

# Risk Factors for Gastrointestinal Leak after Operative Repair of Perforated Peptic Ulcer Disease

## Original Article

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## ABSTRACT

**Background:** Peptic ulcer disease (PUD) is a frequent outpatient diagnosis. Although medications and precautions have advanced to control this disease, the prevalence of PUD remains high. The complication of perforated peptic ulcer disease (PPUD) is the most common reason for urgent PUD surgery. Therefore, it is critical to determine the risk factors for developing a postoperative leak.

**Objectives:** This study aims to identify the risk factors for gastrointestinal leak after operative repair of PPUD to guide for appropriate intraoperative decisions and postoperative care.

**Patients and Methods:** This is a retrospective cohort study of 60 patients who had PPUD surgically repaired at a tertiary medical facility. The possible risk factors for postoperative leak development were recorded. Age, sex, BMI, preoperative usage of steroids, preoperative usage of tobacco, comorbidities, vital signs at admission, preoperative albumin, preoperative complete blood count, and perforation size were among the risk factors that were investigated.

**Results:** In this study, the leak occurred among six (10%) patients, and a burst abdomen among four (5%) patients, while 50 (85%) patients did not develop postoperative complications. Our results revealed that the risk factors after repair of PPUD include older age ( $56.33 \pm 15.9$  years), higher BMI ( $35.9 \pm 16.7$  kg/m<sup>2</sup>), tobacco use, presence of comorbidities (Chronic obstructive pulmonary disease, diabetes mellitus, hypertension, and liver cirrhosis), and larger size of perforation at  $3 \pm 3$  cm.

**Conclusion:** The study demonstrated that older age, higher BMI, tobacco use, the presence of comorbidities, and a larger size of perforation are risk factors for the development of leaks after operative repair of PPUD.

**Key Words:** Emergency surgery, gastrointestinal leak, operative repair, peptic ulcer disease, perforated peptic ulcer.

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## INTRODUCTION

Peptic ulcer disease (PUD) is still often identified in outpatient settings. The incidence of PUD has dropped since the development of drugs and treatment plans. On the other hand, there has not been nearly as significant a drop in the mortality rate linked to PUD or the frequency of emergency surgery<sup>[1]</sup>.

Bleeding, perforation, and blockage are among PUD complications. The most common and serious reason for urgent surgery for PUD is perforated peptic ulcer disease (PPUD)<sup>[2]</sup>. It affects 2–10% of PUD patients and is associated with a 30% death rate and a 50% morbidity rate<sup>[1,3]</sup>. The currently practiced surgical procedure of PPUD is an omental plug by Cellan-Jones or Graham repairs which uses a pedicled or free omental patch<sup>[4]</sup>.

One typical postoperative consequence of PPUD surgical repair has been reported to be postoperative leak<sup>[5]</sup>. Postoperative morbidity is influenced by various factors such as age, operational technique, patient comorbidity status, degree of perforation, and degree of physiologic impairment<sup>[6]</sup>. It has also been demonstrated that other variables, such as female gender, old age, and malnourishment (hypo-albuminemia), raise the chance of death<sup>[7]</sup>. For risk classification and triage, it is crucial to accurately and promptly identify high-risk surgical patients with PPUD.

In order to improve intraoperative guidance and postoperative treatment, the purpose of this study is to determine the risk factors for gastrointestinal leak following operational repair of PPUD.

## PATIENTS AND METHODS

This retrospective cohort study involved 60 patients who were presented to the emergency department of a tertiary hospital with perforated peptic ulcers from January to June 2023.

All patients indicated for emergency exploration for suspected PPUD based on a clinical or radiological diagnosis that underwent Graham's patch repair were included in our study.

## ETHICAL CONSIDERATION

The institutional research and ethics committee reviewed and permitted the research protocol. After participants were adequately briefed on the study's goals, their written informed consent was obtained. The patient could withdraw from the study at any moment; participation was voluntary. According to the Declaration of Helsinki, all steps of data collecting, entry, and analysis were conducted in a highly confidential and private manner.

For every patient, possible risk factors for postoperative leakage following PPUD repair were noted. The study examined various risk factors, such as age, sex, BMI (patients were deemed 'obese' if their BMI was greater than 30 kg/m<sup>2</sup>), comorbidities, preoperative complete blood count, preoperative albumin (albumin <3.5 g/dl is abnormal), size of perforation, and preoperative tobacco and steroid use (any utilize one month before surgery). The study also assessed hospital length of stay, postoperative morbidity, requirement for re-operation, and mortality among the study cohort.

### Clinical evaluation and diagnosis

Patients with PPU were suspected when presenting with severe, sudden-onset epigastric pain, which can become generalized peritonitis with board-like rigidity. Further imaging and laboratory testing were required to rule out differential diseases in cases when clinical images were unclear, such as obese, immunocompromised, patients with decreased levels of consciousness, patients on steroids, elderly, and children.

### Laboratory markers and radiological imaging

Laboratory investigations were done to assess severity and organ function and exclude differential diagnoses involving acute pancreatitis. Total leucocytic count (TLC), hemoglobin, international normalized ratio, albumin, sodium (Na), potassium (K), and lactate levels were all assessed preoperatively. Blood cultures were taken early, before starting broad-spectrum antibiotics.

Upon presentation at the emergency room, an erect chest or upright abdominal radiography was done to confirm the diagnosis and detect complications. For a differential diagnosis, an abdominal computed tomography with

contrast was done. Pelvi-abdominal ultrasound (PAUS) was used to detect the presence of free fluid collection.

### Surgery and follow-up

The operational technique involved midline exploration, lavage with warm saline, repair of the perforation with Graham's omental patch, and insertion of drains (Figure 1).

The postoperative regimen to start was clear fluids on day one. If tolerated, it was upgraded to a soft diet and then a regular diet accordingly.

Based on this primary outcome, patients were stratified into two groups: patients who developed an upper gastrointestinal leak after repair (leak group) and patients who did not develop a leak after repair (no leak group).

Clinical criteria were used to define leaks, or computerised tomography imaging was utilized to show a new fluid collection and a shift in the drain's nature to bilious.

The existence of potential risk variables for leak development was evaluated between the leak and no-leak groups to see if there were any notable differences.

All patients had a nasogastric tube inserted intra-operative and maintained for 2–3 days according to patients' follow-up. The urinary catheter was removed on day one post-surgery unless indicated to promote ambulation and avoid bedridden complications. All patients had intra-abdominal drains that were removed one at a time, according to clinical and laboratory findings, and all were removed before discharge.

All patients followed a similar postoperative management routine unless otherwise required. Routine antibiotics (Third-generation cephalosporins) and metronidazole were prescribed during hospital admission and up to 1 week after discharge.

Patients admitted to the ICU or those with higher sepsis parameters were prescribed varying types of antibiotics (this was individualized on a patient-to-patient basis). All patients received intravenous proton pump inhibitors and analgesics (paracetamol) during their stay.

### Sampling size

We employed a clinical sample size calculator for the analytical study, with a 0.05 alpha error and a 0.80 power of the study, confidence interval (CI) of 95%. According to the literature (6), the Sample size computed is 68 cases, including a 10% increase to cover the follow-up duration.

### Statistics data analysis

SPSS (Statistical Program for Social Science) version 21 (IBM, SPSS, USA) was used to analyse the data. Quantitative data were shown as mean, SD, median, and

interquartile range; qualitative data were shown as numbers and percentages. Tests of significance, both parametric and nonparametric ( $\chi^2$ , Student t test, and Mann–Whitney test) were conducted. The risk factors for postoperative complications, mortality, and leak development were predicted using logistic regression. The significance threshold was established at or below 0.05.

## RESULTS

The study involved 60 patients who fulfilled our inclusion criteria; 95% were males and 5% were females, with a mean age of  $42.02 \pm 14.7$  years and a mean BMI of  $29.01 \pm 7.4$  kg/m<sup>2</sup>, respectively. Nearly half (58%) of the patients did not suffer any comorbidity; however, 78.3% and 73.3% experienced steroid and tobacco use, respectively. Most patients (80%) were vitally stable upon admission; however, the majority had a free fluid collection observed on the pelvi-abdominal US (95%), as shown in Table (1).

Laboratory investigations showed normal ranges of hemoglobin, Na, K, and International normalized ratio and elevated levels of both total leucocytic count and lactate, with an average of  $15.4 \pm 7.05$  and  $2.92 \pm 2.6$  mmol/l, respectively, (Table 1).

Regarding operative details, the majority of patients (86.7%) underwent open Graham's patch, 5% underwent open modified Graham's patch, 5% underwent laparoscopic Graham's patch, and 3.3% underwent laparoscopic converted to open Graham's patch.

The most encountered sizes of perforation were  $0.5 \times 0.5$  cm (50%) and  $1 \pm 1$  cm (30%); 11.7% of patients had  $2 \times 2$  cm perforation, 5% of patients had  $3 \times 3$  cm perforation, 1.7% of patients had  $1.5 \times 1.5$  cm perforation and 1.7% of patients had  $4 \times 4$  cm perforation.

Also, most patients (85%) had three drains inserted, 8.3% had four drains inserted, 5% had no drains inserted, and 1.7% had one drain inserted.

Regarding postoperative events, leaks occurred among six (10%) patients and burst abdomens among four (5%) patients. Only one patient experienced both leaks and a burst abdomen, while 51 (85%) patients did not develop postoperative complications. Twelve (20%) patients needed ICU admission, and five of the reoperated patients did not survive due to severe sepsis, as shown in (Table 2). Only nine of our patients needed re-operation. Our study cohort's median length of hospital stay was 6.0 (5.0–7.0) days.

Table (3) shows that patients who experienced a postoperative leak were significantly more likely to be older ( $P=0.011$ ), have a higher BMI ( $P=0.031$ ), have more comorbidities ( $P<0.001$ ), and have a larger size of perforation ( $P=0.001$ ) when comparing potential risk

factors between the leak and no leak groups.

Accordingly, we determined five factors that were independently correlated with postoperative leak development: older age (odds ratio (OR)=1.08, 95% CI 1.01–1.15), higher BMI (OR=1.1, 95% CI 1.007–1.2), tobacco use (OR=1.9, 95% CI 2.07–18.5), presence of comorbidities (OR=0.016, 95% CI 0.01–0.172), and larger size of perforation at  $3 \times 3$  cm (OR=5.8, 95% CI 2.5–13.1).

The identified risk factors, each of older age, greater BMI, and presence of comorbidities, were more likely to predict both postoperative complication and mortality. At the same time, tobacco use and the presence of leaks were significantly associated with postoperative complications, as shown in Table (4).

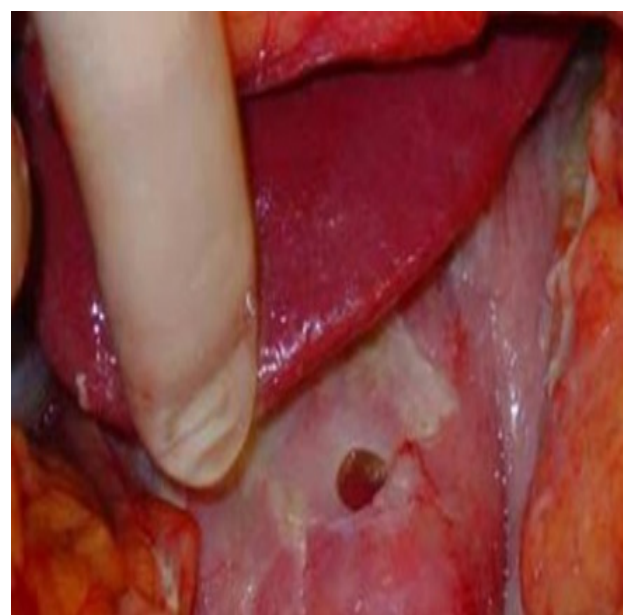
**Table 1:** Basic clinical, demographic data and laboratory findings ( $n=60$ ).

	Frequency, percent
Sex, n (%)	
Male	57 (95)
Female	3 (5)
Age (mean $\pm$ SD) in years	42.02 $\pm$ 14.7
BMI (mean $\pm$ SD)	29.01 $\pm$ 7.4
Comorbidities, n (%)	
COPD, heart failure, cirrhotic	1 (1.7)
DM	2 (3.3)
HTN	1 (1.7)
Both HTN and DM	3 (5)
Leukemia	1 (1.7)
Rheumatoid arthritis	1 (1.7)
Free	51 (85)
Steroid abuse, n (%)	47 (78.3)
Tobacco abuse, n (%)	44 (73.3)
Vitals, n (%)	
Stable	48 (80)
Unstable	12 (20)
PAUS, n (%)	
Minimal FF	5 (8.3)
Mild FF	29 (48.3)
Moderate FF	16 (26.7)
Marked FF	7 (11.7)
No FF	3 (5)
Laboratory investigations	Mean $\pm$ SD
TLC	15.4 $\pm$ 7.05
Hb (gm/dl)	13.2 $\pm$ 2.6
INR	1.2 $\pm$ 0.25
Albumin (gm/dl)	2.98 $\pm$ 0.63
Na (mEq/l)	135.8 $\pm$ 5.1
K (mEq/l)	4.08 $\pm$ 0.72
Lactate (mmol/l)	2.92 $\pm$ 2.6

BMI, Body mass index; COPD, Chronic obstructive pulmonary disease; DM, Diabetes mellitus; FF, Free fluid collection; Hb, hemoglobin; HTN, hypertension; INR, International normalized ratio; K, Potassium; Na, Sodium; PAUS, Pelvi-abdominal ultrasound; TLC, total leucocytic count.

**Table 2:** Postoperative events among study participants.

	Frequency (percent)
Complications	
Burst abdomen	3 (5)
Leakage	5 (8.3)
Both Leakage and burst abdomen	1 (1.7)
No	51 (85)
Leak	6 (10)
ICU admission	12 (20)
Reoperation ( <i>n</i> =9)	
Closure of abdomen in layers	2 (22.2)
Closure of Skin with Bogota.	1 (11.1)
Falciform patch and closure of skin with Bogota	2 (22.2)
Open Graham's patch	1 (11.1)
Open serosal patch.	2 (22.2)
Distal gastrectomy	1 (11.1)
Mortality	5 (8.3)

**Fig. 1:** Intraoperative perforated gastric ulcer.**Table 3:** Comparison of possible risk factors for developing a leak after operative repair of PPU in cases who leaked compared to cases who did not.

	Leak ( <i>N</i> =6) [ <i>n</i> (%)]	No leak ( <i>N</i> =54) [ <i>n</i> (%)]	<i>P</i> value
Sex			0.241 <sup>a</sup>
Male	5 (83.3)	52 (96.3)	
Female	1 (16.7)	2 (3.7)	
Age (mean±SD) in years	56.33±15.9	40.4±13.8	0.011 <sup>b</sup>
BMI (mean±SD)	35.9±16.7	28.2±5.4	0.031 <sup>b</sup>
Albumin <3.5 gm/dl	6 (100)	42 (77.8)	0.333 <sup>a</sup>
Comorbidities			
COPD, heart failure, cirrhotic	0	1 (1.9)	<0.001 <sup>c</sup>
DM	1 (16.7)	1 (1.9)	
HTN	1 (16.7)	0	
Both HTN and DM	3 (50)	0	
leukemia	0	1 (1.9)	
Rheumatoid arthritis	0	1 (1.9)	
Free	1 (16.7)	50 (92.6)	
Steroid abuse	6 (100)	41 (75.9)	0.324 <sup>a</sup>
Tobacco abuse	5 (83.3)	39 (72.2)	0.421 <sup>a</sup>
Vitals			0.088 <sup>a</sup>
Stable	3 (50)	45 (83.3)	
Unstable	3 (50)	9 (16.7)	
Size of perforation			0.001 <sup>c</sup>
0.5 ×0.5 cm	1 (16.7)	29 (53.7)	
1 ×1 cm	1 (16.7)	17 (31.5)	
1.5 ×1.5 cm	0	1 (1.9)	
2 ×2 cm	1 (16.7)	6 (11.1)	
3 ×3 cm	2 (33.3)	1 (1.9)	
4 ×4 cm	1 (16.7)	0	
Drains			
0 (no drain)	0	3 (5.6)	0.759 <sup>a</sup>
1	0	1 (1.9)	
3	6 (100)	45 (83.3)	
4	0	5 (9.3)	

a: Fisher's exact test; b: Independent samples T test; c: Chi-square test.

**Table 4:** Logistic regression to assess the probability of developing a leak, postoperative complication, and mortality dependent on controlled patient demographics, baseline features, and operative details.

	Leak development			Post-operative complication			Mortality		
	Odds ratio	95% CI	P value	Odds ratio	95% CI	P value	Odds ratio	95% CI	P value
Age	1.08	1.01–1.15	0.022	1.075	1.01–1.1	0.01	1.08	1.01–1.1	0.027
Sex (Male)	0.0	0.0–0.0	0.999	0.0	0.0–0.0	0.999	0.0	0.0–0.0	0.999
BMI	1.1	1.007–1.2	0.035	1.13	1.03–1.2	0.012	1.1	1.03–1.3	0.011
Albumin <3.5 gm/dl	0.0	0.0–0.0	0.999	0.0	0.0–0.0	0.999			
Steroid abuse	0.0	0.0–0.0	0.999	0.0	0.0–0.0	0.999	0.0	0.0–0.0	0.999
Tobacco abuse	1.9	2.07–18.5	0.01	4.5	1.04–19.8	0.044	4.8	0.7–3.2	0.1
Comorbidities (no)	0.016	0.01–0.172	0.001	0.07	0.01–0.3	0.002	0.025	0.002–0.2	0.002
Size of perforation (0.5×0.5 cm) 3×3 cm	5.8	2.5–13.1	0.01	18.0	1.2–26.2	0.035	0.0	0.0–0.0	0.999
Leak				0.04	0.005–0.3	0.003	0.0	0.0–0.0	0.999

Male, no, 0.5×0.5 cm were set as reference category.

## DISCUSSION

One of the most frequent surgical emergencies that present in the emergency room is a PPU. The results of patients undergoing emergency surgery for PPUD are influenced by some identified risk factors, including age greater than 60, shock upon admission, and concurrent systemic disorders<sup>[8]</sup>. Up to 30% of all deaths have been documented in the literature<sup>[1,7]</sup>. The treatment of people with PPUD has essentially not changed<sup>[1]</sup>. Rather than using evidence-based approaches, the routine management of patients with PPUD is primarily focused on traditional methods. In view of new surgical facts based on evidence, traditional surgical techniques are currently being re-examined<sup>[1]</sup>.

A comparatively high overall rate of postoperative complications, ranging from 17 to 63%, was described in the literature<sup>[9,10]</sup>. Mortality and morbidity rates were previously reported to be around 10.1 and 24.2%, respectively<sup>[11]</sup>.

The present study result supports previous studies that found considerable postoperative morbidity (OR=0.04, 95% CI 0.005–0.3) following operation repair of PPUD due to leaks. Determining which patients are at a higher risk of developing a postoperative leak is, therefore, crucial.

There were 60 patients in the current study. Patients had emergency exploration of a perforated peptic ulcer in the General Surgery Emergency Unit of a tertiary hospital. It investigated possible risk factors for the occurrence of a postoperative leak following PPUD repair.

Analyzing the postoperative complications of the present study cohort, leak occurred among six (10%) patients, burst abdomen among four (5%) patients, while 50 (85%) patients did not develop postoperative complications. Twelve (20%) patients needed ICU admission, and five (8.3%) patients of the reoperated patients did not survive due to severe sepsis.

The mean age of the study participants was 42.02±14.7 years. Our results revealed that older age (56.33±15.9) significantly increased the risk of developing a postoperative leak after Graham's patch repair. Numerous investigations have shown that advanced age is an independent risk factor for leak, morbidity, and death in patients with PPU<sup>[12–20]</sup>.

Our study's sex distribution comprised 95% males and 5% females, showing no significant difference between sexes in developing postoperative leaks after Graham's omental patch. In concordance, a study conducted in 2021 revealed that gender was not identified as a risk factor for postoperative leakage<sup>[21]</sup>. The same results were obtained in a more recent study by *Liu et al.* in 2023<sup>[20]</sup>.

The mean BMI in our study cohort was 29.01±7.4 kg/m<sup>2</sup>. Our analysis demonstrated that a higher BMI (35.9±16.7 kg/m<sup>2</sup>) is correlated with the development of postoperative leak, with a *P value* of 0.031. However, previous studies found that higher BMI was not correlated with a raised likelihood of postoperative leak or mortality after PPUD surgery<sup>[21,22]</sup>.

Regarding the relation between laboratory findings and postoperative leak incidence or mortality, the patients' findings failed to be considered risk factors; however, other studies found hypoalbuminemia to be a strong single predictor of mortality in PPU cases<sup>[23,24]</sup>.

Concerning medications and smoking, 78.3 and 73.3% experienced steroid and tobacco use, respectively. We found that tobacco utilization is correlated with a higher risk of developing postoperative leaks. In contrast, in the studies conducted by *Lund et al.* and *Liu et al.*, tobacco use was not identified as a risk factor for postoperative leak<sup>[20,21]</sup>.

We investigated the presence of comorbidities in our study, more than half (58%) of the current study patients did not experience any comorbidity; however, the presence of comorbidities such as COPD, heart failure, liver



cirrhosis, diabetes mellitus, and hypertension increased the risk of development of postoperative leak among the study population with a *P value* less than 0.001. In 2019, Safaan and colleagues showed that preoperative comorbidities were significantly correlated with 30-day morbidity<sup>[25]</sup>.

Another element correlated with an elevated risk of a postoperative leak is having a more extensive perforation at 3 ×3 cm, with a *P value* of 0.001. In concordance, *Guadagni et al.*'s study concluded that larger perforations at 1.5 cm increased the risk of developing a postoperative leak<sup>[26]</sup>.

## CONCLUSION

Our study demonstrated that older age, higher BMI, tobacco abuse, presence of comorbidities, and larger size of perforation are risk factors for developing leaks after operative repair of PPUD.

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Declaration: The manuscript has been read and approved by all the authors. The requirements for authorship of this document have been met. Each author believes that the manuscript represents honest work.

## CONFLICTS OF INTEREST

There are no conflicts of interest.

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