

Original Article



Surgical Outcomes and Survival Prognostic Factors for Palliative Gastrectomies in Stage IV Resectable Gastric Cancer Outlet Obstruction Patients

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ABSTRACT

Purpose: Currently, there is no clear evidence to support any specific treatment as a principal therapy for stage IV gastric cancer outlet obstruction (GCOO) patients. This study evaluated the outcomes of palliative gastrectomies and survival prognostic factors in patients with stage IV resectable GCOO.

Materials and Methods: We retrospectively reviewed the medical records of 48 stage IV GCOO patients who underwent palliative gastrectomies between June 2010 and December 2019. Palliative gastrectomies were performed only in patients with resectable disease. Early surgical outcomes and prognostic factors were analyzed using univariate and multivariate analyses.


Results: There were no specific risk factors for postoperative complications, except for being underweight. Severe postoperative complications developed in five patients, and most of the patients underwent interventional procedures and received broad-spectrum antibiotics for intra-abdominal abscesses. The multivariate survival analysis showed that palliative chemotherapy is a positive prognostic factor, while the specific type of hematogenous and lymphatic metastasis is a negative prognostic factor.

Conclusions: We recommend that the treatment method for stage IV GCOO should be selected according to each patient's physical condition and tumor characteristics. In addition, we suggest that palliative gastrectomies can be performed in stage IV resectable GCOO patients without unfavorable prognostic factors (types of hematogenous and lymphatic metastases).

Keywords: Gastric cancer; Palliative care; Gastric outlet obstruction; Gastrectomy; Survival

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Conflict of Interest

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

INTRODUCTION

Gastric outlet obstruction is a late-stage complication of advanced gastrointestinal cancer. If the obstruction is not resolved, the patient will eventually become malnourished and develop cachexia [1-3]. It is especially difficult to plan a treatment strategy that offers symptom relief and survival improvement for stage IV gastric cancer outlet obstruction (GCOO) patients.

Many surgical and interventional treatments, such as gastrojejunostomies (GJ), are used as palliative treatment methods for stage IV patients with GCOO [2]. Self-expanding metal stents (SEMS) are increasingly preferred for use in palliative methods because they offer fast symptom relief, low complication rates, and short hospital stays. Despite the controversy regarding survival benefits gained from the procedure [4-7], palliative gastrectomies are theoretically a good option for pain relief.

SEMS are currently being used as a preferred palliative method because many physicians believe that surgical treatments, including GJs or palliative gastrectomies, present a high postoperative complication risk for stage IV GCOO patients [8,9]. However, SEMS have a higher re-obstruction rate than surgery because of tumor ingrowth and outgrowth [10]. Therefore, SEMS are recommended for patients with the shortest life expectancies [11].

In clinical practice, some stage IV gastric cancer patients exceed survival expectations because of favorable clinical conditions or slow disease progression. Therefore, patients with longer survival prospects may require different treatment options.

The authors of a representative study indicated that palliative gastrectomies do not improve survival rates and generally cannot be justified [12]. However, the authors conceded that palliative gastrectomies can be considered when severe and complicated symptoms, such as obstructions, emerge during chemotherapy.

The current study aimed to evaluate the outcomes of palliative gastrectomies and analyze prognostic factors in patients with stage IV resectable GCOO.

MATERIALS AND METHODS

Patients

We retrospectively reviewed prospectively collected data from 48 stage IV gastric cancer patients who underwent palliative gastrectomies between January 2010 and December 2019 at Hanyang University Guri Hospital. Each surgeon chose the surgical procedure according to the individual needs of the patients and their caretakers. The decision to perform a palliative gastrectomy was based on observations from laparoscopic or open explorations. Palliative gastrectomies were performed only in resectable gastric cancer patients. We defined resectable gastric cancer cases as those in which the affected part of the stomach, including the tumor, could be easily mobilized. We defined unresectable gastric cancer cases as those in which the affected part of the stomach, including the tumor, is immobilized due to fixation of the pancreas, hepatoduodenal ligament, or major arteries.

We excluded stage IV patients with near or total obstructions of the small bowel, colon, or rectum due to advanced peritoneal dissemination.

Approval was obtained from the Institutional Review Board of Hanyang University Guri Hospital of Korea, College of Medicine (2017-02-014-006).

Technical assessment for resectability

We evaluated resectability by lifting the stomach, including the portion with the tumor, because in cases of distal gastric cancer, it is especially necessary to ensure that the first part of the duodenum is free from the pancreas and the hepatoduodenal ligament. If it was difficult to evaluate resectability through laparoscopic exploration, we added a mini-laparotomy incision and confirmed resectability by lifting the stomach with the thumb and index finger.

Clinical analysis

Clinical data, including patient age, sex, body mass index (BMI, kg/m²), American Society of Anesthesiologist (ASA) score, history of major abdominal surgery, and other patient information, were obtained from medical records. The operation method, extent of the gastrectomy (total versus distal gastrectomy), operation time, postoperative complications, postoperative mortality, and length of postoperative hospital stay were also recorded. The pathologic results were analyzed for tumor size, number of retrieved lymph nodes, and the 8th American Joint Committee on Cancer (AJCC) staging system score.

The underweight classification was defined as a BMI below 18.5 kg/m². The ASA classification for each patient was determined by anesthesiologists on the day before the surgery. Patient preoperative albumin levels were measured when the patient was admitted to the hospital. Hypoalbuminemia was defined as serum albumin levels below the normal range (<3.5 g/dL).

Postoperative complications were defined as any condition requiring conservative or surgical treatment. Severe postoperative complications were defined as those that required management with endoscopic or interventional procedures or re-operation (the accordion expanded classification, >level 3) [13]. Thirty-day mortality (i.e., death within 30 days of surgery) was estimated as the postoperative mortality rate.

Follow-up of gastric cancer patients

Postoperative palliative chemotherapy was recommended to most patients. The follow-up program consisted of a physical examination, laboratory tests with tumor markers, gastrofiberscopy, and abdomen and pelvic computed tomography. All the patients were followed-up every 3 months until death. The last follow-up date was June 2020.

Statistical analyses

The statistical analyses were performed using SPSS version 21.0 for Windows (SPSS, Inc., Chicago, IL, USA). All values are expressed as means±standard deviations (SD). The categorical variables were analyzed using the χ^2 test, and the continuous variables were analyzed with the Student's t-test. A multivariate analysis was performed to identify the risk factors associated with early surgical outcomes. Factors with relatively small P-values (P<0.1) in the univariate analyses were selected as variables in the multivariate logistic regression models. Hazard ratios with 95% confidence intervals were estimated for each variable from the multivariate model. A P-value <0.05 was considered statistically significant.

RESULTS

Clinical characteristics

The clinical characteristics of the 48 patients are shown in **Table 1**. The median age was 69.5 years. Twenty-four of the patients (50.0%) were 70 years or older. About half of the patients had one or more comorbid conditions. Sixteen patients (33.3%) had BMIs ≤ 18.5 and were defined as underweight. Low hemoglobin anemia was observed in 21 patients (43.8%). Low serum albumin levels were detected in 17 patients (35.4%).

Operative findings and surgical outcomes

According to the operative findings (**Table 2**), 33 patients showed peritoneal dissemination. Twenty-five patients underwent laparoscopic gastrectomies, and D2 gastrectomies were performed on 15 patients (31.3%). The mean operation time was 170.2 minutes. Total gastrectomies were performed on 25.0% of the patients. Postoperative complications occurred in 11 patients (22.9%), 5 (10.4%) of whom experienced severe postoperative complications. Two patients experienced postoperative mortality (4.2%). The mean postoperative hospital stay length was 16.3 days. Thirteen patients presented with Borrmann type IV gastric cancer, and lymph node metastasis was seen in most patients. More than half the patients required soft oral intake for more than six months after surgery. A total of 31 patients received palliative chemotherapy after surgery. **Fig. 1** shows the overall survival (OS) curve for all the patients.

Univariate and multivariate analyses of postoperative complications and survival rates

Table 3 shows the results of the univariate analysis of the postoperative complication and 1-year survival rates. The severe postoperative complication rate was significantly higher in the underweight patients (BMI < 18.5) than in the non-underweight patients. The univariate analysis of the 1-year survival rate showed that being elderly (> 70 years old), having a high ASA score (over 3), tumor spread pattern (peritoneum, hematogenous, lymphatic), and palliative chemotherapy administration are all significant prognostic factors.

Table 1. Clinical characteristics of the gastric outlet obstruction patients (n=48)

Variables	Values
Age (yr)	66.2 \pm 15.6
≥ 70	24 (50.0)
Sex	
Male	28 (58.3)
Female	20 (41.7)
Comorbidity	
Yes	24 (50.0)
BMI (kg/m ²)	20.8 \pm 3.3
< 18.5	16 (33.3)
Weight change ($> 10\%$)	29 (60.4)
History of major abdominal surgery	1 (2.1)
ASA score	
1 or 2	22 (45.8)
≥ 3	26 (54.2)
Symptom onset before surgery (days)	30.5 \pm 17.8
Hemoglobin level (g/dL)	
< 10.0	21 (43.8)
Albumin level (g/dL)	
< 3.5	17 (35.4)

Values are presented as mean \pm standard deviation or number (%).
BMI = body mass index; ASA = American Society of Anesthesiologist.

Table 2. Operative findings and surgical outcomes from gastric outlet obstruction (n=48)

Variables	Values
Causes of M1 stage	
Peritoneal carcinomatosis	33 (68.8)
Hematogenous metastasis (lung, liver, and others)	8 (16.7)
Lymphatic metastasis	7 (14.6)
Type of surgery	
Open	23 (47.9)
Laparoscopy	25 (52.1)
Extent of the gastrectomy	
Distal	36 (75.0)
Total	12 (25.0)
Extent of the lymph node dissection	
<D2	33 (68.8)
D2	15 (31.3)
Operation time (min)	170.2±42.7
Overall postoperative complications	11 (22.9)
Severe postoperative complications	5 (10.4)
Mortality (within 30 days)	2 (4.2)
Hospital stay after surgery (days)	16.3±7.4
Macroscopic type	
Borrmann type IV	13 (27.1)
Others	35 (72.9)
Tumor size (cm)	9.1±4.3
Depth of tumor invasion	
T3	2 (4.2)
T4a	46 (95.8)
Lymph node metastasis	
N0	3 (6.3)
N1	2 (4.2)
N2	7 (14.6)
N3	36 (75.0)
Number of retrieved lymph nodes	
<15	1 (2.1)
Histology	
Differentiated	20 (41.7)
Undifferentiated	28 (58.3)
Administration of palliative chemotherapy	31 (64.6)
Period of oral soft food (mon)	9.1 (0.2–68.8)
Oral soft diet lasting over 6 months	32 (66.6)
Survival period (mon)	
Peritoneal carcinomatosis	12.1 (0.6–70.0)
Hematogenous metastasis	7.6 (4.5–14.5)
Lymphatic metastasis	5.6 (0.6–12.1)

Values are presented as mean±standard deviation, median (range), or number (%).

Table 4 shows the Cox multivariate proportional hazard analysis results for OS. The OS rates were affected by the M1 tumor spread pattern and palliative chemotherapy.

Patients with severe postoperative complications

Five severe postoperative complications were observed (**Table 5**). Of the 2 patients who died, the causes of death were myocardial infarction and brain infarction during the recovery period. The deceased patients were 78 and 82 years old, respectively. The three other patients with severe postoperative complications had intra-abdominal abscesses and were treated with a pigtail insertion procedure.

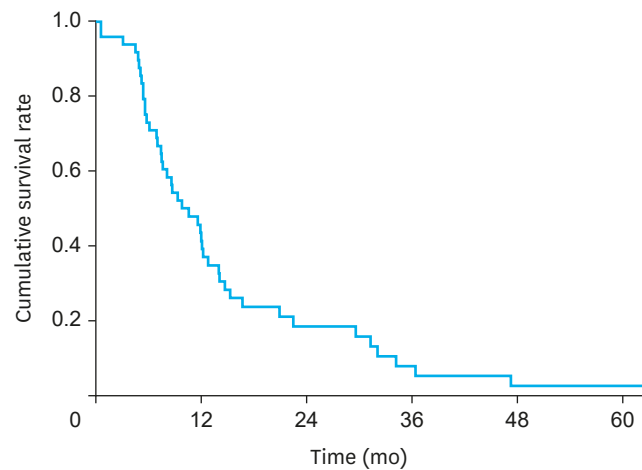


Fig. 1. OS curve of the stage IV GCOO patients.
OS = overall survival; GCOO = gastric cancer outlet obstruction.

DISCUSSION

GCOO can occur as a late-stage complication of gastric cancer [14]. Furthermore, obstruction is a pre-terminal state associated with limited life expectancy. Therefore, the treatment goal should focus on enabling and maintaining oral intake for as long as possible. We argue that the manifestations of a GCOO patient's deteriorating clinical condition, including vomiting, dehydration, and nutritional deficiencies, can be prevented or slowed down with near-normal oral food intake. We also have concluded that proper oral intake can increase compliance with palliative chemotherapy, which is an important prognostic factor for OS of stage IV gastric cancer patients.

Gastrectomies, gastrojejunostomies, and SEMS are representative palliative treatment methods for stage IV GCOO patients. In practice, many clinicians prefer gastrojejunostomies or SEMS as the primary palliative treatment methods for stage IV GCOO patients because of the high morbidity and mortality rates associated with palliative gastrectomies.

Although SEMS have the benefits of low complication rates and rapid patient oral intake during recovery [8,9], stent re-insertion may be required sooner than expected for some patients due to stent re-obstructions caused by tumor ingrowth or overgrowth [10]. Most patients who undergo SEMS insertions cannot return to their previous dietary lifestyle and must eat soft food because of the small diameter of the SEMS. Therefore, because of the high risk of stent obstruction, SEMS should only be inserted in patients whose prognoses are poor [11].

Therefore, it is questionable whether SEMS should be applied as a primary palliative method for all stage IV GCOO patients. Considering the possibility for stent re-obstruction and the poor diet quality associated with SEMS, gastrojejunostomies might be a good alternative option for patients whose life expectancies are longer. However, one study found that half the patients with non-resected gastric cancer developed severe tumor-related complications at some point after the procedure [15]. There is also the possibility that some patients who have undergone gastrojejunostomies might not be able to maintain oral food intake as tumor growth progresses. Therefore, considering these factors, palliative gastrectomies are considered the most reasonable palliative method [4,16].

Stage IV Gastric Cancer Outlet Obstruction

Table 3. The univariate analyses of postoperative complications and 1-year survival rate

Variables	Number	Overall complications	P-value	Severe complications	P-value	1-year survival rate (%)	P-value
Age (yr)			0.303		0.636		0.002
≥70	24	7 (29.2)		3 (12.5)		16.7	
<70	24	4 (16.7)		2 (8.3)		70.6	
Sex			0.061		0.279		0.193
Male	28	9 (32.1)		4 (14.3)		49.7	
Female	20	2 (10.0)		1 (5.0)		35.0	
Comorbidity			0.731		0.636		0.619
Yes	24	5 (20.8)		2 (8.3)		41.7	
No	24	6 (25.0)		3 (12.5)		45.8	
BMI (kg/m ²)			0.339		0.023		0.119
≥18.5	32	6 (18.8)		1 (3.1)		50.0	
<18.5	16	5 (31.3)		4 (25.0)		29.2	
ASA score			0.473		0.781		0.001
1 or 2	22	4 (18.2)		2 (9.1)		72.4	
≥3	26	7 (26.9)		3 (11.5)		19.2	
Hemoglobin level (g/dl)			0.897		0.441		0.414
<10.0	21	5 (23.8)		3 (14.3)		37.5	
≥10.0	27	6 (22.2)		2 (7.4)		48.1	
Albumin level (g/dl)			0.433		0.236		0.791
<3.5	17	5 (29.4)		3 (17.6)		35.3	
≥3.5	31	6 (19.4)		2 (6.5)		47.8	
M1 classification			0.438		0.904		0.004
Peritoneum	33	6 (18.2)		3 (9.1)		51.3	
Hematogenous	8	2 (25.0)		1 (12.5)		37.5	
Lymphatic	33	6 (18.2)		3 (9.1)		14.3	
Type of surgery			0.616		0.567		0.491
Open	23	6 (26.1)		3 (13.0)		43.5	
Laparoscopic	25	5 (20.0)		2 (8.0)		43.3	
Extent of the gastrectomy			0.844		0.434		0.269
Distal	36	8 (22.2)		3 (8.3)		44.1	
Total	12	3 (25.0)		2 (16.7)		41.7	
Extent of the lymph node dissection			0.257		0.552		0.073
<D2	15	5 (33.3)		1 (10.4)		26.7	
≥D2	33	6 (18.2)		4 (12.1)		51.0	
Macroscopic type			0.440		0.507		0.076
Borrmann type I, II, and III	35	7 (20.0)		3 (8.6)		45.2	
Borrmann type IV	13	4 (30.8)		2 (15.4)		38.5	
Lymph node metastasis			0.335		0.434		0.681
N0, N1, and N2	12	4 (33.3)		2 (16.7)		41.7	
N3	36	7 (19.4)		3 (8.3)		44.3	
Histology			0.261		0.936		0.758
Differentiated	20	3 (15.0)		2 (10.0)		44.4	
Undifferentiated	28	8 (28.6)		3 (10.7)		42.9	
Palliative chemotherapy			0.137		0.236		<0.001
Yes	31	5 (16.1)		2 (6.5)		64.2	
No	17	6 (35.3)		3 (17.6)		5.9	

BMI = body mass index; ASA = American Society of Anesthesiologist.

Several studies have concluded that palliative gastrectomies do not contribute to significant survival gains for stage IV gastric cancer patients, however [4,6]. In fact, some authors have concluded that palliative surgical procedures, including GJ, are associated with poor surgical outcomes, including postoperative mortality, longer recovery times, and poor quality of life [6,17]. One study reported that pre-pyloric invasion may increase the incidence of duodenal stump leakage [18]. However, it should be noted that these studies were conducted among a large number of high-risk stage IV patients with low resectability.

Table 4. The multivariate analysis of prognostic factors associated with OS

Variables	OS		
	Hazard ratio	95% confidence interval	P-value
Classification of M1 stage			
Peritoneum			
Hematogenous	0.241	0.096–0.604	0.002
Lymphatic	0.135	0.040–0.460	0.001
Chemotherapy (yes/no)	6.522	2.833–15.013	<0.001
Elderly (≥ 70 / < 70)	0.490	0.210–1.146	0.100
Borrmann type (IV/others)	0.527	0.244–1.139	0.103
ASA Score (≥ 3 / < 3)	0.305	0.064–1.448	0.135

OS = overall survival; ASA = American Society of Anesthesiologist.

Table 5. Patients with severe postoperative complications

Patient	Age	Sex	Type of M1	Operation name	Comorbidity	Complication	Treatment	Outcome	Hospital stay
Patient 1	78	Male	Peritoneum	Total gastrectomy		Myocardial infarction	Medical treatment	Death	18
Patient 2	77	Male	Peritoneum	Distal gastrectomy		Intra-abdominal abscess	Pig-tail insertion	Improved	30
Patient 3	48	Male	Lymphatic	Distal gastrectomy	Hypertension	Intra-abdominal abscess	Pig-tail insertion	Improved	47
Patient 4	26	Male	Peritoneum	Total gastrectomy		Intra-abdominal abscess	Pig-tail insertion	Improved	27
Patient 5	82	Female	Lymphatic	Distal gastrectomy	Diabetes, Parkinson's disease	Brain infarction	Medical treatment	Death	18

Several guidelines suggest that palliative gastrectomies should only be performed to relieve symptoms [19,20]. Therefore, it is necessary to evaluate the impact of palliative gastrectomies on outcomes for stage IV patients with complicated symptoms. Some meta-analyses have concluded that palliative gastrectomies might offer benefits for survival and quality of life [21,22]. Additionally, other studies have reported that palliative gastrectomies are more helpful when selectively performed on patients with stage IV GCOO [23]. Therefore, it is necessary to select only patients whose clinical conditions can safely endure palliative gastrectomies and evaluate whether the patients have prognostic factors favorable to the procedure. Accordingly, we excluded patients with extremely low resectability, which is directly associated with serious postoperative complications.

In our study, the median survival time was 9.8 months, and the 1-year survival rate was 43.5%. Contrary to previous studies that identified several postoperative complication risk factors associated with nutritional deficiencies [24-26]. We did not find any risk factors, except for low BMI (underweight). Severe postoperative complications developed in five patients. Two of the 5 patients died within 30 days of surgery, but the causes of death were myocardial infarction and brain infarction, which were not directly related to the surgeries. The other three patients underwent pigtail insertion procedures and received broad-spectrum antibiotics to treat intra-abdominal abscesses. Considering that the two patients who died were elderly (82 and 78 years old) and that serious complications requiring re-operation did not occur, we are confident that palliative gastrectomies can be safely applied for patients with stage IV GCOO. Thirty-one patients (64.6%) received palliative chemotherapy after surgery. Most of the patients were able to return to their previous diet within a month of surgery. The soft diet maintenance period of oral food intake was 9.1 months. Thirty-two patients (66.6%) were able to maintain oral food intake (soft diet) for at least 6 months. Ultimately, most of the patients were unable to have oral intake due to the progression of extensive peritoneal dissemination in the last stage.

Our multivariate analysis showed that palliative chemotherapy is an important favorable factor for OS among stage IV GCOO patients. On the other hand, the specific type of lymphatic or hematogenous metastasis was an unfavorable prognostic factor. We found that the extent of the lymph node dissection (D2 versus D1+) and gastrectomy (total versus distal) and the type of surgery (open versus laparoscopy) had no impact on the OS of stage IV GCOO patients. Crucially, D2 lymph node dissections did not affect survivability. Additionally, we found that there was no impact of advanced age, a high ASA score, hypoalbuminemia, being underweight, or the extent of the lymph node dissection on OS.

There are some limitations to extracting any strong conclusions from this study. This was a retrospective study with a small sample population, and it was conducted in a single group without a control. A well-designed prospective study is necessary to overcome these problems.

In conclusion, we recommend that the treatment method for stage IV GCOO should be selected according to each patient's physical condition and tumor characteristics. Our results suggest that palliative gastrectomies can be performed in stage IV resectable GCOO patients without incurring unfavorable prognostic factors. Palliative gastrectomies can be considered for treatment of stage IV gastric cancer outlet obstruction patients who have: 1) resectable tumors, 2) moderate peritoneal metastasis, and 3) good physical conditioning and can withstand postoperative chemotherapy.

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