

## Factors Predicting the Mortality and Morbidity in the Management of Perforated Duodenal Ulcer

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### ABSTRACT

**Background:** Peptic ulcer perforation continues to be a major surgical problem. In this study, risk factors that influence morbidity and mortality in perforated peptic ulcer disease were examined. **Objective:** The aim of this study is to assess the usefulness of the prognostic factors in terms of morbidity and mortality in the treatment of perforated duodenal ulcer patient. **Patients and Methods:** The study is comprised of patients who presented with peptic ulcer perforation between July 2014 and July 2015 in the department of surgery in Aswan University. Data regarding age, gender, complaints, time elapsed between onset of symptoms and hospital admission, physical examination findings, co-morbid diseases, laboratory and imaging findings, morbidity and mortality were recorded. The study group included 82(82.0%) male and 18 (18%) female patients. The mean age was  $54.34 \pm 10.45$  (18-78) years. **Results:** The results of this study showed that the most common cause of mortality was cardiovascular failure. Mortality was observed in 8 patients (8.0%). 37 patients (37.0%) had complications. The most common complication was wound infection. Analysis revealed age over 50 years, presence of co-morbidities as independent risk factors for morbidity. Age over 50 years, time to admission and purulent peritoneal fluid were detected as independent risk factors for mortality. **Conclusions:** We can conclude that the early diagnosis and proper treatment are important in patients presenting with peptic ulcer perforation.

### INTRODUCTION

Peptic ulcer disease (PUD) is a disease that results from an imbalance between aggressive factors such as stomach acid and pepsin and mucosa defense barriers<sup>1</sup>. Every year peptic ulcer disease (PUD) affects 4 million people around the world<sup>2</sup>. Over the last several decades, the development of potent antisecretory agents (H2 blockers and proton pump inhibitors) and the recognition that treatment for Helicobacter pylori infection can eliminate most ulcer recurrences have essentially eliminated the need for elective surgery<sup>2</sup>.

Mortality and morbidity following perforated peptic ulcer (PPU) is substantial, and mortality proportions of 25–30% have been reported in population-based studies<sup>3,4,5,6</sup>. When PPU are diagnosed expeditiously and promptly treated, outcomes are excellent with mortality ranges from 6% to 14%<sup>1,7,8,9</sup>.

A large number of prognostic factors for morbidity and mortality following PPU have been reported<sup>10,11,12</sup>.

Poor outcomes have been associated with increasing age, major medical illness, peri-

operative hypotension<sup>13</sup>, and delay in diagnosis and management (greater than 24 hours)<sup>14</sup>.

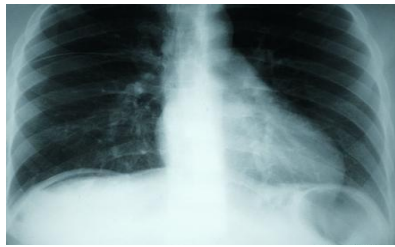
Several scoring systems including the Boey scoring system and the Mannheim Peritonitis Index (MPI)<sup>14</sup> have been used to stratify the risk of the patients and predict the outcomes of patients with perforated peptic ulcer. The Boey score is the most commonly and easily implemented among these scoring systems, and accurately predicts perioperative morbidity and mortality. The Boey score seeks to predict mortality based on the presence of major medical illness, pre-operative shock, and perforation longer than 24 h. In the original study by Boey et al., the in-hospital mortality proportion increased progressively with the number of prognostic variables, being 0%, 10%, 45.5%, and 100% in patients with none, one, two, or all three variables, respectively.

### PATIENTS AND METHODS

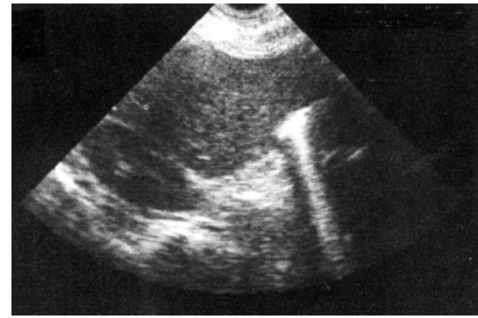
The study included 100 cases of perforated chronic duodenal ulcer. They were treated in the department of surgery in Aswan University Hospital between July 2014 and July 2015. The

criteria of case selection were thorough history, clinical examination & radiological findings with diagnosis of perforation of chronic duodenal ulcer and undergone operative treatment. Data on patient co-morbidities, presenting symptoms, vital signs, laboratory studies, and diagnostic procedures were documented.

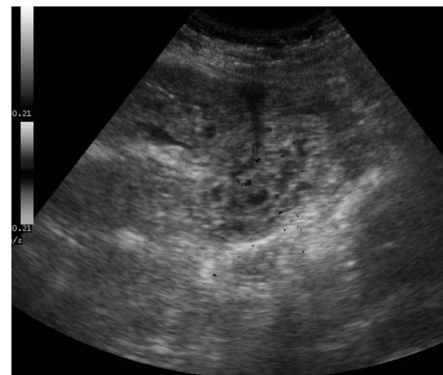
Erect abdominal x- ray was performed followed by urgent surgery which included simple closure with omental patch reinforcement together with peritoneal toilet and tube drainage. Briefly, three sutures through the ulcer were placed using 3/0 vicryl. The needle was passed through the normal duodenum a few millimeters away from the edge in order to avoid tearing the ulcer. Then, a patch of epiploon was applied to the perforation site and the sutures were tied (Fig. 1, 2,3,4). A drain was left in the right subhepatic region. In case of general peritonitis, the abdominal cavity was irrigated with warm saline and a second drain was placed at the pelvis. Peri-operative complication details, mortality and the results of follow-up data were obtained postoperatively.



**Fig. 1:** Abdominal radiography in standing position showing free air under the diaphragm.



**Fig. 2:** The sonographic appearance of free intraperitoneal air



**Fig. 3:** Intraperitoneal free fluid and reduced intestinal peristalsis at sonographic examination are considered indirect signs of gastroduodenal perforation



**Fig. 4:** Primary closure of perforated duodenal ulcer by interrupted sutured covered with pedicled omentoplasty.

The following clinical variables were evaluated for their putative influence on morbidity and mortality: age, associated medical illness, duration of symptoms, nature of peritoneal fluid, extent of peritonitis, and preoperative shock. The significance of differences was assessed. A p value of <0.05 was accepted as significant.

The duration of symptoms was defined as the time span between the initial pain perception due to perforation and the operation. A delay in treatment was defined as an interval of more than 24 hours until surgery from the suspected time of perforation. The study was divided into two groups : "early admission"– within 24 hours –, and "late admission" – later than 24 hours –, according to the duration of symptoms.

Haemodynamic instability at the time of presentation was defined as a systolic blood pressure less than 90 mmHg. Patients were arbitrarily divided into two groups (<49 years and >49years). Treatment outcome was elaborated by postoperative complications and death.

#### Statistical analysis

The essential information was entered into the computer spreadsheet. Statistical package for social sciences (SPSS) for windows version 21.0 (SPSS Inc.) was used to analyze the data using the appropriate descriptive and inferential statistical methods and displayed by means of varied statistical presentations. The degree of agreement of the various clinically related procedure tools in terms of a specific diagnosis was determined by the use of Kappa statistics, which indicated the degree of agreement beyond chance. The Kappa value could range from 0 to 1. Statistical significance was set at  $P < 0.05$ .

#### Ethical consideration

Written informed consent was obtained from all the study subjects and approval for the study was obtained from the Hospital Ethical and Research Committee of the OAUTHC, Ile-Ife, Osun State.

## RESULTS

In this study, age of the patients ranges from 18 to 78years with mean age  $54.34 \pm 10.45$  years.

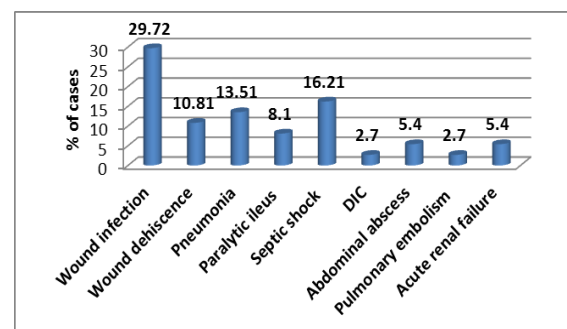
The maximum distribution belongs to 4<sup>th</sup> decade of life .There were 82 males (82%) and 18 females (18%).

A variety of post-operative complications occurred in a number of patients. These were pneumonia, paralytic ileus, wound infection, acute renal failure, septic shock, pulmonary embolism, wound dehiscence, duodenal fistula, abdominal abscess and disseminated intravascular coagulation (DIC)

Complications developed in 37 (37%) patients as listed in table 1

**Table 1:** Distribution of complications raised in patients with perforated DU.

Complication	No. "n=37"	%
Wound infection	11	29.72
Wound dehiscence	4	10.81
Pneumonia	5	13.51
Paralytic ileus	3	8.10
Septic shock	6	16.21
DIC	1	2.70
Abdominal abscess	2	5.40
Pulmonary embolism	1	2.70
Acute renal failure	2	5.40
Duodenal fistula	2	5.40%
Total	37	37%



**Fig 1:** Distribution of complications raised in patients with perforated DU.

The overall mortality in 100 cases was 8%. The details of postoperative mortalities are shown in table 2

**Table (2):** Postoperative mortalities.

<i>Serial No.</i>	<i>Sex</i>	<i>Age</i>	<i>Co- morbidities</i>	<i>Causes of death</i>
No.1	female	78	Ischaemic heart disease	Cardiovascular failure
No.2	male	71	Liver cirrhosis, hypertension	Cardiovascular failure
No.3	male	68	Chronic obstructive pulmonary disease	Respiratory infection and failure
No.4	male	73	Diabetes Mellitus, Hepatitis	Sepsis with multi organ failure
No.5	female	55	Rheumatoid arthritis	Renal failure
No.6	male	59	None	Pulmonary embolism
No.7	male	44	None	Sepsis with DIC
No.8	male	48	None	Duodenal fistula

This study indicates that some factors play a role and have high association with the outcome. Table 3

**Table (3):** Some of the influencing factors to mortality observed in the study group.

<i>Factors</i>	<i>No. of patients</i>	<i>No. of death</i>	<i>P. value</i>
<b>Age of the patients :</b>			
< 50 years	52 (52%)	2 (25.0% )	P<0.000***
> 50 years	48 (48%)	6 (75.0% )	
<b>Time interval between onset of symptom and operation:</b>			
< 24 hours	38 (38 % )	2 (25.0%)	P<0.000***
> 24 hours	62 (62 % )	6 (75.0%)	
<b>Nature of peritoneal fluid:</b>			
Billous	34 (34%)	1(12.50 %)	P<0.000***
Purulent	66 (26%)	7(87.5%)	
<b>Extent of Peritonitis :</b>			
Generalized	74 (74%)	7(87.5%)	P<0.000***
Localized	26(26%)	1(12.5%)	
<b>Pre operative shock :</b>			
Present	11(11%)	5(62.5 %)	P<0.02*
Absent	89(89%)	3(37.5%)	
<b>Concurrent medical diseases:</b>			
Present	23(23%)	5(62.5%)	P<0.02*
Absent	77(77%)	3(37.5%)	

**Table (4): Some of the influencing factors to morbidity observed in the study group .**

<b>Factors</b>	<b>No. of patients</b>	<b>Complications "n=37"</b>	<b>P. value</b>
<b>Age of the patients :</b>			
< 50 years	52 (52%)	15 (40.54%)	P=0.392n.s
> 50 years	48 (48%)	22 (59.45 %)	
<b>Time interval between onset of symptom and operation :</b>			
< 24 hours	38 (38 %)	7 (18.91%)	P<0.000***
> 24 hours	62 (62 %)	30 (81.08%)	
<b>Nature of peritoneal fluid:</b>			
Billous	34 (34%)	9 (24.3 %)	P<0.000***
Purulent	66 (26%)	28 (75.67%)	
<b>Extent of Peritonitis :</b>			
Generalized	74 (74%)	34 (91.89%)	P<0.000***
Localized	26 (26%)	3(8.10 %)	
<b>Pre operative shock :</b>			
Present	11(11%)	8(21.62 %)	P<0.001**
Absent	89(89%)	29(78.37%)	
<b>Concurrent medical diseases:</b>			
Present	23(23%)	16 (43.24 %)	P=0.385n.s
Absent	77(77%)	21 (56.75 %)	

## DISCUSSION

Perforated peptic ulcer (PPU) is relatively rare, but life-threatening with the mortality varying from 10% to 40%<sup>15,16</sup>.

This study indicates that there are many factors, which are mostly connected to each other affecting the prognosis regarding morbidity and mortality rates, such as age, duration of perforation, extent of peritonitis, preoperative shock and concomitant medical disease.

The incidence of perforated duodenal ulcer disease increases with advanced age and this increase has been attributed to the high frequency of risk factors for PUD among elderly patients, e.g., *Helicobacter pylori* colonization or use of non-steroidal anti-inflammatory drugs. A decreasing incidence of perforations in the younger age groups has been reported earlier<sup>17</sup>, contrary to our observation. A possible explanation for our findings of a higher incidence of perforations in young men (52% of patients were <50 years old) is that use of a diet high in salt and smoking among young people is common in Aswan, which was earlier shown to be associated with an increased risk of perforation. These factors have in common that they affect acid secretion in the gastric mucosa<sup>18</sup>. Defining

the exact etiological factor in any given patient may often be difficult, as more than one risk factor may be present and they tend to interact.

It is also known that the size of perforation is more likely associated with higher mortality and morbidity due to increased peritoneal contamination<sup>19</sup>. In our study, we have not come across giant perforation.

Sixty two patients were admitted to our department later than 24 hours after their initial pain started. The present study showed that the risk of morbidity was statistically significant when the patient was submitted to surgery with a perforation later than 24 hours, in agreement with literature which emphasizes the importance of early surgical intervention to improve the outcome<sup>20</sup>.

It is clearly evident from other publication<sup>21,22,23</sup> and as in our study that there are more deaths among patients with longstanding perforation. It is highly statistically significant in all analyses that, delayed treatment after perforation causes reduced survival, increased complications and prolonged hospital stay<sup>24</sup>.

Previous studies have reported the strong negative prognostic impact of delayed surgery for PPU<sup>24</sup>. D.L. Buck et al.,<sup>25</sup> in their nationwide cohort study of 2668 patients treated surgically

for PPU demonstrated that every hour of surgical delay was associated with a 2-4 per cent decreased probability of surviving 30 days.

A possible reason for the strong association between delay and adverse outcome could be the increased risk of developing severe sepsis. Longstanding perforation is associated with peritoneal contamination, positive peritoneal cultures, septic complications and development of postoperative abscesses<sup>25</sup>.

The critical for delayed presentation having negative effects seems to be approximately 24 hours. Recent studies showed that duodenal perforations are sterile for the first 12 hours and then become contaminated<sup>21</sup>. This may explain why frequency of adverse effects increases with increasing delay. Hemodynamic instability and extensive peritoneal soiling was seen in delayed cases. Hemodynamic instability was mainly evident among the delayed cases and may be due to sepsis.

Most of our patients were referred from peripheral hospitals of long distance, this itself delayed the treatment. Reasons behind delayed surgery for PPU in our sixty two patients seem to be associated with out-of-hospital perforation, late attendance by the surgeon, attendance by a non-senior surgeon and lack of peritoneal signs. The recognition of symptoms was significantly later in elderly patients which were probably due to a low sensibility of older people to the symptoms of disease.

Another factor frequently noted in the literature regarding morbidity and mortality is the co-existence of significant co-morbidities<sup>22, 26</sup>. In our series, this factor was found to be important for morbidity and it was associated with mortality. However, in a study done by G. Bas et al.,<sup>22</sup> this factor was not found to be important for morbidity but it was associated with mortality.

Co-morbidity alone cannot explain the increase in the mortality but other factors like duration of perforation, extent of peritonitis, preoperative shock, as well as the ongoing functional and biological deterioration associated with advanced age may play a role<sup>27, 28</sup>.

Elderly patients are another vulnerable group suffering from chronic duodenal ulcer perforation with vague and atypical presentation. The frequency of complication increases markedly in age group more than 50 years which is reflected in the series of Sakhawat Mahmud Khan et al<sup>21</sup>.

Lethality in patients less than 50 years was low. Morbidity and mortality in this series are higher among elderly. İlhan et al.<sup>1</sup> reported that mortality significantly increased in PUP patients above the age of 60. Kocer et al.<sup>34</sup> stated that mortality was 1.4% below the age of 65, while it was 75% above 50 years of age. In our study, being above the age of 50 was found to have a significant influence on mortality. A similar observation was made in our study. While some authors found that old age alone did not predict the outcome<sup>29, 30</sup>, age is an established prognostic factor after surgery for PPU for many authors<sup>31, 32</sup>. However, we determined that sex did not have an influence on mortality.

The present study confirms the value of age as a prognostic factor, patients who survived after surgical treatment of PPU were significantly younger than patients who died. Elderly patients have several unfavourable prognostic conditions caused by their advanced age and co-existing diseases, which lead to poorer results and higher mortality.

Gross peritoneal sepsis poses a great therapeutic problem and accounts for most of the deaths in perforation patient. There are more complications in the form of wound infection, wound dehiscence and fistula in that group even with optimum supportive efforts. All these ultimately prolong hospital stay of the patients with various long term complications.

The diagnosis of suspected duodenal ulcer perforation was made clinically and confirmed radiologically by erect abdominal X- ray in more than 87% of cases. Abdominal CT was more sensitive and specific than X- ray and was indicated in doubtful cases. History of peptic ulcer disease and NSAID usage was found in 23% of cases.

In the era of H. pylori eradication therapy and acid reducing medication, up to 90% of perforations can be treated by simple closure with or without omental patch. Definitive ulcer surgery is no longer required in the majority of the patients, as recurrence rates have dropped dramatically with post-operative medical therapy<sup>33</sup>.

## CONCLUSION

In spite of the developments in peptic ulcer disease treatment, peptic ulcer perforation

remains a serious surgical problem. Patients above the age of 50, with a time to presentation longer than 24 hours, presence of shock at the time of presentation and concomitant diseases are patients at high risk for post-operative morbidity and mortality. We believe that close post-operative follow-up of patients under risk can help in reducing morbidity and mortality rates. Limiting surgical delay is of paramount importance in treating patients with PPU.

We suggest Erect CXR as initial routine diagnostic assessment in case of acute abdomen from suspected free perforation of PU. If free peritoneal air is detected with conventional radiography, other imaging investigations are not indicated. In the absence of direct or indirect findings of pneumoperitoneum, US examination could help to confirm the evidence of intraperitoneal free fluid.

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