

Evaluation of clinico-radiological factors affecting morbidity and mortality in peptic ulcer perforation surgery

Mustafa Yeni¹, Murat Kartal², Tolga Kalaycı³

Department of General Surgery, Erzurum Regional Training and Research Hospital, Erzurum, Turkey

ABSTRACT

Objectives: Peptic ulcer perforation (PUP) remains a surgical emergency with high early period morbidity and mortality. In this study, it was aimed to evaluate clinico-radiological factors affecting morbidity and mortality in peptic ulcer perforation surgery.

Methods: Patients who were operated for PUP at Erzurum Regional Training and Research Hospital General Surgery Clinic, Erzurum, Turkey between 2010 and 2020 were selected retrospectively. The patients' clinical and radiological parameters were retrieved from their medical records. Patients who developed complications in the 30 days after surgery were considered the morbidity-positive group, and the patients who developed mortality in the 30 days after surgery were considered the mortality-positive group. The relationship between investigated factors and morbidity and mortality was investigated with suitable statistical tests. A p value < 0.05 was considered statistically significant.

Results: The study included 81 patients and, 74 (91.4%) patients were males. Complications were observed in 15 (18.5%) patients and mortality was seen in 3 (3.7%) patients in the first 30 days postoperatively. Preoperative comorbidity, low systolic blood pressure, high Boey score had negative effect on both morbidity and mortality. In addition, lower amylase levels played a protective role in both morbidity ($p = 0.011$) and mortality ($p = 0.018$). Mortality increased significantly with increasing age. However, no radiological factor affected either morbidity or mortality.

Conclusions: Both morbidity and mortality increased in cases with poor clinical condition at the time of diagnosis. In addition, the mortality rate was higher in patients with comorbidities and postoperative complications.

Keywords: Amylase, Boey score, comorbidity, morbidity, mortality, peptic ulcer perforation

Peptic ulcer perforation (PUP) is one of the most important complications of peptic ulcer disease (PUD) [1]. Although the incidence of PUD decreased during the last few decades due to the successful treatment of *Helicobacter pylori*, the decrease in perforation cases was not as desired [2]. Perforation accounts for most deaths associated with PUD [3, 4]. PUP remains a surgical emergency, with high early period

mortality of 10-30% and early period morbidity of 21-43% [4, 5].

Surgical repair with or without omentum is the most common surgical technique in PUP surgery. While surgical repair is most commonly performed with open surgery, laparoscopy are preferred in appropriate cases [6]. The laparoscopic treatment of PUP has been shown to be applicable and safe, but its im-

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Address for correspondence: Mustafa Yeni, MD., Erzurum Regional Training and Research Hospital, Department of General Surgery, Atatürk Mah., Çat Yolu Cad., Yakutiye, Erzurum, Turkey. E-mail: mustafayeni3@hotmail.com, Tel (Mobil): +90 505 314 63 00, Tel (Office): +90 442 232 55 55

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plementation into routine clinical practice has been slow [5]. A Denmark study reported that only 6% of patients with PPU were treated with laparoscopic surgery [7].

The aim of this study is to evaluate clinico-radiological factors affecting morbidity and mortality in PUP surgery.

METHODS

Patients who were operated for PUP at Erzurum Regional Education and Research Hospital General Surgery Clinic, Erzurum, Turkey, between 2010 and 2020 were selected for the study retrospectively. Age and gender of the patients, preoperative comorbidity, systolic blood pressure (above or below 100 mm Hg), time from pain to hospital admission (longer or shorter than 24 hours) were evaluated. Since smoking is an important parameter in perforation etiology, the smoking of the patients was also evaluated. Boey scores of all patients were calculated. The components of the Boey score are as follows: concomitant medical illness, preoperative shock, perforation time greater than 24 hours. Each factor scores 1 point if positive. The total Boey score is calculated based on the individual scores of the parameters.

Preoperative laboratory parameters and imaging tools were also investigated. In hematological analysis, white blood cell (WBC) and platelet counts, hemoglobin values, leukocyte and lymphocyte counts were searched. In addition, amylase and lactate dehydrogenase (LDH) levels were investigated in biochemical analysis. Presence of free air both X-Ray radiograph and computed tomography (CT) scan were investigated. Also, on CT scan, presence of intra-abdominal fluid was searched.

Surgery type, perforation location, postoperative

complications, hospital stay, and mortality were also evaluated. After collecting the evaluated parameters, the relationship between the parameters and morbidity and mortality was analyzed.

Ethics committee approval was received from Non-invasive Clinical Research Ethics Committee of Erzurum Regional Education and Research Hospital, Erzurum, Turkey (Decision No: 2021/05-84).

Statistical Analysis

Statistical evaluation was made with SPSS v22.0 (IBM, Armonk, NY, USA). The normality distribution of quantitative variables were checked with Shapiro-Wilk test. The Mann-Whitney U test was used according to the results of the Shapiro-Wilk test. In addition, Chi-square test, and Likelihood ratio test were used to compare qualitative variables. A p value below 0.05 was considered statistically significant.

RESULTS

Between 2010 and 2020, 94 patients were operated on for PUP in Erzurum Regional Training and Research Hospital General Surgery Clinic, Erzurum, Turkey. Thirteen patients were excluded from the study because all data of these patients were not accessible. Thus, 81 patients were included in the study. After collecting the evaluated parameters, the effect of the collected parameters on morbidity and mortality was investigated. Complications were observed in 15 (18.5%) patients and mortality was seen in 3 (3.7%) patients in the first 30 days postoperatively. Patients were divided into groups according to morbidity and mortality.

74 (91.4%) patients were males and 7 (8.6%) were females, and male to female ratio was 10.57. The mean age of all patients was 44.81 years (range: 18-

Table 1. Comorbid diseases of the patients

Comorbidity	n (%)
Hypertension	10 (62.5)
Chronic obstructive pulmonary disease (COPD)	3 (18.75)
Hypertension with COPD	2 (12.5)
Hypertension with diabetes mellitus	1 (6.25)
Total	16 (100)

Table 2. Comparison of clinical parameters according to morbidity

Preoperative factors	Morbidity positive n = 15	Morbidity negative n = 66	p value
Age (years) (mean)	46.27	39.80	0.337*
Gender			0.114**
Female	3 (42.9%)	4 (57.1%)	
Male	12 (16.2%)	62 (83.8%)	
Comorbid disease			0.001**
Yes	8 (50%)	8 (50%)	
No	7 (10.8%)	58 (89.2%)	
Preoperative systolic blood pressure			0.001**
< 100 mmHg	7 (58.3%)	5 (41.7%)	
≥ 100 mmHg	8 (11.6%)	61 (88.4%)	
Time from pain to admission			0.932**
≥ 24 hours	8 (18.2%)	36 (81.8%)	
< 24 hours	7 (18.9%)	30 (81.1%)	
Boey score			0.004***
0	5 (15.2%)	28 (84.8%)	
1	2 (6.3%)	30 (93.8%)	
2	4 (40%)	6 (60%)	
3	4 (66.7%)	2 (33.3%)	
Cigarette usage			0.701**
Yes	9 (20%)	36 (80%)	
No	6 (16.7%)	30 (83.3%)	
Laboratory test results (mean)			
WBC ($10^3/\text{mm}^3$)	15.27	13.02	0.484*
Neutrophil ($10^3/\text{mm}^3$)	10.87	10.46	0.670*
Lymphocyte ($10^3/\text{mm}^3$)	3.44	1.83	0.555*
Platelet ($10^3/\text{mm}^3$)	292.53	274.23	0.870*
Amilase (U/L)	58.07	95.70	0.011*
LDH (U/L)	261.20	247.67	0.359*
Free air on X-Ray			0.983**
Yes	8 (18.6%)	35 (81.4%)	
No	7 (18.4%)	31 (81.6%)	
Free air on CT scan			0.113**
Yes	15 (22.1%)	53 (77.9%)	
No	0 (0%)	13 (100%)	
Fluid at CT scan			0.742**
Yes	10 (19.6%)	41 (80.4%)	
No	5 (16.7%)	25 (83.3%)	
Operative factors			
Type or surgery			0.464**
Open	14 (17.9%)	61 (82.1%)	
Laparoscopic	1 (33.3%)	2 (66.7%)	
Perforation localization			0.001***
Pre-pyloric area	9 (39.1%)	14 (60.9%)	
Juxta-pyloric area	4 (23.5%)	13 (76.5%)	
Post-pyloric area	2 (4.9%)	39 (95.1%)	

* Mann-Whitney U Test, **Chi-square test, ***Likelihood ratio test. WBC = White Blood Cell, LDH = Lactate Dehydrogenase, CT = Computed Tomography

Table 3. Comparison of clinical parameters according to mortality

	Mortality positive n = 3	Mortality negative n = 78	p value
Preoperative factors			
Age (years) (mean)	78.17	39.57	< 0.001*
Gender			0.240**
Female	1 (14.3%)	6 (85.7%)	
Male	2 (2.7%)	72 (97.3%)	
Comorbid disease			0.007**
Yes	3 (18.8%)	13 (81.2%)	
No	0 (0%)	65 (100%)	
Preoperative systolic blood pressure			0.003**
< 100 mmHg	3 (25%)	9 (75%)	
≥ 100 mmHg	0 (0%)	69 (100%)	
Time from pain to admission			0.246**
≥ 24 hours	3 (6.8%)	41 (93.2%)	
< 24 hours	0 (0%)	37 (100%)	
Boey score			< 0.001***
0	0 (0%)	33 (100%)	
1	0 (0%)	32 (100%)	
2	0 (0%)	10 (100%)	
3	3 (50%)	3 (50%)	
Cigarette usage			0.084**
Yes	0 (0%)	45 (100%)	
No	3 (8.3%)	33 (91.7%)	
Laboratory test results (mean)			
WBC (10 ³ /mm ³)	17.38	13.33	0.934*
Neutrophil (10 ³ /mm ³)	13.58	10.42	0.480*
Lymphocyte (10 ³ /mm ³)	3.38	2.08	0.953*
Platelet (10 ³ /mm ³)	272.67	277.81	0.543*
Amilase (U/L)	36.00	90.76	0.018*
LDH (U/L)	360.33	245.94	0.053*
Free air on X-Ray radiograph			0.598**
Yes	1 (2.3%)	42 (97.7%)	
No	2 (5.3%)	36 (94.7%)	
Free air on CT scan			> 0.999**
Yes	3 (4.4%)	65 (95.6%)	
No	0 (0%)	13 (100%)	
Fluid at CT scan			0.292**
Yes	3 (5.9%)	48 (94.1%)	
No	0 (0%)	30 (100%)	
Operative Factors			
Type or surgery			> 0.999**
Open	3 (3.8%)	75 (96.2%)	
Laparoscopic	0 (0%)	3 (100%)	
Perforation localization			0.258***
Pre-pyloric area	1 (4.3%)	22 (95.7%)	
Juxta-pyloric area	2 (11.8%)	15 (88.2%)	
Post-pyloric area	0 (0%)	41 (100%)	
Morbidity			0.005**
Yes	3 (20%)	12 (80%)	
No	0 (0%)	66 (100%)	

*Mann-Whitney U Test, **Chi-square test, ***Likelihood ratio test. WBC = White Blood Cell, LDH = Lactate Dehydrogenase, CT = Computed Tomography

84 years). While no relationship was found between age and morbidity, mortality increased with increasing age ($p < 0.001$). Sixteen (19.8%) patients had at least one comorbid disease. Comorbid diseases of the patients are shown in Table 1.

In 12 (14.9%) patients, preoperative systolic blood pressure was under 100 mm/Hg. In 44 (54.3%) patients, time from pain to hospital admission was longer than 24 hours. The most common Boey score of the study was Boey 0 ($n = 33$, 40.7%). The percentages for Boey 1, 2, and 3 were 39.5%, 12.3% and 7.4%, respectively. In addition, cigarette consumption was present in 55.6% ($n = 45$) of all patients. There was a correlation between the presence of comorbid disease, low systolic blood pressure, high Boey score, and both morbidity and mortality. While the morbidity rate was 66.7% in patients with Boey 3 score, the mortality rate was 50%. As the Boey score increased, the possibility of both morbidity and mortality increased.

On laboratory, 58 (71.6%) patients had leukocytosis, and 57 (70.4%) patients had neutrophilia. According to laboratory evaluation, only amylase levels played a role in both morbidity ($p = 0.011$) and mortality ($p = 0.018$). Both morbidity and mortality were inversely proportional to the rising amylase level.

On imaging tools examination, subdiaphragmatic free air on right side was observed in 43 (53%) patients on plain radiography. Plain radiography was not taken in 20 (24.7%) patients under emergency conditions. However, free air was also present on tomography in all patients with free air on plain radiography. On CT scan, 68 (84%) patients had intra-abdominal free air, 51 (63%) patients had free fluid in the abdomen. On the other hand, there was no pathological finding on CT scan in 13 (16%) patients. The presence of free air and free fluid in imaging methods affected

neither morbidity nor mortality.

Open surgery was preferred surgery type in 78 (96.3%) patients. The remaining operations were performed via laparoscopy. Graham's omental patch closure was performed in all patients to close the perforation defect. Most of the surgery notes could not be evaluated because there was no information about the perforation diameter in operation notes. In addition, the most common area of perforation was the post-pyloric area ($n = 41$, 50.6%). Other perforation areas and percentages were as follows: 28.4% at pre-pyloric area, and 21% at juxta-pyloric area. Morbidity rate was higher in pre-pyloric area perforations with 39.1% ($p = 0.001$). In the patients with morbidity, mortality was also higher ($p = 0.005$). Evaluation of morbidity and mortality according to clinical and radiological parameters is shown in Table 2 and Table 3.

The morbidity rate of the study was 18.5%. The most common postoperative complication was surgical site infection with 46.7%. The incidence of pulmonary complications was 33.3%. Postoperative complications and treatment of these complications are shown in Table 4. The mean length of hospital stay was 8.23 days (3-16 days). Mortality rate of our study was 3.7% ($n = 3$). All patients died because of multi organ failure and sepsis.

DISCUSSION

This study's results demonstrate that morbidity of PUP surgery was higher at the patients with preoperative comorbidity, shock, higher Boey score, and perforation localized pre-pyloric area. In addition, mortality of PUP surgery was higher at the patients with advanced age, preoperative comorbidity, shock,

Table 4. Postoperative complications and treatment of these complications

Postoperative complications	Treatment	n (%)
Surgical site infection	Local drainage with daily cleaning	7 (46.7)
Multi organ failure and sepsis (all these patients died)	Combine antibiotherapy with fluid support therapy	3 (20)
Atelectasis	Breathing exercises	2 (13.3)
Pleural effusion	Drainage without chest tube	2 (13.3)
	Drainage with chest tube	1 (6.7)
Total		15 (100)

higher Boey score, and morbidity. However, lower amylase level had a protective effect on both morbidity and mortality.

In literature, PUP cases are more likely to be seen in male gender and are mostly seen in the 4th and 5th decades [8-11]. In the present study, the male/female ratio was 10.57, which was consistent with the literature. On the other hand, the mean age of all patients was 44.81 years, which was consistent with the literature too.

There was no consensus on a specific gender and age limit that determined morbidity and mortality. In the study of Kim *et al.* [12], age above sixty and female gender were affected morbidity. However, Kocer *et al.* [10] showed that PUP cases were mostly seen in the male gender (88.8 vs. 11.2). Yıldırım *et al.* [13] showed that age over 50 years increased both morbidity and mortality. In this study, gender did not affect both morbidity and mortality. However, advanced age only affected mortality.

Since smoking is more preferred in male gender and the incidence of smoking increases, perforation rates are higher in male gender [14, 15]. The smoking prevalence of present study was 55.6% and was not correlated with higher morbidity and mortality. On the contrary, Kocer *et al.* [10] showed that smoking increased mortality but did not affect morbidity. Contrary to the literature, smoking did not affect both morbidity and mortality in the present study.

As in the literature, the presence of preoperative shock increases mortality like our study [10, 16, 17]. Tas *et al.* [18] did not identified correlation between shock and morbidity. In contrast, preoperative shock increased morbidity in the present study. Comorbidities, higher ASA (American Society of Anesthesiologist) score and from pain to hospital application are also important factors for morbidity and mortality [5, 9-11, 19]. However, in the recent study, no relationship was found between the time of onset of pain and both morbidity and mortality. But comorbid diseases played an important role in increasing morbidity and mortality. As a limitation of our study, ASA scores of the patients could not be accessed and evaluated.

Boey score is a useful tool for assessing the prognosis of operated cases due to PUP and helps in the evaluation of both morbidity and mortality [14]. While mortality is between 30-60% in patients with a Boey score of 2, in Boey score 3 cases, mortality reaches

100%. In our study, all deaths had a Boey score of 3.

Laboratory parameters can also help to predict PUP. Yamamoto *et al.* [20] showed that while serum WBC count and platelet count were higher in perforation group, hemoglobin level, total protein and albumin levels, AST and ALT levels were higher in non-perforation group. Amylase levels were higher in patients with morbidity and mortality in follow-up and higher amylase levels were correlated with duration of perforation, size of perforation, and amount of fluid determined intraoperatively [21]. However, in contrast to the literature in the present study, both morbidity and mortality were high in patients with low serum amylase levels.

In plain radiography, 47.2-80% of patients with perforation had sub-diaphragmatic free air on the right side [10, 22]. On the other hand, CT scan has a high diagnostic accuracy of 98% in the diagnosis of PUP [12]. In 35% of gastroduodenal perforations, there is no direct or indirect finding in imaging methods [23]. In this study, while subdiaphragmatic free air on right side was observed in 53% of the patients on plain radiography, free air was also present on tomography in 84% of all patients. On the other hand, there was no pathological finding on CT scan in 16% of the patients.

In the studies of Tas *et al.* [18] and Yıldırım *et al.* [13] free air on plain radiograph and perforation localization were not affected both morbidity and mortality. There was no relationship between the presence of free air in imaging tools and morbidity and mortality.

Type of surgery, perforation diameter wider than 5 mm and performing definitive procedures for treatment were also factors on morbidity and mortality [10, 18]. However, Yıldırım *et al.* [13] showed that the perforation diameter larger than 5 mm and the amount of fluid detected intraoperatively did not affect morbidity, but did affect mortality. Additionally, one study showed that even intra-abdominal fluid above 200 cc affected morbidity [24]. Effects on morbidity and mortality could not be evaluated since most of the surgery notes did not have any information about the perforation diameter and intra-abdominal fluid in our study. In addition, surgical procedures could not be compared since all patients were operated with primary closure with omental patch. But in the study of Yıldırım *et al.* [13], treatment with only primary suture increased both morbidity and mortality.

The post-operative morbidity rate in PUP surgery ranges between 21-42% [10, 25]. Pulmonary and surgery site infections are often the main cause of post-operative complications [11]. The morbidity rate in the presented study was 18.5%, which was partially lower than the literature.

In literature, length of stay after surgery in patients with PUP ranges between 7-12.5 days [9, 26]. In line with the literature, the average length of hospital stay in this study was 8.23 days.

Limitations

There were some limitations in this study. This study was a retrospective study, and the patients were excluded because the data of 13 patients were not available. The relationship between ASA score, perforation diameter and amount of intra-abdominal fluid and early outcomes could not be evaluated due to the lack of information. In addition, the small number of patients included in the study is an important limitation.

CONCLUSION

Peptic ulcer perforation (PUP) is a serious disease that every surgeon may encounter. PUP remains a surgical emergency with high early period morbidity and mortality. From our study's results, both morbidity and mortality increased in cases with poor clinical condition at the time of diagnosis. In addition, the mortality rate was higher in patients with comorbidities and postoperative complications. Diagnosis and necessary surgical treatment should be done as early as possible to prevent morbidity and mortality.

Authors' Contribution

Study Conception: MY, TK; Study Design: MY, MK; Supervision: MY; Funding: MK, TK; Materials: MY, MK; Data Collection and/or Processing: MY, TK; Statistical Analysis and/or Data Interpretation: MY, TK; Literature Review: MY, MK, TK; Manuscript Preparation: MY, TK and Critical Review: MY.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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