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A Perforated Gastric Carcinoma: A Single-Center Experience

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Objective: In this study, we aimed to describe clinicopathologic characteristics of the patients with a perforated gastric carcinoma, and to assess surgical approaches and possible factors affecting mortality and morbidity.

Material and Method: We retrospectively reviewed data of 18 patients who underwent emergent surgery for a perforated gastric carcinoma between January 2002 and December 2012. Data including surgical procedure, pathologic findings, complications, morbidity and mortality rates, and outcomes were evaluated.

Results: The mean age was 58 years. The most common tumor localization was antrum (55%), and 11 patients (61.1%) had Stage IV disease. Nine patients (50%) had a comorbid disease. Of the patients, primary suture + omentopexy was performed in 11 (61.1%) whereas total gastrectomy with D0 or D1 lymph node dissection in 5 (27.7%), subtotal gastrectomy with D0 lymph node dissection in 2 (11.1%), and 2-stage total gastrectomy with D2 lymph node dissection in 2 (11.1%). The complication rate was 50% with a mortality rate of 50%. Overall survival was 79 ± 97.89 days. Sepsis and the presence of comorbidities were found to increase early mortality ($P = 0.00$ and $P = 0.028$)

Conclusion: Our study results show that postoperative morbidity and mortality rates are still high in patients with a perforated gastric carcinoma. In stable patients, 1-step radical gastrectomy should be performed, while palliative surgery or 2-stage radical gastrectomy can be performed in patients with poor overall status and diffuse peritonitis. Early diagnosis and perforation management before the onset of diffuse peritonitis can decrease high mortality and morbidity rates.

Key words: Surgical treatment – Prognostic factor – Gastric tumor – Perforation

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Gastric tumor perforation, which is uncommon in clinical practice, is suggestive of an advanced tumor and presence of lymphatic metastasis.[1] The incidence of perforation has been reported as 0.56% to 3.9% in gastric tumors.[1,2] Based on the literature review, gastric ulcers are the main cause of gastric perforation, and about 10% to 16% of the cases are caused by a gastric tumor.[3] There is a limited number of studies on gastric tumor perforation and its outcomes in the literature.[4] Although a limited number of case control studies are available in the literature, several case reports and small case series have been recently published.[5–8] All these findings show the rarity of study subjects for this issue.

Since history and symptoms in patients with a perforated gastric carcinoma are similar to those with benign gastric perforation, it is difficult to make a definite diagnosis before surgery. Frozen section and biopsy should be performed in all gastric perforations, as treatment strategies of gastric perforations caused by benign and malignant causes are different.[9] Primary suture is used in most of the cases in many centers, as the patient is ineligible for major surgery or has an advanced tumor. More recently, radical surgery in the initial operation has been introduced in selected cases who are stable and have a resectable tumor without generalized peritonitis.[3,5,8,10] On the other hand, either palliative surgery alone or 2-stage surgical approach to manage perforation by palliative surgery and to delay radical surgery later is used. It is difficult, however, to make a decision on the surgical approach in patients with a perforated gastric carcinoma, as these patients often are hemodynamically unstable with peritonitis, comorbidities, and an advanced disease. In addition, surgery is associated with an increased mortality in these patients up to 8%–82%, depending on the surgical approach selected.[1,2,5]

In the present study, we aimed to present our 10-year experience including typical characteristics, surgical methods, and outcomes in patients with a perforated gastric carcinoma, and to investigate surgical approaches and possible factors affecting mortality and morbidity.

Patients and Methods

An approval of the local Ethics Committee was obtained for this study. A written informed consent was obtained from each patient. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Between January 2002 and December 2012, a total of 874 patients underwent surgery for a gastric tumor in General Surgery clinic of Erciyes University, Faculty of Medicine. We retrospectively reviewed data of 18 patients who underwent emergent surgery for a perforated gastric carcinoma, as confirmed by histopathologic examination. Data including age, sex, comorbidity, tumor localization and histopathology, presence of distant metastasis, presence of ascites, lymph node involvement, inflammatory peritonitis, surgical procedure performed, and causes of morbidity and mortality were assessed using the hospital records.

All patients were assessed preoperatively in the emergency room. The diagnosis of perforation was made based on the history and physical examination findings. The diagnosis was supported by the presence of free-air under diaphragm on plain abdominal radiographs. Once fluid and electrolyte imbalance was corrected, an emergent surgery was performed. All patients were managed as a surgical emergency and laparotomy was performed with the midline incision. Intraoperative diagnosis, surgical staging, and decision about resection or palliative procedure were performed by the surgeon. The TNM staging was applied to all patients, based on the criteria established by the American Joint Committee of Cancer (AJCC).[11] Sepsis was defined according to the guidelines criteria for the diagnosis of sepsis.[12]

The surgical procedures applied were classified as follows: (1) resection surgery including (a) subtotal gastrectomy and (b) total gastrectomy; (2) palliative surgery, primary suture + omentopexy; and (3) staged surgery, primary suture + omentopexy initially, followed by resection through relaparotomy. If total gastrectomy was performed with perigastric lymph nodes including the right and left cardiac lymph nodes, those with lesser and greater curvatures, and supra- and infrapyloric lymph nodes (N1), lymph node dissection was defined as follows: D0 for incomplete dissection of perigastric lymph nodes (N1); D1 for complete dissection of N1 lymph nodes; D2 for excision of lymph nodes along left gastric artery, common hepatic artery, splenic artery, arteries, celiac trunk, and splenic hilus (N2) in addition to N1 lymph nodes; D3 for extended lymph node dissection including dissection of lymph nodes in the hepatoduodenal ligament, posterior surface of the pancreatic head and

mesenteric root (N3), in addition to N1 + N2 lymph nodes.

The term operative mortality for death events occurring within the first 30 days, term late mortality for deaths after 30 days, and postoperative morbidity for postoperative complications, which increased the duration of hospital stay or required an additional treatment were used. Data including age, sex, comorbidity, tumor localization, presence and extent of peritonitis, distant metastasis, tumor stage, and surgical procedures applied were recorded.

Statistical Analysis

Statistical analysis was performed using SPSS version 20.0 software (IBM Corporation, Armonk, New York). Descriptive data were expressed in mean and SD or median and percentage. The correlation between mortality and comorbidities, sepsis, and complications was investigated using the chi-square test. T-test was used to analyze the correlation between surgical type and surveillance. A P value of <0.05 was considered statistically significant.

Results

Of 18 patients who underwent emergent surgery for tumor-related gastric perforation, 11 (61%) were men and 7 (39%) were women. The mean age was 58 years (range: 44 to 75 years). Demographic characteristics and perioperative findings are shown in Table 1.

There was $\geq$1 comorbidities in 10 patients, including hypertension in 4 (22%), diabetes mellitus in 2 (11.1%), chronic obstructive pulmonary disease in 1 (5.5%), and ischemic heart disease in 3 (16.6%).

Tumor was localized at the antrum and prepyloric region in 10 (55%), at the lesser curvature in 4 (22%), at the greater curvature in 2 (11%), at fundus in 1 (5%), and at kardia in 1 (5%). There was diffuse peritonitis in 9 (50%) and liver metastasis in 11 patients (61.1%). Biopsy samples were obtained from metastatic lesions and perforation site in all patients. The diagnosis of a gastric carcinoma was made by perioperative frozen sections in 4 patients (22.2%) and by postoperative histopathological examination in 14 patients (77.7%; Table 1).

Primary suture + omentopexy was performed in 11 patients (61.1%; poor general condition of patients, extensive tumor spread with adjacent organs invasion, technical difficulties in respective procedures, and severe diffuse fibro-purulent peritonitis), whereas total or subtotal gastrectomy was performed in 5 patients (27.7%) and 2-stage radical gastrectomy was performed in 2 patients (11.1%). For 2-stage surgery, D0 or D1 total gastrectomy was performed on Day 12 or 14 following the initial surgery among those who underwent primary suture + omentopexy. In all patients who underwent resection, histopathologic examination reported tumor-free proximal and distal surgical margins. Therefore, tumor resection rate in the initial surgery was 27.7% (n = 5), which increased to 38.8% (n = 7), when the patients who underwent staged surgery were included (Table 2). Table 2 shows postoperative findings and survival data of the patients.

According to the TNM staging, 7 patients (38.8%) had Stage III disease, while 11 patients (61.1%) had Stage IV disease. On the histopathologic examination, an adenocarcinoma was detected in 17 patients

Table 1 Clinicopathologic features of patients with perforated gastric cancer

Variable	N
Age, mean (range), year	
Range (y), mean	58 (44-75)
Male	56.7 (44-65)
Female	61 (45-75)
Sex, n (%)	
Male	11 (61.1%)
Female	7 (38.8%)
Location, n (%)	
Lower-third	10 (55.5%)
Middle-third	6 (33.3%)
Upper-third	2 (11.1%)
Disease stage, n (%)	
I	0 (0%)
II	0 (0%)
III	5 (27.7%)
IV	13 (72.2%)
Surgery, n (%)	
Gastrectomy	7 (38.8%)
Total	5 (27.7%)
Subtotal	2 (11.1%)
Local repair	11 (61.1%)
Lymph node dissection, n (%)	
Extended (D2,D3)	0 (0%)
Limited (D0, D1)	5 (27.7%)
Diagnosis, n (%)	
Frozen section	4 (22.2%)
Histopathology	14 (77.7%)
Cancer type, n (%)	
Adenocarcinoma	17 (94.4%)
Mucinous adenocarcinoma	12 (66.6%)
Signet ring cell carcinoma	5 (27.7%)
Others	0 (0%)
Gastric lymphoma	1 (5.5%)

Table 2 Postoperative survival data

Case	Sex	Age	TNM	Stage	Type of surgery	Comorbidities	Postoperative complications	Survival (day)	Cause of death	Sepsis status, Yes (+), No (−)
1	M	44	T3N1M0	III-A	Subtotal gastrectomy	HT	Wound infections	200	Primary cancer	(−)
2	F	55	T4N1M1	IV	Repair		(−)	45	Primary cancer	(−)
3	M	62	T4N2M1	IV	Repair	Cardiac disease	(−)	Perioperative exitus	Hospital mortality	(+)
4	F	54	T4N1M1	IV	Repair + Feeding jejunostomy	Cardiac disease	(−)	3	Hospital mortality	(+)
5	M	57	T4N1M1	IV	Repair	HT	Bleeding	4	Hospital mortality	(+)
6	F	74	T4N1M1	IV	Repair			15	Hospital mortality	(+)
7	M	61	T4N2M1	IV	Repair	Pulmonary disease	Pulmonary embolism	10	Hospital mortality	(+)
8	F	45	T3N2M0	III B	Total gastrectomy		Wound infection	165	Primary cancer	(−)
9	M	56	T3N1M0	III A	Total gastrectomy		Wound infection	100	Primary cancer	(−)
10	F	75	T4N1M1	IV	Repair	DM		7	Hospital mortality	(+)
11	M	55	T3N1MO	III A	Total gastrectomy (initial repair)		Anastomotic leakage	25	Hospital mortality	(+)
12	M	65	T4N2M1	IV	Repair	HT	Fistula	12	Hospital mortality	(+)
13	M	56	T4N1M1	IV	Repair			38	Primary cancer	(−)
14	F	65	T4N1M1	IV	Repair	Cardiac disease	Bleeding	11	Hospital mortality	(+)
15	M	54	T4N1M1	IV	Repair			45	Primary Cancer	(−)
16	M	58	T3N1M0	IIIA	Total gastrectomy	HT	Wound infections	200	Primary cancer	(−)
17	M	58	T3N1M0	III A	Subtotal gastrectomy	DM		300	Primary cancer	(−)
18	F	59	T3N1MO	IIIA	Total gastrectomy (initial repair)			250	Primary cancer	(−)

DM, diabetes mellitus; HT, hypertension; TNM, tumor-node-metastasis.

and a mixed-cell lymphoma in 1. Of the patients with adenocarcinoma, 5 had a signet ring cell carcinoma.

Nine patients had ≥1 complication in 9 patients (50%). The most common complications included wound site infection in 4 (22.2%), postoperative bleeding in 2 (11.1%), anastomosis leakage in 1 (5.5%), fistula in 1 (5.5%), and pulmonary embolism in 1 patient (5.5%). Operative mortality rate was 50% (n = 9). Five patients (27.7%) who experienced complications died. Possible causes of death was sepsis in 3 (33.3%), bleeding in 2 (22.2%), heart failure in 1 (11.1%), pulmonary embolism in 1 (11.1%), and perioperative death in 1 patient (11.1%). In addition, D0 total gastrectomy was performed in 1 patient (5.5%), while primary suture in 8 of the non-survivors (50%). The mean ages of non-survivors and survivors were 63.1 years (range: 54 to 75 years) and 53.8 years (range: 44 to 59 years), respectively. Moreover, 70% patients with comorbidities were in the operative mortality group, while 30% were in the late mortality group, indicating a significant correlation between the presence of comorbidities and mortality ($P < 0.05$). Furthermore, all patients with sepsis were in the operative mortality group, indicating a significant correlation between sepsis status and mortality ($P < 0.05$). However, the operative mortality rate was 55.6% and late mortality rate was 44.4%, suggesting no significant correlation between complications and mortality ($P > 0.05$; Table 3). The overall survival rate was 79.44 ± 97.89 days in all patients, while the mean survival was 17.27 ± 16.96 days in patients who underwent repair surgery and 177.14 ± 91.9 days in patients who underwent resection. There was a significant difference in the mean survival

Table 3 Factors affecting mortality

	Mortality			
	Operative mortality	Late mortality	Total	*P*
Comorbidities				
Yes				
n	7	3	10	0.028*
%	70	30	100.0	
No				
n	2	6	8	
%	25.0	75.0	100.0	
Sepsis				
Yes				
n	9	0	9	0.000*
%	100	0.0	100.0	
No				
n	0	9	9	
%	0.0	100.0	100.0	
Complications				
Yes				
n	5	4	9	0.500
%	55.6	44.4	100.0	
No				
n	4	5	9	
%	44.4	55.6	100.0	

*$P < 0.05$.

between the patients who underwent repair surgery and those who were resected ($P < 0.05$; Table 4).

Discussion

Until the second half of the 20th century, only primary suturing was used to prevent further spread of a tumor and to manage peritonitis, based on the idea that resection for a perforated gastric carcinoma was associated with a high-risk of mortality and morbidity.[4] Using this approach, the mortality rate varied between 62% and 82%.[13–15] However, with the report of Heimlich who suggested that longer survival could be achieved by an emergent resection in 1963,[16] curative and palliate resection methods were introduced for eligible patients within previous decades. In many studies, the mortality rate was reported as lower with this approach, compared to palliative approaches.[7,10,17,18] In 2000, Lehnert *et al*[19] suggested 2-stage radical surgery in stable, but ineligible patients for the first-line radical surgery with resectable tumors. In addition, there are recent publications reporting that staged surgery is safe yielding similar oncological outcomes.[3,8] The surgical method should be selected based on the clinical status of the patient

Table 4 Surgical types

	N	Mean	SD	*P*
Repair surgery	11	17.27	16.96	0.000
Resection	7	177.14	91.92	
General surgery	18	79.44	97.89	

*$P < 0.05$.

SD, standard deviation.

and the main goal should be to resolve the acute condition for the patient.

In several countries in which a screening program for gastric carcinomas is not implemented, 55.82% of the patients with a gastric carcinoma have advanced disease, and lymph node metastasis is already present in 57% to 67% of the patients.[1,4] In addition, the fact that overall status is usually poor with the presence of comorbidities and peritonitis makes it difficult to select the surgical approach that would be employed. Based on the literature: *(i)* total or subtotal gastrectomy + D2 or D3 lymphadenectomy should be performed in stable patients with a resectable tumor (no findings of shock, no comorbid disease, no peritonitis); *(ii)* palliative surgery should be performed in stable patients with a non-resectable tumor; *(iii)* staged radical gastrectomy should be performed in unstable patients with a resectable tumor; and *(iv)* simple repair surgery or omental patch should be performed in unstable patients with an advanced disease.[3,7,8,19,20]

The fact that tumor stage is usually advanced in tumors with perforation is a critical factor, which decreases the resection rate.[21] In our study, resection was able to be performed in only 5 patients (27.7%) during the initial surgery. In these patients in whom the histopathologic examination result reported no involvement at the surgical margins, we decided not to perform a redo surgery for extended lymph node dissection due to potential mortality/morbidity risks, taking postoperative overall status, comorbidities, and tumor stage into consideration. Primary suture + omentopexy was performed in 61.1% of the patients (n = 11); this rate is similar to that reported by Ozmen *et al*.[20] In addition, these patients (n = 11) had a distant metastasis that precluded resection. As a result, we decided not to perform a redo surgery in these patients, considering the fact that curative surgery is not feasible and palliative surgery including resection alone would not provide any survival benefit.

In the literature, it is recommended to obtain a biopsy sample and to study frozen section during surgery, where applicable, as it affects the selection

of surgical method and approach to the patient.[3,9] There are many differences in the treatment strategies between benign or malignant causes of gastric perforation, and radical surgery in the same session can be performed in eligible patients, as diagnosed by frozen section at the intraoperative period. In our study, frozen sections were studied in 22.2% of the patients at the intraoperative period. Of the patients diagnosed with gastric cancer by frozen section, no resection was performed due to diffuse peritonitis in 2 patients (11.1%), despite the presence of Stage III disease. As resection and lymph node dissection are extremely challenging in the presence of diffuse peritonitis, it is appropriate to prefer staged surgery and to delay major surgery in these patients.[1,21] In addition, total gastrectomy with D2 lymph node dissection was performed in 2 patients at the early postoperative period following the recovery of peritonitis. Of these, anastomosis leakage was developed in one patient who died on Day 25.

In the present study, resection was performed in five patients (27.7%) in whom the diagnosis of gastric carcinoma was unable to be confirmed by histopathologic examination and or frozen section, as the clinical findings suggested a perforated gastric carcinoma. In these patients, a definitive diagnosis was made by postoperative histopathologic examination. Roviello *et al*[1] also suggested to perform resection in gastric perforation in patients without an established diagnosis of gastric cancer preoperatively or no frozen-section study, who had suspicious clinical appearance for malignity with a stable general status and resectable tumor, as cure can be achieved with low morbidity risk in these patients, although perforation is caused by a benign condition. On the other hand, another advantage of this approach is that elective radical gastrectomy can be performed with an appropriate preparation, if the histopathologic examination reports a gastric carcinoma as the cause of perforation.[4]

Gastric cancer-related complications result in a very high mortality rate (0 to 82%), depending on the surgical intervention performed, and require an emergent surgery.[1,4] In the present study, perioperative morbidity and mortality rates were found to be 50% and 50%, respectively. Although no death occurred among patients who underwent resection in the initial surgery, 1 of 2 patients who underwent 2-stage total gastrectomy died on Day 25. In the literature, it was reported that mortality rate (7% to 20%) was lower in patients who underwent resection in the initial surgery, compared to those in whom resection was unable to be performed.[4,10,17–19] This can be due to fact that resection is performed in selected patients with a good overall status without diffuse peritonitis, while primary repair is mostly preferred in complicated and severe patients.[3,7,20] In our study, the overall survival rate was 79.44 ± 97.89 days in all patients, while the mean survival was 17.27 ± 16.96 days and 177.14 ± 91.9 days in patients who underwent repair surgery and resection, respectively. This finding indicates a significant difference in the mean survival between these patient groups ($P < 0.05$; Table 4), consistent with the previous findings. Ignjatovic *et al*[5] reported that survival was 75.77 ± 68.88 days with curative resection and 18.00 ± 24.43 days with surgery. These findings are also consistent with the literature data.

In this study, only short-term results were reviewed in patients with a perforated gastric carcinoma. In the literature, there is a limited number of studies reporting long-term results. The disease becomes more diffuse due to seeding by the tumor cells after perforation; thus, long-term results are poorer in patients with perforation, compared to those without.[22] However, in a more recent study, no significant difference was found in the long-term results after resection between the patients with a gastric carcinoma complicated by perforation and those without.[18] This finding indicates that perforation alone does not affect the surgical approach and that radical surgery, either 1- or 2-stage, should be performed in eligible patients.

Moreover, most of gastric tumor perforations occur in advanced age patients. In the series of Roviello *et al*,[1] age was 68 years, while in the study of So *et al*[23] age was 59 years. In our study, the mean age was 58 years and 61% of the patients were males. This is consistent with the literature data.

In addition, perforation frequently develops in the antrum and prepyloric region.[1,8,17] In the present study, perforation was most frequently observed in these regions; however, only 1 patient had perforation in the fundus and kardia.

Korkmaz *et al*[21] reported that the majority of postoperative deaths were related to comorbid diseases. In our study, we found that comorbidities were prognostic factors for the mortality and the complications increased the length of stay in the hospital. Analysis of the relationship between comorbidities and mortality revealed that 70% patients with comorbidities were in the operative mortality group, while 30% were in the late mortality group, indicating a significant correlation between the presence of comorbidities and mortal-

ity, consistent with the literature data. Furthermore, the major cause of mortality is the presence of sepsis.[1,21] However, it has been reported that 82.8% of the patients with a perforated gastric tumor develop sepsis.[21] In a study by Kotan *et al*,[24] a significant relationship was found between the operative mortality and sepsis. In the present study, all 9 patients with early mortality were septic, and death occurred due to sepsis or sepsis-related multiple organ failure. All patients with sepsis were in the operative mortality group, indicating a significant relationship between sepsis status and mortality ($P < 0.05$). These results indicate that peritonitis treatment and perioperative treatment of diffuse peritonitis reduce the mortality rates of peritonitis treatment and major surgeries in patients with perforated peritonitis and sepsis.

Nonetheless, this study has some limitations. Our sample size is small and we need further large-scale studies to generalize these results. However, as the incidence of perforated gastric carcinomas is extremely low, only small-scale studies have been reported in the literature, to date. Therefore, we believe that our results would contribute to the current literature data.

In conclusion, preoperative diagnosis is challenging and postoperative morbidity and mortality rates are high in perforated gastric carcinomas. In patients with suspected or confirmed gastric perforation, 1-stage radical gastrectomy should be employed in stable patients with resectable tumors, while palliative surgery or 2-stage radical gastrectomy should be performed in those with resectable tumors and poor overall status. However, reduction in high mortality and morbidity rates at the early postoperative period depends on establishing the diagnosis before the development of peritonitis and early management of perforation, irrespective of the surgical approach applied.

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