomach. The operative approach consisted of a right posterolateral thoracotomy with laparotomy in 52, thoracoscopic esophagectomy with laparotomy in 18, and transhiatal esophagectomy without thoracotomy in 4. The esophagogastric anastomosis had been performed at the neck in 39 patients and at the highest portion of the intrathoracic esophagus in 35 patients.

All 74 patients underwent upper gastrointestinal endoscopy to assess mucosal breaks in the residual esophagus. The severity of reflux esophagitis was determined according to the Los Angeles classification.

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Table 1. Incidence and severity of reflux esophagitis in this study (according to the Los Angeles classification).

Grade of esophagitis	No. of patients (n = 74)
No esophagitis	21 (28.4%)
Esophagitis	53
Grade A	8/53 (10.8%)
Grade B	5/53 (6.8%)
Grade C	23/53 (31.0%)
Grade D	17/53 (23.0%)

See text for explanation of esophagitis grades.

Data on reflux symptoms, pharyngeal regurgitation, and cervical heartburn were obtained from the patients' clinical records. The patients with reflux symptoms were defined as those who had reflux symptoms more than once a week. The patients were divided into two groups based on the presence or absence of symptoms (group I consisted of 43 patients with reflux symptoms, and group II comprised 31 patients without reflux symptoms). Data on medication with antacid agents, such as proton pump inhibitors (PPIs) and histamine receptor-2 blockers (H₂-blockers), were obtained from the patients' clinical records. H₂-blocker-resistant esophagitis was defined as esophagitis that did not improve after treatment with an H₂-blocker for 8 weeks or more.

Chi-square and Mann-Whitney nonparametric statistical tests were used as appropriate. A value of *p* < 0.05 was considered statistically significant.

Results

As shown in Table 1, endoscopy revealed that 71.6% of the patients (53/74) had reflux esophagitis in the remnant esophagus. Severe esophagitis (i.e., grade C or D) was found in more than 75% of the patients with esophagitis, grade A in 15.1%, and grade B in 9.4%. Of the 74 patients, 32 were found to have columnar epithelium in the residual esophagus; 2 of these patients were not found to have reflux esophagitis, but the remaining 30 patients did have it. Barrett's esophagus was found in four patients with columnar epithelium, and the other patients had short-segment Barrett's esophagus. The follow-ups for four patients with Barrett's esophagus were more than 5 years. New carcinoma in the residual esophagus was not found in any of the patients at follow-up, although one patient was diagnosed as having adenocarcinoma of the reconstructive gastric tube.

There was no significant difference in the age of the patients between groups I and II. Group I consisted of 11 patients without endoscopic findings in the esophagus and 32 patients with mucosal breaks. Group II consisted of 10 patients without endoscopic findings in the esophagus and 21 patients with mucosal breaks. No significant correlation (*p* = 0.6) was found between reflux symptoms and the endoscopic findings of reflux esophagitis (Fig. 1).

Antacid agents (e.g., PPIs and H₂-blockers) had been administered to 57 patients (77%). Five patients without esophagitis had taken antacid agents for reflux symptoms. As for the 53 patients with esophagitis, H₂-blockers were effective against the esophagitis and symptoms in only 35%; 65% of those patients needed PPIs for the esophagitis and symptoms because H₂-blockers had not been effective.

As for the relation of reflux esophagitis to the anastomotic sites

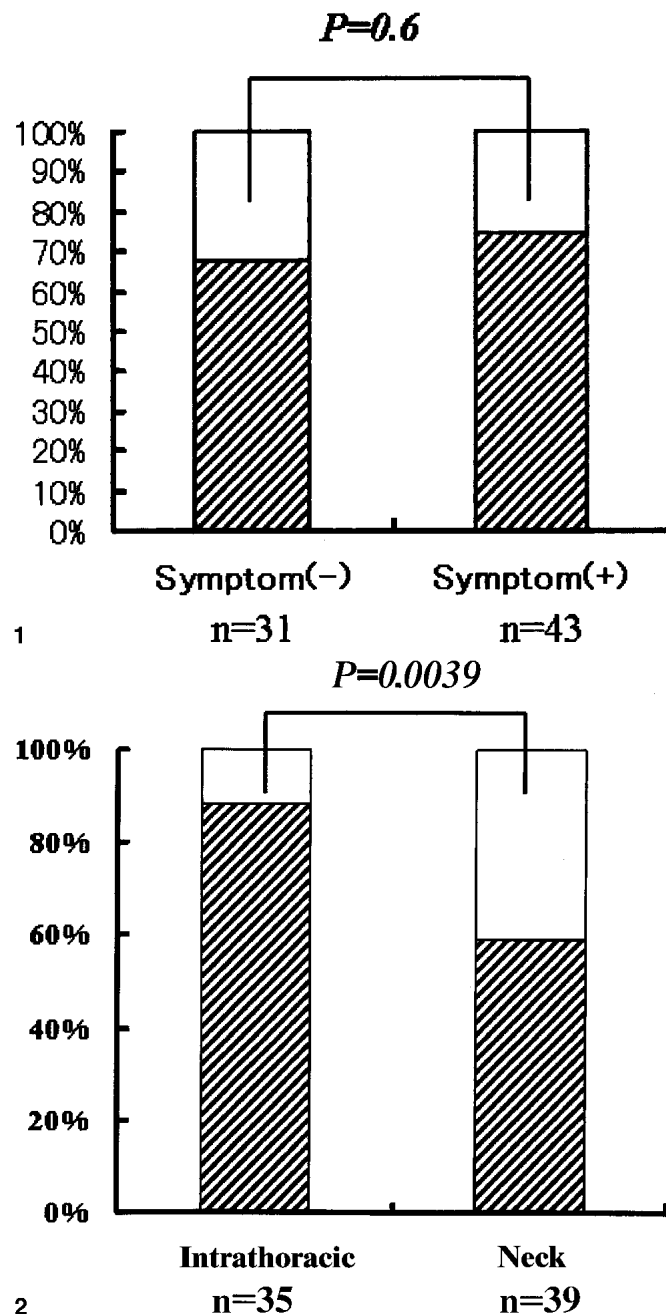


Fig. 1. Correlation between reflux symptoms and reflux esophagitis was not significant (chi-square test, *p* = 0.6). Open bars: esophagitis-negative; hatched bars: esophagitis-positive.

Fig. 2. Incidence of reflux esophagitis with neck and intrathoracic anastomoses was 56.4% and 88.6%, respectively (chi-square test, *p* = 0.0039). Open bars: esophagitis-negative; hatched bars: esophagitis-positive.

(Fig. 2), among the patients with neck anastomosis 22 had esophagitis and 17 did not. Among the patients with an intrathoracic anastomosis, 31 had esophagitis and 4 did not. The incidences of reflux esophagitis in the neck anastomosis group and the intrathoracic anastomosis group were 56.4% and 88.6%, respectively, with a significant difference between them (*p* = 0.0039).

Discussion

The results of our study showed a high incidence of reflux esophagitis in the remnant esophagus of the patients who underwent reconstruction using a gastric tube via the posterior mediastinal route after esophagectomy in our hospital. Severe esophagitis was common in these patients. Moreover, there was no significant correlation between reflux symptoms and reflux esophagitis.

The occurrence of reflux esophagitis in our patients (71.6%) was higher than that found in previous studies [1–4]. The number of long-term survivors after esophagectomy increased during this decade thanks to advances in surgical techniques and perioperative management [5]. Upper gastrointestinal (GI) endoscopic examinations were routinely performed at follow-up in our hospital even if they did not complain of any other reflux symptoms because of detecting abnormalities of the residual esophagus and gastric tube such as an ulcer of the gastric tube and cancer of the residual esophagus. Reflux esophagitis was observed in patients who did not survive long after esophagectomy during the previous decade or did not complain of any other symptoms after esophagectomy. Because our patients with esophagitis in the past were evaluated together with the most recent ones, the occurrence of reflux esophagitis was high in this study.

Severe esophagitis was observed in more than 75% of the patients with esophagitis after esophagectomy. After esophagectomy, there are no structures that may prevent gastroesophageal or duodenogastric reflux due to resection of the esophagogastric junction and pyloroplasty. Accordingly, peristaltic waves of the residual esophagus were not observed in our experience if the patients had had peristalsis before surgery. Gastric and duodenal contents then easily regurgitated into the residual esophagus, and it was difficult to clear them out of that area. It seems that these phenomena were the main risk factors for esophagitis. Based on the effectiveness of PPIs as treatment for reflux esophagitis, it seems that gastric acidity in the denervated stomach is strongly related to the incidence of reflux esophagitis.

Gutshow and colleagues noted that early after vagotomy intraluminal acidity decreased in two-thirds of the patients, but the stomach recovered its normal pH profile with time [2]. However, there have been other, different reports on acidity of the denervated stomach. Domergue et al. [6] and Bonavina et al. [7] noted that gastric acidity decreased after esophagectomy. Hashimoto and colleagues noted that gastric acidity did not decrease after esophagectomy and that the postoperative acidity in the gastric tube was high in patients with high preoperative acidity [8]. Other studies to evaluate the acidity of a denervated gastric tube including the infection rate with *Helicobacter pylori* (HP) and the degree of mucosal atrophy, are needed to solve this problem, because HP infection influences the acidity of the stomach, especially in Japan [9].

Although most of the patients complained of reflux symptoms (e.g., cervical heartburn and pharyngeal regurgitation) after esophagectomy, there was no significant relation between reflux symptoms and reflux esophagitis in our series. Cervical heartburn and pharyngeal regurgitation were considered to be reflux symptoms in this study; only three patients complained of cervical heartburn. The remaining patients with symptoms complained of pharyngeal regurgitation without cervical heartburn. It seemed that the perception of the cervical esophagus is lost after esophagectomy, and patients felt “reflux” as regurgitation of gastric or duodenal con-

tents into the pharynx. Patients with esophagitis did not complain of any other reflux symptom if they did not have pharyngeal reflux.

We also had four cases of esophageal bleeding from an esophageal ulcer caused by reflux esophagitis in the remnant esophagus; however, two of them did not have reflux symptoms and were diagnosed at endoscopy during a survey of anemia. Therefore it seems that routine endoscopic examination is necessary after gastric pull-up esophagectomy to determine whether reflux esophagitis is present. If so, adequate acid suppression therapy for esophagitis is necessary.

The incidence of reflux esophagitis in our patients with a neck anastomosis was significantly lower than that in the patients with an intrathoracic anastomosis. This finding was in agreement with those of previous reports. Demeester et al. stated that it was generally accepted that an esophagogastric anastomosis at the level of the neck resulted in less postoperative esophagitis and stricture formation than one performed within the chest [10, 11]. However, Johansson et al. [12] noted that exposure of the esophageal remnant to acid increased during the first postoperative year in patients with a neck anastomosis but not in patients with a proximal chest anastomosis. It seems that these contradictory findings were due to differences in the duration of follow-up. Johansson et al. did not evaluate the patients who probably developed esophagitis later because their study was shorter than that of Demeester et al. and the present one.

Although gastric advancement is the best method of reconstruction after esophagectomy from the viewpoint of safety and ease, an intrathoracic stomach is a poor long-term substitute. Skinner showed that stomach should not be used for reconstruction in patients with benign disease because of the high incidence of late esophagitis due to reflux and the risk of serious aspiration pneumonia [1]. In addition, Demeester and colleagues also suggested that in patients with benign disease a colon interposition is usually preferred to obviate the late problems associated with a cervical esophagogastrostomy because patients undergoing a cervical esophagogastrostomy for benign disease may develop problems associated with the anastomosis during the fourth or fifth postoperative year, whereas this is less likely to develop in patients who have had a colon interposition [10, 11].

Based on this concept, we think that the cancer patients who are expected to survive long may be found to have the same late problems as patients with benign disease. For that reason, gastric advancement might be avoided for reconstruction after esophagectomy in these patients. Therefore, we recommend a colon interposition for reconstruction after esophagectomy in patients who are expected to survive long or who have benign disease, if possible. However, this procedure is less safe and less easy to perform than gastric advancement. Patients with cancer are subjected to greater surgical stress by esophagectomy than are those with benign disease with combined two- or three-field lymphadenectomy. It might be difficult for many surgeons to accept the change from gastric advancement to colon interposition. Okada et al. reported a technique involving modified gastric advancement [3]. This technique was added to an antireflux structure for esophagogastric anastomosis; it is called the “invagination technique.” It might be acceptable for many surgeons to modify gastric advancement in this way. It is desirable with a gastric pull-up esophagectomy to add an antireflux structure.

Routine endoscopic examination is useful for detecting reflux

esophagitis of the remnant esophagus in patients after gastric pull-up esophagectomy. In patients who are expected to survive a long time, colon interposition is recommended for reconstruction after esophagectomy, if possible. Even if the stomach is used for reconstruction after esophagectomy, neck anastomosis is recommended to reduce the risk of reflux esophagitis.

Résumé. Après oesophagectomie pour cancer de l'œsophage, l'estomac est souvent utilisé pour reconstruire le tube digestif. Comme on a constaté souvent un reflux dans les suites opératoires de cette intervention, on a étudié, rétrospectivement, les facteurs de risque de l'œsophagite par reflux après oesophagectomie chez 74 patients opérés d'un cancer de l'œsophage thoracique. Le diagnostic de reflux a toujours été par endoscopie. On a classé l'œsophagite selon la classification de Los Angeles. On a analysé les symptômes de reflux, les médicaments et les procédés chirurgicaux utilisés. Le rapport entre les symptômes et l'œsophagite et son influence sur le site de l'anastomose ont été évalués. On a observé un reflux chez 53 patients. Une œsophagite sévère, grades C ou D, a été retrouvée chez 75.6% de ces patients. Tous ces patients ont pris des médicaments anti-acides; les anti-H₂ n'ont été efficaces que chez 35% des patients. La corrélation entre les symptômes de reflux et l'œsophagite n'était pas significative. On a observé les signes d'œsophagite chez 56.4% des patients ayant une anastomose au cou et chez 88.6% des patients ayant eu une anastomose intra-thoracique ($p = 0.0039$). Nous concluons qu'un examen endoscopique de routine est nécessaire après oesophagectomie et reconstruction par tube gastrique car le reflux n'est pas toujours évident cliniquement, en se basant sur les symptômes de reflux. Lorsqu'on utilise un tube gastrique pour reconstruction après oesophagectomie, une anastomose au cou pourrait réduire le risque d'œsophagite par reflux.

Resumen. La tubulización gástrica es un procedimiento muy utilizado en la reconstrucción del esófago tras esofagectomía por cáncer gástrico. Sin embargo, es frecuente que aparezca una esofagitis por reflujo. Por ello, analizamos retrospectivamente los factores de riesgo de reflujo esofágico tras tubulización gástrica, en 74 pacientes esofagectomizados por cáncer del esófago torácico. La esofagitis de reflujo se diagnosticó mediante endoscopia y su gravedad se evaluó de acuerdo con la clasificación "Los Angeles." Se revisaron tanto los síntomas como la medicación y el proceder quirúrgico empleado. Se evaluó también la relación entre los síntomas de reflujo y el grado de esofagitis, así como el papel que podría desempeñar la posición de la anastomosis esofago-gástrica. En 53 pacientes se constató esofagitis por reflujo. En el 75.6% de ellos la esofagitis era grave (C o D). Aunque todos los pacientes con esofagitis ingerían antiácidos y seguían un tratamiento con antagonistas de los receptores H₂ de la histamina, la

terapia sólo fue efectiva en el 35%. No existió correlación significativa entre los síntomas y el grado de esofagitis por reflujo. En pacientes con anastomosis gastroesofágica cervical la esofagitis por reflujo afectó al 56.4%, si la anastomosis era intratorácica al 88.6% ($p = 0.0039$). Tras una anastomosis gastroesofágica por esofagectomía la endoscopia rutinaria es obligatoria ya que el grado de esofagitis no guarda relación con la sintomatología. La anastomosis de la tubulización gástrica con el esófago debe realizarse en el cuello, pues el riesgo de esofagitis de reflujo es menor.

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