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A perforated Gastric Carcinoma: A Single-Center Experience

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Abstract:	<p>Objective: In this study, we aimed to describe clinicopathological characteristics of the patients with a perforated gastric carcinoma, and to assess surgical approaches and possible factors affecting mortality and morbidity.</p> <p>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, pathological findings, complications, morbidity and mortality rates, and outcomes were evaluated.</p> <p>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 five (27.7%), subtotal gastrectomy with D0 lymph node dissection in two (11.1%), and two-stage total gastrectomy with D2 lymph node dissection in two (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)</p> <p>Conclusion: Our study results show that postoperative morbidity and mortality rates are still high in patients with a perforated gastric carcinoma. In stable patients, one-step radical gastrectomy should be performed, while palliative surgery or two-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.</p>

A perforated Gastric Carcinoma: A Single-Center Experience

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2 **Abstract**

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4 with a perforated gastric carcinoma, and to assess surgical approaches and possible factors
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9 mortality rates, and outcomes were evaluated.

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11 and 11 patients (61.1%) had Stage IV disease. Nine patients (50%) had a comorbid disease. Of
12 the patients, primary suture + omentopexy was performed in 11 (61.1%) whereas total
13 gastrectomy with D0 or D1 lymph node dissection in five (27.7%), subtotal gastrectomy with
14 D0 lymph node dissection in two (11.1%), and two-stage total gastrectomy with D2 lymph node
15 dissection in two (11.1%). The complication rate was 50% with a mortality rate of 50%. Overall
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18 **Conclusion:** Our study results show that postoperative morbidity and mortality rates are still
19 high in patients with a perforated gastric carcinoma. In stable patients, one-step radical
20 gastrectomy should be performed, while palliative surgery or two-stage radical gastrectomy can
21 be performed in patients with poor overall status and diffuse peritonitis. Early diagnosis and
22 perforation management before the onset of diffuse peritonitis can decrease high mortality and
23 morbidity rates.

24 **Keywords:** Surgical treatment, prognostic factor, gastric tumor, perforation.

25

26 **Introduction**

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

35 Since history and symptoms in patients with a perforated gastric carcinoma are similar
36 to those with benign gastric perforation, it is difficult to make a definite diagnosis before
37 surgery. Frozen-section and biopsy should be performed in all gastric perforations, as treatment
38 strategies of gastric perforations caused by benign and malignant causes are different [9].
39 Primary suture is used in most of the cases in many centers, as the patient is ineligible for
40 major surgery or has an advanced tumor. More recently, radical surgery in the initial operation
41 has been introduced in selected cases who are stable and have a resectable tumor without
42 generalized peritonitis [3,5,8,10]. On the other hand, either palliative surgery alone or two-stage
43 surgical approach to manage perforation by palliative surgery and to delay radical surgery later
44 is used. It is difficult, however, to make a decision on the surgical approach in patients with a
45 perforated gastric carcinoma, as these patients often are hemodynamically unstable with
46 peritonitis, comorbidities, and an advanced disease. In addition, surgery is associated with an
47 increased mortality in these patients up to 8-82%, depending on the surgical approach selected
48 [1,2,5].

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

52

53 **Patients and Methods**

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

57 Between January 2002 and December 2012, a total of 874 patients underwent surgery
58 for a gastric tumor in General Surgery clinic of Erciyes University, Faculty of Medicine. We

59 retrospectively reviewed data of 18 patients who underwent emergent surgery for a perforated
60 gastric carcinoma, as confirmed by histopathological examination. Data including age, sex,
61 comorbidity, tumor localization and histopathology, presence of distant metastasis, presence of
62 ascites, lymph node involvement, inflammatory peritonitis, surgical procedure performed, and
63 causes of morbidity and mortality were assessed using the hospital records.

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

73 The surgical procedures applied were classified as follows: 1) resection surgery
74 including a) subtotal gastrectomy and b) total gastrectomy; 2) palliative surgery, primary suture
75 + omentopexy; and 3) staged surgery, primary suture + omentopexy initially, followed by
76 resection through re-laparotomy. If total gastrectomy was performed with perigastric lymph
77 nodes including the right and left cardiac lymph nodes, those with lesser and greater curvatures,
78 and supra- and infra-pyloric lymph nodes (N1), lymph node dissection was defined as follows:
79 D0 for incomplete dissection of perigastric lymph nodes (N1); D1 for complete dissection of
80 N1 lymph nodes; D2 for excision of lymph nodes along left gastric artery, common hepatic
81 artery, splenic artery, arteries, celiac trunk and splenic hilus (N2) in addition to N1 lymph nodes;
82 D3 for extended lymph node dissection including dissection of lymph nodes in the
83 hepatoduodenal ligament, posterior surface of the pancreatic head and mesenteric root (N3) in
84 addition to N1 + N2 lymph nodes.

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

90

91 **Statistical Analysis**

92 Statistical analysis was performed using SPSS version 20.0 software (IBM Corporation,
93 Armonk, NY, USA). Descriptive data were expressed in mean and standard deviation or median
94 and percentage. The correlation between mortality and comorbidities, sepsis, and complications
95 was investigated using the chi-square test. T-test was used to analyze the correlation between
96 surgical type and surveillance. A p value of <0.05 was considered statistically significant.

97 98 **Results**

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

102 There was ≥ 1 comorbidities in 10 patients, including hypertension in four (22%),
103 diabetes mellitus in two (11.1%), chronic obstructive pulmonary disease in one (5.5%), and
104 ischemic heart disease in three (16.6%).

105 Tumor was localized at the antrum and prepyloric region in 10 (55%), at the lesser
106 curvature in four (22%), at the greater curvature in two (11%), at fundus in one (5%), and at
107 kardia in one (5%). There was diffuse peritonitis in 9 (50%) and liver metastasis in 11 patients
108 (61.1%). Biopsy samples were obtained from metastatic lesions and perforation site in all
109 patients. The diagnosis of a gastric carcinoma was made by perioperative frozen-sections in
110 four patients (22.2%) and by postoperative histopathological examination in 14 patients
111 (77.7%) (Table 1).

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

123 According to the TNM staging, seven patients (38.8%) had Stage III disease, while 11
124 patients (61.1%) had Stage IV disease. On the histopathological examination, an

125 adenocarcinoma was detected in 17 patients and a mixed-cell lymphoma in one. Of the patients
126 with adenocarcinoma, five had a signet-ring-cell carcinoma.

127 Nine patients had ≥ 1 complication in nine patients (50%). The most common
128 complications included wound site infection in four (22.2%), postoperative bleeding in two
129 (11.1%), anastomosis leakage in one (5.5%), fistula in one (5.5%), and pulmonary embolism in
130 one patient (5.5%). Operative mortality rate was 50% (n=9). Five patients (27.7%) who
131 experienced complications died. Possible causes of death was sepsis in three (33.3%), bleeding
132 in two (22.2%), heart failure in one (11.1%), pulmonary embolism in one (11.1%), and
133 perioperative death in one patient (11.1%). In addition, D0 total gastrectomy was performed in
134 one patient (5.5%), while primary suture in eight of non-survivors (50%). The mean ages of
135 non-survivors and survivors were 63.1 years (range: 54 to 75 years) and 53.8 years (range: 44
136 to 59 years), respectively. Moreover, 70% patients with comorbidities were in the operative
137 mortality group, while 30% were in the late mortality group, indicating a significant correlation
138 between the presence of comorbidities and mortality ($p < 0.05$). Furthermore, all patients with
139 sepsis were in the operative mortality group, indicating a significant correlation between sepsis
140 status and mortality ($p < 0.05$). However, the operative mortality rate was 55.6% and late
141 mortality rate was 44.4%, suggesting no significant correlation between complications and
142 mortality ($p > 0.05$) (Table 3). The overall survival rate was 79.44 ± 97.89 days in all patients,
143 while the mean survival was 17.27 ± 16.96 days in patients who underwent repair surgery and
144 177.14 ± 91.9 days in patients who underwent resection. There was a significant difference in
145 the mean survival between the patients who underwent repair surgery and those who were
146 resected ($p < 0.05$) (Table 4).

147

148 **Discussion**

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

159 surgery is safe yielding similar oncological outcomes [3,8]. The surgical method should be
160 selected based on the clinical status of the patient and the main goal should be to resolve the
161 acute condition for the patient.

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

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

184 In the literature, it is recommended to obtain a biopsy sample and to study frozen-section
185 during surgery, where applicable, as it affects the selection of surgical method and approach to
186 the patient [3,9]. There are many differences in the treatment strategies between benign or
187 malignant causes of gastric perforation, and radical surgery in the same session can be
188 performed in eligible patients, as diagnosed by frozen-section at the intraoperative period. In
189 our study, frozen sections were studied in 22.2% of the patients at the intraoperative period. Of
190 the patients diagnosed with gastric cancer by frozen-section, no resection was performed due
191 to diffuse peritonitis in two patients (11.1%), despite the presence of Stage III disease. As
192 resection and lymph node dissection are extremely challenging in the presence of diffuse

193 peritonitis, it is appropriate to prefer staged surgery and to delay major surgery in these patients
194 [1, 21]. In addition, total gastrectomy with D2 lymph node dissection was performed in two
195 patients at the early postoperative period following the recovery of peritonitis. Of these,
196 anastomosis leakage was developed in one patient who died on Day 25.

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

208 Gastric cancer-related complications result in a very high mortality rate (0 to 82%),
209 depending on the surgical intervention performed, and require an emergent surgery [1,4]. In the
210 present study, perioperative morbidity and mortality rates were found to be 50% and 50%,
211 respectively. Although no death occurred among patients who underwent resection in the initial
212 surgery, one of two patients who underwent two-stage total gastrectomy died on Day 25. In the
213 literature, it was reported that mortality rate (7 to 20%) was lower in patients who underwent
214 resection in the initial surgery, compared to those in whom resection was unable to be
215 performed [4, 10, 17-19]. This can be due to fact that resection is performed in selected patients
216 with a good overall status without diffuse peritonitis, while primary repair is mostly preferred
217 in complicated and severe patients [3,7,20]. In our study, the overall survival rate was $79.44 \pm$
218 97.89 days in all patients, while the mean survival was 17.27 ± 16.96 days and 177.14 ± 91.9
219 days in patients who underwent repair surgery and resection, respectively. This finding
220 indicates a significant difference in the mean survival between these patient groups ($p < 0.05$)
221 (Table 4), consistent with the previous findings. **Ignjatovic et al. [5] reported that survival was**
222 **75.77 ± 68.88 days with curative resection and 18.00 ± 24.43 days with surgery. These findings**
223 **are also consistent with the literature data.**

224 In this study, only short-term results were reviewed in patients with a perforated gastric
225 carcinoma. In the literature, there is a limited number of studies reporting long-term results.
226 The disease becomes more diffuse due to seeding by the tumor cells after perforation; thus,

227 long-term results are poorer in patients with perforation, compared to those without [22].
228 However, in a more recent study, no significant difference was found in the long-term results
229 after resection between the patients with a gastric carcinoma complicated by perforation and
230 those without [18]. This finding indicates that perforation alone does not affect the surgical
231 approach and that radical surgery, either one- or two-stage, should be performed in eligible
232 patients.

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

237 In addition, perforation frequently develops in the antrum and prepyloric region
238 [1,8,17]. In the present study, perforation was most frequently observed in these regions;
239 however, only one patient had perforation in the fundus and kardia.

240 Korkmaz et al. [21] reported that the majority of postoperative deaths were related to
241 comorbid diseases. In our study, we found that comorbidities were prognostic factors for the
242 mortality and the complications increased the length of stay in the hospital. Analysis of the
243 relationship between comorbidities and mortality revealed that 70% patients with comorbidities
244 were in the operative mortality group, while 30% were in the late mortality group, indicating a
245 significant correlation between the presence of comorbidities and mortality, consistent with the
246 literature data. Furthermore, the major cause of mortality is the presence of sepsis [1,21].
247 However, it has been reported that 82.8% of the patients with a perforated gastric tumor develop
248 sepsis [21]. In a study by Kotan et al. [24], a significant relationship was found between the
249 operative mortality and sepsis. In the present study, all of nine patients with early mortality
250 were septic, and death occurred due to sepsis or sepsis-related multiple organ failure. All
251 patients with sepsis were in the operative mortality group, indicating a significant relationship
252 between sepsis status and mortality ($p < 0.05$). These results indicate that peritonitis treatment
253 and perioperative treatment of diffuse peritonitis reduce the mortality rates of peritonitis
254 treatment and major surgeries in patients with perforated peritonitis and sepsis.

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

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

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