Primary gastric cancer in an oesophageal gastric graft after oesophagectomy

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Received 29 July 2010; received in revised form 10 February 2011; accepted 28 February 2011; Available online 24 August 2011

Abstract

Objective: Recent advances in surgical treatment of oesophageal cancer have improved the prognosis of early, locally advanced oesophageal cancer. Primary cancer from oesophageal graft is rare, but has been detected in long-term survivor. We analyzed data from patients who developed primary gastric cancer in an oesophageal graft to evaluate strategies of treatment and their outcomes. Methods: We retrospectively reviewed data from patients who developed primary gastric cancer in oesophageal graft at Samsung Medical Center between September 1994 and December 2009. The clinico-pathologic features and prognoses were investigated. Long-term survival rate was determined by Kaplan–Meier analysis. Results: Ten primary gastric graft cancers (five early gastric cancer (EGC), five advanced gastric cancer (AGC)) were diagnosed. The mean age was 69.0 (range 59.6–74.6). Initial operation was Ivor-Lewis transthoracic oesophagectomy in eight cases and three-field lymphadenectomy in two. The median period to detection of the primary gastric cancer graft after oesophagectomy was 50 (9–102) months. Seven gastric graft cancers were diagnosed by regular endoscopic examination. EGCs were treated with ESD in two cases, partial resection of stomach in one, and oesophagogastrojejunostomy in three, including one patient who underwent the operation after ESD. AGCs were treated with chemotherapy in one case, supportive care in one, and oesophagogastrojejunostomy in three. There was no adjuvant chemotherapy used in any case. The median follow-up period after second operation was 14 months (range 1–97). Six patients survived during this period. Three of the five AGC patients died. The estimated median survival rate of our cases was 70%. Conclusions: In areas of high prevalence of stomach cancer, regular endoscopic examinations of oesophageal gastric grafts may help in the early detection of primary gastric graft cancer. Reoperation with a colon graft is a potential treatment option for primary gastric graft cancer.

Keywords: Oesophageal cancer; Oesophagectomy; Gastric cancer; Survival rate; Graft

1. Introduction

Oesophageal cancer is an aggressive cancer with a high mortality rate [1–3]. The management of loco-regional oesophageal cancer has benefitted from major advances over the past 15 years. The low cure rates for oesophageal cancer after loco-regional therapy alone have prompted the inclusion of systemic chemotherapy in multimodality treatment regimens in order to control distant micrometastatic disease and enhance local radiation effects over the last 15 years [4]. The 5-year survival for all patients with oesophageal cancer improved only modestly over the last 30 years [1,3].

The stomach is the most commonly used oesophageal substitute after oesophagectomy in patient with oesophageal cancer. Primary cancer in oesophageal graft is a rare late complication, but has been detected in long-term survivors [5,6]. Therefore the primary gastric cancer could occur in the gastric graft [7,8]. However, little information is available regarding the treatment and outcome of primary gastric cancer after oesophagectomy in patient with oesophageal cancer.

The purpose of this study was to review our experiences of primary gastric cancer in oesophageal gastric graft after oesophagectomy to evaluate possible treatment strategies and outcomes.

2. Materials and methods

2.1. Population

We retrospectively reviewed the medical records of patients with primary gastric cancer in an oesophageal gastric graft after oesophagectomy performed for treatment of oesophageal cancer at Samsung Medical Center, Seoul,
Korea between September 1994 and December 2009, the observation period ended on May 1, 2010. A total of 1227 patients underwent curative surgery for oesophageal cancer during the study period. We excluded patients with other oesophageal graft substitute, oesophageal cancer recurrence in the gastric graft, and patients with oesophagectomy due to gastro-esophageal junction tumor. A total of 1111 patients underwent curative oesophageal cancer surgery with a gastric substitute during the study period. The initial operation for oesophageal cancer with a gastric graft included transthiatal oesophagectomy, Ivor-Lewis transthoracic oesophagectomy, tri-incisional oesophagectomy, and oesophagectomy plus a three-field lymphadenectomy. Only 10 patients (0.9%) were diagnosed as primary gastric cancer during follow-up period.

2.2. Medical and surgical treatment and follow-up

Early gastric cancer (EGC) could be treated by endoscopic submucosal dissection (ESD), if it met the indications described by the Japanese Society for Gastroenterological Endoscopy (JSGE) for endoscopic mucosal resection (EMR) of an EGC, such as type I lesion less than or equal to 2 cm, type IIb and IIc less than or equal to 1 cm, and intestinal type adenocarcinoma limited to the mucosa [9]. ESD was performed under local anesthesia while monitoring vital signs.

If surgical resection was possible in good performance patients with EGC that could not be resected by ESD or locally advanced gastric cancer (AGC), we performed gastrectomy and colon interposition for intrathoracic gastric graft replacement. In one patient with EGC and supposed submucosal invasion by tumor, we resected the tumor with adjacent tissue and repaired it primorally. Colon interposition for intrathoracic gastric graft replacement was performed under general anesthesia with controlled ventilatory support.

If surgical treatment was impossible or a patient was the poor general condition, we evaluated the status of patient and treated medically. Chemotherapy was performed in the patient with a good performance status.

After colon interposition, all patients were followed at regular intervals of one to three months by physical examination, chest radiography, computed tomography (CT) of the lung and abdomen, annual endoscopy and the 2-deoxy-2 [18F] Fluoro-o-glucose position emission tomography/computed tomography (F-18 FDG PET/CT), as needed, if any abnormality was detected.

2.3. Statistical analysis

The Kaplan–Meier method was used to estimate survival probabilities. PASW statistical software (Statistical Package for the Social Sciences, Version 17.0 for Windows) was used. All data were collected retrospectively and stored in a database using PASW software.

3. Results

Ten primary gastric graft cancers (five EGC, five AGC) were diagnosed in all male patients. The mean age of all patients was 69.0 (range 59.6–74.6). The oesophageal cancer was squamous cell carcinoma in type in all patients. The initial operation performed was the Ivor-Lewis transthoracic oesophagectomy in eight cases and oesophagectomy plus a three-field lymphadenectomy in two cases. The median period to detect the primary gastric graft cancer after oesophagectomy was 50 (range 9–102) months. Only three patients presented with symptoms of gastric graft cancer, such as epigastric soreness, regurgitation, and dysphagia. The other seven patients were diagnosed by regular endoscopic examination. The cell type of gastric cancer was adenocarcinoma in all patients including one signet ring cell carcinoma (Table 1).

EGCs were treated with ESD in two cases, partial resection of gastric graft in one, and colon interposition for intrathoracic gastric graft replacement in three, including one patient who underwent the operation after ESD due to pathologic diagnosis of signet ring cell carcinoma. AGCs were treated with chemotherapy in one patients, supportive care in one, and colon interposition for intrathoracic gastric graft replacement in three. No patients received adjuvant chemotherapy (Table 1).

For retrosternal colon interposition for an intrathoracic gastric graft replacement, the median operating time was 485 min (range 430–590 min). The median operating time for taking down the gastric graft thoracically a right thoracotomy was 203 min (range 185–255 min). The median operating time of retrosternal colon interposition thorou
The median follow-up period after second operation or the diagnosis of primary gastric graft cancer was 14 months (range 1–97). During this period, six patients survived. Three out of five AGC patients died (Table 1). The causes of death were cancer bleeding in one patient, and pneumonia-induced septic shock in two patients. The estimated 5-year survival rate was 70%. Gastric cancer did not recur in any operated patients during follow-up period. However, oesophageal cancer recurred on left upper lobe as a single pulmonary nodule in one patient and was treated by thoracoscopic left upper lobectomy.

4. Discussion

The improvement of surgical techniques, better post-operative management, and multimodality treatment have allowed longer postoperative survival for patients with oesophageal cancer [1–3]. According to data from the Surveillance, Epidemiology and End Results (SEER) Program, the 5-year survival for all patients with oesophageal cancer improved only modestly over the last 30 years, from 5% in 1975–1977 to 17% in 1996–2004 [1]. Among these survivors, some develop gastric graft cancer, especially in areas with a high prevalence of stomach cancer [5,6]. Matsubara et al. reported that the overall relative risk (RR) of the secondary primary malignancy after oesophagectomy was 2.98, and that the relative risk of stomach cancer was 2.00 [5]. Motoyama et al. reported that 30% of the secondary primary malignancies were located in stomach and that 3.5% of patients developed a gastric carcinoma after oesophagectomy [6]. In our cases, only 10 patients (0.9%) were diagnosed with primary gastric graft cancer during follow-up period.

The etiology of secondary malignancy in gastric graft is still unclear [7,8,10]. Irradiation to the mediastinum during adjuvant therapy may cause carcinogenesis during long-term follow-up [7]. In a vagotomized gastric tube, the toxic effect of refluxed duodenal juice containing bile may lead to a reflux-induced gastric cancer [7,8]. However, Helicobacter pylori may not be considered as a cause of gastric graft cancer because this bacteria has not been routinely detected in such cases [7,11].

Koyanagi et al. reported that the differences in the proportion of second gastric cancer according to the route of reconstruction are attributable to differences in initial symptoms according to the route [12]. Dysphagia was the most frequent symptom in patients with new primary gastric graft cancer who underwent retrosternal and posterior mediastinal route reconstructions for their oesophagectomies [12]. In our study, only one patient had dysphagia. Seven patients had no symptoms and were diagnosed by routine annual endoscopic screening. Therefore, regular endoscopic exams allowed us to detect five asymptomatic EGCS and two AGCs. Cancers that are diagnosed clinically are associated with poor short-term survival, whereas cancers detected by periodic endoscopic screening tend to have a better prognosis as they are detected at earlier stages [10]. In our report, the median period to detection of primary gastric graft cancer after oesophagectomy was 50 months. The longest period to detection was 102 months. Sugita et al. reported that the average interval between oesophagectomy and detection of gastric tube carcinoma was 62.8 months [8], and Suzuki et al. reported that the mean interval was 72 months [13]. These results suggest that regular endoscopic examination is important for detecting primary gastric graft cancer as well as any recurrence of oesophageal cancer and should be continued beyond 5 years of follow-up [13].

In Korea as well as Japan, where stomach cancer is the most common cancer, an organized screening program for stomach cancer has been used. The screening test for stomach cancer, recommended as part of the National Cancer Screening Program in South Korea, is biannual upper endoscopy or upper gastrointestinal series are recommended for men and women over the 40 years old [14]. We think that the long-term follow-up including annual endoscopic exams of the oesophageal gastric graft could help to detect the gastric graft cancer early, especially in a high prevalence area of stomach cancer.

The opportunity of curative treatment of gastric graft cancer depends on the tumor stage and patient condition [7,10]. Early, single, mucosal cancers can be treated by EMR or ESD [8,9,15]. The indications for EMR or ESD for early-stage

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**Table 2. Complications after colon interposition for intrathoracic oesophageal gastric graft.**

<table>
<thead>
<tr>
<th>Complication</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laparotomy wound dehiscence</td>
<td>1</td>
</tr>
<tr>
<td>Prolonged air leak</td>
<td>2</td>
</tr>
<tr>
<td>Vocal cord palsy</td>
<td>3</td>
</tr>
<tr>
<td>Cervical anastomotic leak</td>
<td>1</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>1</td>
</tr>
</tbody>
</table>

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**Table 3. Literature review of surgical results of total gastrectomy and colon interposition.**

<table>
<thead>
<tr>
<th>Authors (published year)</th>
<th>Number of case</th>
<th>Anastomotic leak</th>
<th>Recurrence of tumor (mean F/U period)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ben-nun et al. (2000)</td>
<td>1</td>
<td>1</td>
<td>NR</td>
</tr>
<tr>
<td>Suzuki (2001)</td>
<td>3</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Sugiura (2002)</td>
<td>7</td>
<td>5</td>
<td>2 cases of GC, 2 cases of EC (NR)</td>
</tr>
<tr>
<td>Ikeda et al. (2003)</td>
<td>1</td>
<td>No</td>
<td>No (18 months)</td>
</tr>
<tr>
<td>Yoon (2010)</td>
<td>6</td>
<td>1</td>
<td>No, 1 cases of EC (14 months)</td>
</tr>
</tbody>
</table>

gastric graft cancer are similar to those for early-stage primary gastric cancer [8, 9]. Sugiyama et al. reported that of 15 patients treated by EMR, three required further surgery because of submucosal tumor invasion. All patients treated by EMR alone were alive without recurrence [8]. Of our cases, two out of 10 patients were treated by ESD. One patient was treated successfully. However, the other required further surgery after ESD due to pathologic diagnosis of signet ring cell carcinoma. These two patients were still alive at the end of the observation period and had no evidence of recurrence.

Total or partial gastrectomy for gastric graft cancer is a complex procedure and carries high morbidity and mortality rates [7, 8, 10]. In this series, one partial resection of residual stomach was performed in a patient who had the stenosis of inferior mesenteric artery orifice (Table 1). Partial gastrectomy is performed when the tumor is distant from the right gastroepiploic artery and does not reach the serosa [10]. Okamoto et al. reported three cases of partial resection of the residual stomach with no subsequent recurrence [7]. Reconstruction with colonic or jejunal grafts after gastrectomy occasionally uses the retrosternal and antero-thoracic route [7, 8, 10, 12]. Suzuki et al. reported three cases of total gastrectomy and reconstruction that were performed using the pedicled colon [13]. Total gastrectomies were performed successfully by Ben-Num et al. [16, 17], while Sugiyama et al. reported high surgical morbidity and treatment failures with this technique [8] (Table 3). In our series, although the complication rate was very high (83%), total gastrectomy and colon interposition for intrathoracic gastric graft replacement were successfully performed in six patients without perioperative mortality (Table 1). There was no evidence of recurrence of gastric cancer, and only one recurrence of oesophageal cancer after partial or total gastrectomy during 14 months follow-up period (Table 3). The estimated 5-year survival rate of patients treated by ESD or surgery was 84.7%. Therefore, we believe that total gastrectomy and retrosternal colon interposition is a good treatment choice in operable patients with locally advanced AGC or EGC in which EMR or ESD is contraindicated, even if there is high morbidity.

In conclusion, early diagnosis is of utmost importance for a better prognosis of gastric graft cancer. Long-term follow-up including annual endoscopic exams of the oesophageal gastric graft could help to detect the gastric graft cancer early, especially in a high prevalence area of stomach cancer. Endoscopic treatment might be the treatment of choice for early gastric graft cancer. Total gastrectomy and colon interposition might be a viable option of treatment of locally advanced gastric graft cancer.

References