

Surgical Treatment of Anastomotic Recurrence after Gastrectomy for Gastric Cancer

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Background: The purpose of this study was to evaluate the outcome of reoperation with curative intent for the treatment of anastomotic recurrent gastric cancer. **Methods:** Ten patients with anastomotic recurrence of gastric cancer who underwent reoperation from November 1995 to February 2011 were analyzed retrospectively. The time interval between the first operation and reoperation, recurrence pattern, type of surgery, survival, and postoperative outcome were analyzed. **Results:** The average time to recurrence after initial surgery was 48.8 months (median, 23.5 months). Of the ten patients, eight (80.0%) had recurrence at the esophagojejunostomy, one (10.0%) at the esophagogastrostomy, and two (20.0%) at the esophagus. Among these patients, five had combined metastasis or invasion to major organs in addition to anastomotic recurrence. Complete resection was achieved in five patients (50.0%), and incomplete resection or bypass surgery was performed in the remaining five patients (50.0%). The overall median survival time was 7.0 months (range, 2.2 to 105.5 months). The median survival time following complete resection and palliative surgery (incomplete resection or bypass surgery) was 28.1 months (range, 4.2 to 105.5 months) and 5.5 months (range, 2.2 to 7.5 months), respectively. **Conclusion:** Surgical resection of anastomotic recurrent gastric cancer should be implemented only in selected patients in whom complete resection is possible.

Key words: 1. Neoplasm recurrence
2. Anastomosis
3. Surgical procedures, operative
4. Stomach neoplasms

INTRODUCTION

Gastric cancer is the fourth most common cancer in the world and a major cause of cancer death worldwide [1]. Currently, the only potentially curative treatment for gastric cancer is radical gastrectomy. Early detection, improvements in extended lymphadenectomy, and adjuvant chemotherapy have all drastically improved the survival rate of gastric cancer. However, despite these advances, recurrence is still

possible and is often the cause of unsuccessful recovery from gastric cancer [2,3]. The main reason for recurrence is the advanced stage of many cases of gastric cancer at the time of diagnosis.

Even after curative resection, death from gastric cancer is primarily due to recurrence. The recurrence rates of gastric cancer after curative resection are not uniform but vary according to the time after surgery. More than 90% of patients relapse within five years after surgery, and 70% relapse with-

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in two years. Wu et al. [4] reported that cumulative recurrence rates were 53.5%, 80.0%, 89.0%, 94.7%, and 96.3% at 1, 2, 3, 4, and 5 years, respectively. These high rates of recurrence have been attributed to abundant lymphatic channels within the gastric wall that provide channels for mucosal skip lesions and numerous potential pathways of lymphatic drainage away from the stomach. Local recurrence may occur in patients who underwent R0 resection. Recurrence patterns of gastric cancer include locoregional, hepatic, or peritoneal lesions [5,6]. Unfortunately, the diagnosis of recurrence is difficult, prognosis is unreliable, and no standard treatment has been established [7]. Gastric cancer carries a poor prognosis when local recurrence has developed, and any attempts at curative treatment are generally considered futile. Although chemotherapy is an important treatment for recurrent gastric cancer, it often produces disappointing results. Indeed, many patients die within one year of diagnosis due to recurrence [7]. Four types of local recurrence can be differentiated according to location and origin: 1) local lymph node metastasis, 2) extraluminal recurrence, 3) recurrence within the remnant stomach, and 4) anastomotic recurrence following gastrectomy. Surgical intervention has been limited to locoregional recurrent gastric cancer [8], and in such cases, surgical treatment may play a role in handling recurrence. The goal of our research was to evaluate the outcomes of surgical treatment for anastomotic recurrent gastric cancer.

METHODS

From November 1995 to February 2011, ten patients with anastomotic recurrent gastric cancer underwent surgical intervention in the Department of Thoracic and Cardiovascular Surgery at Samsung Medical Center, Seoul, Republic of Korea. The eligibility criteria for this study included 1) histologically confirmed gastric carcinoma, 2) curative total or subtotal gastrectomy (R0 resection) with lymph node dissection for gastric cancer, 3) anastomotic recurrence after operation for gastric cancer, and 4) reoperation of recurrent gastric cancer with curative intent. We collected and analyzed patient characteristics including sex, age, type of recurrence, time to recurrence, surgical procedure performed during primary and secondary operations, previous hospital location for

primary operation, original T and N staging, number of lymph node metastases, and pathology at primary operation. Follow-up evaluation consisted of patient history, physical examination, and laboratory testing including tumor markers, chest radiography, endoscopy, computed tomography (CT), and position emission tomography (PET).

Recurrences were classified as locoregional, lymphatic (regional and distant lymph node metastases), hematogenous, and peritoneal. Locoregional recurrence was defined as cancer recurrence at the resection margin, within the lymph nodes (including regional, retropancreatic, retrocrural, and para-aortic nodes), or in the operation bed within the region of the resection and above the pancreas and abdominal wound. Peritoneal recurrence was defined as cancer recurrence in the abdominal cavity. Hematogenous recurrence was defined as any metastatic lesion in the liver, lung, bone, ovary, spleen, testis, or other distant organ.

Surgical resection was performed for recurrent lesions in patients for whom surgery was indicated based on multidisciplinary team discussion. All patients in this study underwent a potentially curative operation for recurrent cancer. The surgery for recurrence was categorized as curative resection or palliative resection. Curative resection was intended to improve survival through removal of metastatic lesions. Complete resection was defined as no macroscopic or microscopic evidence of residual tumor, and incomplete resection was defined as macroscopic or microscopic evidence of residual tumor due to invasion of a major organ or vessel. Palliative resection such as bypass surgery was performed solely to alleviate symptoms.

RESULTS

1) Patient characteristics

This study included seven males and three females, ranging in age from 38 to 70 years (mean, 56.5 years). The major clinicopathologic characteristics of the patients are listed in Table 1. Eight of ten patients received postoperative chemotherapy after total or subtotal gastrectomy. The median time between recurrence and initial operation was 23.2 months (range, 5.1 to 156.7 months). Of the ten patients, nine underwent total gastrectomy and one had subtotal gastrectomy.

Table 1. The characteristics of patients with first operation (n=11)

Variable	Value
Age (yr)	54.3 (30-68)
Gender	
Male	7 (70.0)
Female	3 (30.0)
Procedure performed at first operation	
Total gastrectomy	9 (90.0)
Subtotal gastrectomy	1 (10.0)
Pathologic T category	
T1	1 (10.0)
T2	3 (30.0)
T3	3 (30.0)
T4	1 (10.0)
Unknown	2 (20.0)
Pathologic N category	
N0	1 (10.0)
N1	1 (10.0)
N2	5 (50.0)
N3	1 (10.0)
Unknown	2 (20.0)
Stage	
IA	1 (10.0)
IIB	2 (20.0)
IIIA	2 (20.0)
IIIB	1 (10.0)
IV	2 (20.0)
Unknown	2 (20.0)
Histology	
Adenocarcinoma	7 (70.0)
Signet ring cell	3 (30.0)

Values are presented as mean (range) or number (%).

2) Recurrence pattern and reoperation types

All ten patients had anastomotic recurrent cancer. The patterns of recurrence among the ten patients are summarized in Table 2. Eight patients (80.0%) had recurrence at the esophagojejunostomy, one (10.0%) at the esophagogastrostomy, and two (20.0%) at the esophagus. Of the ten patients, five had combined metastasis or invasion to major organs in addition to anastomosis recurrence. Among these five patients, pulmonary metastatic lesions were found in two patients during reoperation. One patient (10.0%) had peritoneal seeding during surgery and two patients had pleural seeding. Major organ invasions (aorta, liver, and diaphragm) of the recurrent tumor were found in two patients during surgery.

The recurrence characteristics and operative techniques are

summarized in Table 3. Seven patients underwent esophagojejunostomy, two underwent esophagocolojejunostomy, one underwent jejunojejunostomy, and two underwent colocolostomy. One patient underwent exploratory laparotomy, seven underwent feeding jejunostomy, and one underwent pulmonary metastasectomy. Complete tumor resection was achieved in five patients (50.0%). Incomplete resection was performed in four patients (40.0%), and a bypass operation was performed in one patient (10.0%) because of peritoneal seeding.

3) Survival after reoperation

The median survival time was 7.0 months (range, 2.2 to 105.5 months). Survival data are summarized in Table 2. The median survival time after surgery for recurrent tumors was 28.1 months (range, 4.2 to 105.5 months) following complete resection. Four patients had incomplete resection, and their median survival time after surgery was 4.9 months (range, 2.2 to 7.5 months). A bypass operation was performed in one patient, who survived for 5.5 months. Postoperatively, five patients underwent adjuvant chemotherapy and three patients had adjuvant radiotherapy.

DISCUSSION

Gastric cancer is one of the most common causes of cancer death worldwide. Even after curative resection, 22% to 50% of patients experience disease recurrence [6,9,10]. Peritoneal, hematogenous, and locoregional recurrences are the most common recurrence patterns in gastric cancer. Hematogenous recurrence occurs most commonly in the liver, followed by the lungs. Locoregional recurrence occurs most commonly at the anastomosis site or stump [6]. An isolated locoregional recurrence was reported in 6% to 46% of patients who underwent surgical resection [4,6,9,11,12]. Locoregional recurrence results from direct tumor proliferation or lymphatic spread within the abdominal cavity [13].

There are many risk factors for recurrence of gastric cancer, including lymph node metastasis, serosal invasion, infiltrative or diffuse type, large tumor size (4 cm or greater), undifferentiated tumor, and proximal tumor location [6]. After surgery, the average length of time until recurrence was 21.8 months. Patients with locoregional recurrence averaged 27.3

Table 2. Postoperative results and survival data

Patients	Type of surgery	Lymph node metastasis	Combined metastasis or invasion to major organs	Survival (mo)	Disease-free survival (mo)	Vital status
1	Incomplete	3/5(+)	Multi-organ invasion	3.4	0	Death
2	Complete	1/12(+)	(-)	4.2	4.2	Death
3	Complete	0/3(-)	(-)	105.5	105.5	Survival
4	Incomplete	Not checked	Aorta invasion	6.4	5.5	Death
5	Incomplete	6/10(+)	Pulmonary metastasis, pleural seeding	7.5	0	Death
6	Complete	0/3(-)	(-)	28.1	20.3	Death
7	Bypass surgery	Not checked	Peritoneal seeding	5.5	0	Death
8	Incomplete	8/10(+)	Pulmonary metastasis, pleural seeding	2.2	1.9	Death
9	Complete	0/5(-)	(-)	48.0	48.0	Survival
10	Complete	4/11(+)	(-)	11.9	10.7	Survival

Table 3. Recurrence characteristics and perioperative details (n=11)

Variable	Value
Site of recurrence	
Esophagojejunostomy	8 (80.0)
Esophagogastrostomy	1 (10.0)
Esophagus (not esophago-jejunostomy)	2 (20.0)
Lung	2 (20.0)
Lymph node metastasis at reoperation	
(+)	5 (50.0)
(-)	3 (30.0)
Unknown	2 (20.0)
Procedure performed at reoperation	
Transthoracic esophagectomy	8 (80.0)
Esophagojejunostomy	7 (70.0)
Esophagocolojejunostomy	2 (20.0)
Explorative laparotomy	1 (10.0)
Jejunojejunostomy	1 (10.0)
Colocolostomy	2 (20.0)
Feeding jejunostomy	7 (70.0)
Pulmonary metastasectomy	1 (10.0)
Adjuvant chemotherapy	6 (60.0)
Adjuvant radiotherapy	4 (40.0)

Values are presented as number (%).

months between surgery and recurrence, while those with peritoneal and hematogenous recurrence averaged 18.1 and 14.6 months, respectively [6].

Diagnosis is improved by modern imaging techniques and is mainly determined by increased expression of tumor markers, endoscopy, CT, and PET-CT. Some studies showed the usefulness of monitoring carcinoembryonic antigen, carbohydrate antigen (CA) 19-9, and CA 72-4 for detecting re-

currence of resected gastric cancer [14,15]. Endoscopic examination is the most accurate tool to identify anastomotic or gastric stump recurrences after subtotal gastrectomy, allowing early diagnosis and radical treatment in highly selected patients [16].

In previous studies, the average survival time after recurrence was 6.0 to 8.7 months: 6.4 months for patients with peritoneal recurrence, 9.4 months for hematogenous recurrence, and 11.0 months for locoregional recurrence. Overall, 70% of the patients died within one year of diagnosis, and 89% died within two years. The mean survival time after complete resection for recurrent tumors was 21.6 months, compared with 11.6 months for patients who had incomplete resection. A bypass operation was performed in one patient, who survived 8.5 months [6,12].

There is no effective or specific diagnostic method for recurrence. Moreover, a standard treatment for patients with recurrence has not yet been established. The goals of treating recurrent gastric cancer are to increase survival and relieve symptoms [17]. Meta-analyses of randomized, controlled trials in patients with recurrent gastric cancer have demonstrated that systemic chemotherapy considerably improves survival compared with the best supportive care [18,19]. However, despite the effectiveness of S-1 and cisplatin combination chemotherapy [20], the median survival time for patients with gastric cancer recurrence remains unsatisfactory at approximately 12 months. Palliative resection is indicated in highly selected symptomatic patients; in such cases, surgery is usually performed to restore the passage of food, and tumor re-

duction is a minor goal [6,12]. Nonetheless, surgery may play a role in the treatment of recurrent gastric cancer. Assuming that complete resection can be achieved and the patient can tolerate surgery, there might be some benefits from reoperation. The resectability of a recurrent tumor may be the most important factor determining survival after resection, as shown by our results and a previous report [6,17].

Surgery is very uncommon for patients with anastomotic site recurrence after surgery for gastric cancer. According to our study, patients with incomplete resection died within a few months after reoperation; however, three of five patients with complete resection survived. Based on biopsy results, surgery is beneficial if there is no lymph node metastasis; however, the survival rate is not significantly improved if there is lymph node metastasis. We believe that an aggressive surgical approach is beneficial whenever there is a completely resectable lesion. To ensure early detection, endoscopy and PET-CT evaluation should be performed periodically during follow-up. This is particularly important for recurrence at the esophagojejunostomy site, where early detection greatly improves the chance of complete resection. In addition, careful use of criteria and thoughtful deliberation are needed when selecting patients with anastomotic site recurrence for reoperation. Because the number of patients in this study was small, we could not perform statistical analysis, and our conclusions may not be generalizable. Therefore, further studies including more patients are necessary to determine the effectiveness of surgery in such cases.

In conclusion, surgical resection of anastomotic recurrent gastric cancer should be implemented only in selected patients in whom complete resection is possible.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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