

# Prognostic factors of peptic ulcer perforation

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## ABSTRACT

**Objectives:** Today a perforated peptic ulcer (PPU) is a rare condition. However, emergency surgery for perforated ulcer presently carries a mortality risk of up to 30%. The aim of this study is to analyze and define factors influencing surgical prognosis in patients operated upon for PPU.

**Methods:** We performed a retrospective analysis of 62 patients treated for PPU in Suleyman Demirel University, Surgical Department between January 1995 to January 2004. Univariate analysis was performed to determine risk factors for mortality in PPU by chi-square test, Pearson and Spearman correlation tests using SPSS for Windows statistical software. We accepted statistical significance for  $p$  values  $<0.05$ .

**Results:** The overall mortality rate was 17.7%. The present study confirms the age, sex, American Society of Anesthesiology (ASA) classification, coexisting medical disease, elapsed time from symptoms to operation, blood pressure, pulse, serum albumin and creatinine levels,

hemoglobin level and diameter of perforation as valid prognostic factors in whole series, whereas a previous history of peptic ulcer disease, chronic ingestion history of nonsteroidal anti-inflammatory drugs, alcohol ingestion, smoking habits, site of perforation, type of surgical treatment (simple suture or resection), postoperative complications did not appear to be related to prognosis.

**Conclusion:** Age, gender, ASA classification, coexisting medical disease, elapsed time from symptoms to operation, blood pressure, pulse, serum albumin and creatinine levels, hemoglobin level and diameter of perforation are factors significantly associated with fatal outcomes in patients undergoing emergency surgery for PPU. Thus, such factors need to be carefully taken into account during the general workup of patients admitted for PPU.

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Over the past 2 decades, treatment of peptic ulcer disease (PUD) has changed dramatically. The first major change occurred after the introduction of histamine  $H_2$  receptor antagonists for gastric acid suppression at the end of the 1970s, followed by proton-pump inhibitors at the end of the 1980s.<sup>1</sup> In addition, the pathophysiological understanding of PUD was completely changed by the discovery that an infective agent, *Helicobacter pylori* (*H. Pylori*), is present in 75-85% of the patients. Today, *H. Pylori* is regarded as a causative factor for the majority of duodenal and gastric ulcers encountered in routine clinical practice.<sup>2</sup> There has been a marked decrease in elective surgery for PUD following the introduction of the above medical

therapies including antibiotics for *H. pylori* eradication. By contrast, the number of acute complications has remained quantitatively constant.<sup>3</sup> Today, surgery is mainly reserved for some patients with complicated PUD, such as bleeding, perforation, and gastric outlet obstruction.<sup>1,4,5</sup> Crisp's description of a perforated ulcer from 1843 would fit into any modern textbook as far as the symptomatology is concerned.<sup>4</sup> Today, ulcer perforation incidence is stable or tends to decline, and most patients with ulcer perforations are elderly men and women, with perforations in the prepyloric and pyloric areas as frequent as perforations in the duodenum.<sup>4</sup> The incidence of PUD has been estimated as 1500-3000 per 100,000 inhabitants per

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year.<sup>1</sup> The lifetime prevalence of hemorrhage, perforation, and obstruction in peptic ulcer patients were estimated to be 15-20%, 5%, and 2%.<sup>6</sup> Approximately 3-10 per 100,000 inhabitants per year are operated on due to peptic ulcer perforation.<sup>7</sup> Approximately two-thirds of operations for complicated PUD are due to perforations with ensuing peritonitis.<sup>8</sup> Overall, PUD accounts for more than 70% of mortality associated with the disease.<sup>9</sup> Several potential predicting factors for perforation have been evaluated in the literature. In this paper, we studied the main factors associated with mortality in patients undergoing surgery for perforated peptic ulcers (PPU) in a referral academic hospital in southern Turkey.

**Methods.** We performed a retrospective analysis of 62 patients treated for PPU in the Surgical Department of Suleyman Demirel University, Isparta, Turkey, between January 1995 to January 2004. Excluded patients had perforated ulcers at the anastomotic site following former ulcer surgery and patients with cancer perforation. Data were recorded in a computerized registry database including gender, patient ages, American Society of Anesthesiology (ASA) status, associated medical conditions (cardiovascular, pulmonary, metabolic, hepatic, renal, or diabetic disease), time between onset of symptoms to surgery, arterial pressure and pulse rate at admission, hematological and biochemical parameters (hemoglobin, albumin and creatinine), complaints attributable to previous ulcer disease, chronic ingestion of non steroidal anti-inflammatory drugs (NSAIDs), alcohol ingestion history and smoking habits, site of perforation, diameter of perforation and type of surgery (suture versus resection). Mortality rate and prognostic factors were evaluated. Follow-up information was obtained by clinical records. Diagnosis of suspected gastroduodenal ulcer perforation was made clinically (acute abdomen) and confirmed by radiological examination (free intra-abdominal air). After the initial diagnosis and the usual reanimation measures (correcting the hydric, metabolic, and preexisting acid-base imbalances, nasogastric intubation and aspiration, intravenous antibiotics), the patients underwent surgical treatment. Preoperatively all patients had intravenous antibiotics (cefotaxime plus metronidazole), which was continued post-operatively. Medical treatment with proton pump inhibitor was started preoperatively (omeprazole 80 mg per day) in all patients and continued for a minimum of 14 days along with oral eradication therapy of *H. pylori*. An open surgical approach was performed in all patients. In 58 patients (93.5%), primary closure of the perforation was performed with an omentoplasty; 2 patients (3.2%) underwent truncal vagotomy with pyloroplasty; and 2 patients (3.2%) underwent subtotal gastrectomy and gastro-

jejunostomy. Each operation was the surgeon's preference for the individual patient. It was seen that the definitive surgery was preferred in 4 patients who had short duration of symptoms and with localized peritonitis. Univariate analysis was performed to determine risk factors for mortality in PPU by chi-square test, Pearson and Spearman correlation tests using SPSS for Windows statistical software (SPSS Inc., 8.0 standard version, Chicago, USA). A value of  $p < 0.05$  was accepted as significant.

**Results.** Patients undergoing surgery included 62 patients with a median age of  $53.5 \pm 19.02$  (range 17-87 ages). Eleven patients (17.7%) died during hospitalization for different reasons, and the factors contributing to mortality are shown in **Table 1**. Causes of the mortality were sepsis in 4 patients (6.5%), respiratory failure in 3 patients (4.8%), myocardial infarction in 2 patients (3.2%) and heart failure in one patient (1.6%). The etiology of mortality could not be found in 2 patients (3.2%). Age and sex distribution are shown in **Table 1**, and the mortality rate was significantly higher in the older age group ( $p=0.022$ ) and females. Patients were classified according to ASA scores as shown in **Table 1**, and statistical comparison between patients with ASA groups showed a significant difference ( $p=0.000$ ). Twenty-five (40.3%) patients had coexisting disease and 37 (59.7%) had not. The associated medical diseases were found in sequence chronic obstructive lung disease in 6 patients (9.7%), diabetes mellitus plus hypertension in 6 patients (9.7%), congestive heart failure in 4 patients (6.5%), diabetes mellitus in 3 patients (4.8%), hypertension in 3 patients (4.8%), epilepsy in 2 patients (3.2%), chronic obstructive lung disease plus hypertension in 2 patients (3.2%). There was coexisting disease in all mortalities. Coexisting disease was associated with higher mortality ( $p=0.000$ ). Duration of symptoms is shown in **Table 1**, and the duration of preoperative symptoms had a profound influence on mortality ( $p=0.011$ ). Low blood pressure (BP) values were associated with higher mortality rate, and patients with systolic BP lower than 100 mm Hg had a mortality risk approximately 16 times higher ( $p=0.000$ ). Patients' pulse rates were also evaluated. Mortality rate was higher in patients who had pulse rates above 100 beats/minute ( $p=0.000$ ). The blood albumin, blood creatinine and hemoglobin levels were evaluated as shown in **Table 1**. Low hemoglobin concentration was associated with higher mortality ( $p=0.009$ ). A previous history of PUD was obtained in 16 patients (25.8%). Mortality was independent from the previous PUD history ( $p=0.942$ ). Six patients (9.7%) had history of chronic ingestion of NSAIDs, however, there was not statistical difference between mortality rate and NSAIDs ingestion ( $p=0.942$ ). Four patients (6.5%) had history of

alcohol ingestion, but no association was found with increased mortality ( $p=0.694$ ). A history of smoking habits was found in 25 patients (40.3%). There was no association between mortality and smoking ( $p=0.768$ ). When the perforation sites were evaluated, in 11 patients (17.7%) gastric perforation, and in 55 patients (82.3%) duodenal perforation were found. No statistical difference was found between mortality rates ( $p=0.966$ ). Diameter of perforation is shown in **Table 1**, with larger defects associated with higher mortality ( $p=0.014$ ). Simple closure and omentopexy were the operative choice in 58 patients (93.5%). Truncal vagotomy with pyloroplasty and subtotal gastrectomy with gastrojejunostomy were performed in 2 patients each (3.2%). There was no death in 4 patients that underwent definitive surgery. Mortality rate was 19% in the simple closer group. Definitive surgery and simple closure groups were not comparable, because the patients in the definitive group were selected. The average hospitalization rate was found

to be  $9.3 \pm 9.2$  days (between 1 - 60 days). No complication was seen in 49 patients (79%). Thirteen patients (21%) incurred complications. Postoperative complications were pneumonia in 4 patients (6.5%), atelectasis in 2 patients (3.2%), wound infection in 2 patients (3.2%), anastomotic leakage, abdominal compartment syndrome, intra-abdominal bleeding, intra-abdominal abscess, small bowel injury due to drain, ARDS, upper gastrointestinal bleeding, acute renal failure, and toxic hepatitis were found in one patient (1.6%) each. No statistical difference was found between mortality and postoperative complications ( $p=0.081$ ).

**Discussion.** The number of patients admitted to hospital because of uncomplicated PUD has continued to decline since the introduction of H<sub>2</sub>-receptor antagonists and proton pump inhibitors, although hospital admissions due to hemorrhage or perforation have remained constant.<sup>8</sup> During the

Table 1 - Factors contributing to mortality among patients with perforated peptic ulcer (N = 62).

Factor	Discharged alive (N = 51) n (%)	Died (N = 11) n (%)	P-value
<b>Age</b>			0.022
< 60) (n=36)	33 (90.9)	3 (9.1)	
>60) (n=26)	18 (69.2)	8 (30.8)	
<b>Gender</b>			0.000
Male (n=51)	46 (90.2)	5 (9.8)	
Female (n=11)	5 (45.5)	6 (54.5)	
<b>ASA Classification</b>			0.000
I (n=37)	37 (100)	0 (0)	
II (n=7)	5 (71.4)	2 (28.6)	
III (n=11)	6 (54.5)	5 (45.5)	
IV (n=7)	3 (42.9)	4 (57.1)	
<b>Coexisting medical disease</b>			0.000
Yes (n=25)	14 (56)	11 (44)	
No (n=37)	37 (100)	0 (0)	
<b>Elapsed time from symptoms to operation (hours)</b>			0.002
0-12 (n=18)	17 (94.4)	1 (5.6)	
12-24 (n=18)	17 (94.4)	1 (5.6)	
24-48 (n=13)	10 (76.9)	3 (23.1)	
>48 (n=13)	7 (53.8)	6 (46.2)	
<b>Blood pressure (mm Hg)</b>			0.011
<100 (n=9)	1 (11.1)	8 (88.9)	
>100 (n=53)	50 (94.3)	3 (5.7)	
<b>Pulse (beats/minute)</b>			0.000
<100 (n=43)	41 (95.3)	2 (4.7)	
>100 (n=19)	10 (52.6)	9 (47.4)	
<b>Blood albumin level (g/dl)</b>			0.000
<2.5 (n=15)	7 (46.7)	8 (53.3)	
>2.5 (n=47)	44 (93.6)	3 (6.4)	
<b>Blood creatinine level (g/dl)</b>			0.000
<2.5 (n=47)	44 (93.6)	3 (6.4)	
>2.5 (n=15)	7 (46.7)	8 (53.3)	
<b>Hemoglobin level (g/dl)</b>			0.009
<10 (n=19)	12 (63.2)	7 (36.8)	
>10 (n=43)	39 (90.7)	4 (9.3)	
<b>Diameter of perforation (mm)</b>			0.014
<0.5 (n=42)	38 (90.5)	4 (9.5)	
>0.5 (n=20)	13 (65)	7 (35)	

ASA - American Society of Anesthesiology

last 50 years, there has been a radical change in the epidemiology of PUD. The rate of PPU has tended to diminish.<sup>9,10</sup> At the same time, a gradual relative increase in elderly persons sustaining a perforation has been observed.<sup>8,10,11</sup> Our study supports these data: 62.9% were more than 50 years old. In fact, an absolute increase has been reported in elderly women.<sup>9,11</sup> But, the present study does not indicate that more women than men sustained a PPU. Also, we observed that the mortality rate of women was higher than the male population (**Table 1**). This outcome is not associated with the sex directly. The specifications of the sex groups were dissimilar. The mean age, ASA score, time between onset of symptoms to surgery, and coexisting medical disease ratio were higher in the female group.

Emergency surgery for perforated ulcer presently carries a mortality risk of up to 30%.<sup>1,4</sup> Our mortality rate (17.7%) was comparable with other recent literature reports.<sup>7,12,13</sup> Within the past decade, several retrospective and prospective studies have identified risk factors predictive of mortality including age, delay to surgery, shock on admission, low albumin concentration, concurrent medical illness, ulcer location, renal failure, liver cirrhosis, and immunosuppression.<sup>1,4,7,14-19</sup> Many scoring systems have been introduced to assess prognosis objectively after emergency surgery that attempt to identify patients with a higher risk of morbidity and mortality.<sup>12,19</sup> The present study confirmed the age, sex, ASA classification, coexisting medical disease, elapsed time from symptoms to operation, blood pressure, pulse, serum albumin and creatinine levels, hemoglobin level and diameter of perforation as valid prognostic factors in whole series (**Table 1**), whereas a previous history of PUD, chronic ingestion story of NSAIDs, alcohol ingestion, smoking habits, site of perforation, type of surgical treatment (simple suture or resection), postoperative complications did not appear to be related to prognosis.

There is an ongoing debate whether PPUs generally need to be operated on or not. It has been estimated that approximately half of the perforations seal by themselves,<sup>20</sup> and a prospective trial comparing conservative treatment with surgical treatment in perforated PUD has shown no advantage of surgical treatment with regard to morbidity and mortality.<sup>21</sup> The results of this trial have been confirmed by the evaluation of a protocol for the non-operative management of PPU in a general hospital over several years. Possibly, conservative treatment can be safely tried in approximately two-thirds of patients.<sup>22</sup> However, it has been shown that delaying time point of an operation beyond 12 hours after the onset of clinical symptoms will worsen the outcome in peptic ulcer perforation.<sup>14-16</sup> Therefore, it is crucial not to pass the time when an operation (laparotomy or laparoscopy) is definitely indicated.<sup>14,16,20,21,23</sup>

Consequently, we believe that surgery is the only treatment for peptic ulcer perforation. For many years, there has been a discussion about which is the operation of choice for patients with peptic ulcer perforation.<sup>7,12,16</sup> In our experience, the type of surgical treatment has not influenced prognosis; it is to be considered that we performed a definitive operation only on selected cases. The simple suture of the perforation with omentoplasty is the treatment of choice, because it is simple and fast.<sup>4,13</sup> We preferred this technique in most of the patients. The need for radical treatment of peptic disease with gastric resection or a vagotomy associated with suture is advocated because of the high rate of recurrent ulcer.<sup>5,13</sup> We also demonstrate that the suture of perforation is safe, and the treatment of underlying peptic disease is to demand medical therapy; the rare recurrences were due to low compliance of patients to therapy.

In conclusion, age, gender, ASA classification, co-existing medical disease, elapsed time from symptoms to operation, blood pressure, pulse, serum albumin and creatinine levels, hemoglobin level and diameter of perforation are factors significantly associated with fatal outcomes in patients undergoing emergency surgery for PPU. Thus, such factors need to be carefully taken into account during the general workup of patients admitted for PPU.

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