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Original Research Article

A Prospective Study on Postoperative Complications in Peptic Ulcer Perforation

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Abstract

Background: Perforated peptic ulcer is a common surgical emergency and the post-operative morbidity is related to the physiological effects of peritonitis, delayed source control and host reserve failure.

Methods: Patients: Adults who underwent emergency surgery for peptic ulcer perforation. Interventions: None. Main outcome measures: Pattern of postoperative complications and factors associated with morbidity. Demographic, clinical, biochemical, operative and outcome data were prospectively collected, and complications were classified according to the Clavien-Dindo classification in 128 consecutive patients who were followed for 30 days after surgery.

Results: The mean age was 47.8±16.3 years, 108 (84.4%) were male, and 51 (39.8%) had at least one postoperative complication. The most common morbid events were surgical-site infection (18.0%), pulmonary complications (14.1%), postoperative sepsis (9.4%), prolonged ileus (7.8%), wound dehiscence (7.0%), intra-abdominal collection (6.3%), and repair-site leak (4.7%). 17 (13.3%) patients experienced Clavien-Dindo grade III-V complications, and 8 (6.3%) died within 30 days. Patients with complications were older (56.4±15.2 vs 42.1±14.2 years; $p<0.001$) and were more likely to have a symptom duration >24 hours, preoperative shock, ASA class III-IV, hypoalbuminemia, large perforations, and Boey scores ≥2. On multivariable analysis, delay beyond 24 hours (adjusted odds ratio [aOR] 3.18; 95% CI 1.38-7.34; $p=0.007$), preoperative shock (aOR 4.26; 95% CI 1.41-12.89; $p=0.010$), and serum albumin <3.0 g/dL (aOR 2.89; 95% CI 1.22-6.86; $p=0.016$) independently predicted postoperative morbidity.

Conclusions: Nutritional and physiological susceptibility, early presentation, rapid resuscitation and source control may decrease complications after peptic ulcer perforation surgery.

Keywords: Peptic Ulcer Perforation; Postoperative Complications; Peritonitis; Omental Patch; Surgical Morbidity; Risk Factors.

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Introduction

Peptic ulcer disease (PUD) is a potentially serious condition that can lead to perforation of an ulcer into the peritoneal cavity (PPU), and is still one of the most important complications of PUD. With the advent of acid suppression and Helicobacter pylori eradication, and more careful use of ulcerogenic medications, elective ulcer surgery has declined, but perforation remains as a sudden generalized peritonitis that requires prompt resuscitation and source control.

The clinical significance of PPU is not commensurate with its prevalence, as a patient with PPU can rapidly deteriorate due to bacterial contamination, systemic inflammation, sepsis, organ dysfunction and postoperative complications. However, despite improvements in anesthesia, critical care, antimicrobial treatment and surgical technique, significant short-term morbidity and mortality remain as described in contemporary reviews [1].

Early diagnosis, physiological stabilization, broad-spectrum antibiotic and prompt operative treatment are stressed in international guidelines for most patients with free perforation and peritonitis. Simple closure with or without an omental patch is the preferred approach for small gastroduodenal perforations, with the choice between open and laparoscopic repair depending on the hemodynamic stability, surgical skills, ulcer characteristics and the degree of contamination [2]. The epidemiology is also variable, with age, comorbidity, NSAID use, smoking, H. pylori prevalence, and early surgical treatment all playing a role in complicated peptic ulcer disease [3].

Perforation has been found to occur with different frequency and severity according to age and sex in population-based studies, with the highest mortality rates in older patients and those who are physiologically compromised [4]. This variation is clinically significant as the postoperative course depends not only on the perforation, but also on the other factors. Risk of surgical-site infection, respiratory complications, intra-abdominal sepsis, repair-site leakage, reoperation, and death depend on the duration of peritoneal contamination, shock, renal dysfunction, nutritional reserve, comorbidity, and the severity of systemic inflammation. In a modern perspective, PPU should not only be considered in terms of technical closure, but also in terms of host response to emergency surgery [5].

Multicenter data has recently been confirmed that postoperative morbidity is still prevalent within various health systems. The Global Research Collaboration for Acute Conditions in Emergency Surgery (GRACE) study reported significant morbidity at 30 days after PPU surgery, and identified differences in patient characteristics, surgical techniques and outcomes between countries [6]. Especially delayed source control. Previous nationwide cohort studies have shown that mortality rates were worse with each hour of delay after admission to theatre [7] and that surgical delay was an independent risk factor for decreased survival [8].

Although there is a wealth of literature on mortality prediction, few prospective studies from routine tertiary-care practice have described the full range of postoperative complications and have also considered modifiable and non-modifiable risk factors for morbidity. There are numerous reports available that are retrospective, that include a mix of different types of perforation, or that only include deaths and not complications that extend hospital stays and necessitate further intervention. The ability to identify high-risk features prior to and during surgery may help to facilitate more intensive monitoring, earlier escalation of care, and more appropriate counseling of patients and families.

The present prospective observational study was thus designed to find the incidence and pattern of postoperative complications in the patients who underwent surgery for peptic ulcer perforation and to identify the independent clinical, biochemical and operative factors which are associated with postoperative morbidity at 30 days.

Materials and Methods

This is a prospective observational study carried out in the Department of General Surgery of a tertiary care teaching hospital. Patients were screened for participation in the study if they were consecutive adult patients undergoing emergency surgery for a perforated gastric or duodenal peptic ulcer.

Patients older than 18 years with radiologic and operative confirmation of perforated gastric and duodenal peptic ulcer were eligible. Patients with incomplete 30-day outcome information, patients with iatrogenic perforation, patients with perforation due to a known gastrointestinal malignancy, patients with perforation due to another segment of bowel and patients with traumatic perforation were excluded. Patients who died prior to operative source control were also excluded as the primary outcome was postoperative morbidity.

The sample size required was calculated for one prospective cohort. With a projected 40% complication rate, a 95% confidence interval and an absolute precision of 9%, a minimum of 114 patients was needed. Recruitment was continued until 132 patients had been operated on, even if they were not followed up. Thirty days follow-up was not completed in four patients, leaving 128 patients for final analysis.

At admission, trained investigators noted age, sex, smoking and alcohol use, previous ulcer symptoms, previous exposure to nonsteroidal anti-inflammatory drugs, major comorbidities, and duration of symptoms, heart rate, blood pressure, temperature, and presence of shock. Preoperative shock was defined as having a systolic blood pressure of less than 90 mmHg and needing active fluid resuscitation and/or vasopressor support. Laboratory parameters measured were hemoglobin, total leukocyte count, serum creatinine, electrolytes and serum albumin. Hypoalbuminemia was considered as serum albumin <3.0 g/dL. ASA physical status and Boey score were recorded prior to surgery.

Initial resuscitation, intravenous fluids, nasogastric decompression, proton pump inhibitors, analgesia, correction of significant electrolyte disturbances and broad-spectrum intravenous antibiotics for gram-negative and anaerobic organisms were used in all patients.

The surgeon on duty chose the operative approach based on the physiological status, contamination and perforation characteristics, and the surgeon's expertise. Perforation size and location, degree of peritoneal contamination, surgical approach, surgical duration and transfusion requirement were recorded in a prospective manner. Primary closure with an omental patch was used to treat small and medium perforations, while resection was performed when clinically indicated for large or suspicious gastric ulcers.

The main outcome was the development of any postoperative complication within 30 days of surgery. Complications were actively documented during admission and at follow-up, and were classified using the Clavien-Dindo classification.

Prespecified events were surgical-site infection, pulmonary complication (pneumonia, clinically significant atelectasis, or prolonged ventilatory support), postoperative sepsis, prolonged ileus (beyond postoperative day 5), wound dehiscence, intra-abdominal collection (requiring antibiotics or drainage), repair-site leak, acute kidney injury, reoperation, and death. Major morbidity was defined as Clavien-Dindo grade III-V and length of hospital stay was defined as the time from surgery to discharge or death.

Data were analysed with SPSS version 29.0. Continuous variables were tested for normality and then expressed as mean±SD or median with IQRs. Categorical variables were presented as numbers and percentages.

The independent-samples t test or Mann-Whitney U test was used for continuous variables and the chi-square test or Fisher exact test was used for categorical variables when comparing patients with and without postoperative complications. Univariable analysis was performed on all variables and those with $p<0.10$ and clinically important variables were selected for multivariable binary logistic regression. Odds ratios (ORs) with 95% confidence intervals (CIs) were presented. The Hosmer-Lemeshow test was used to evaluate model calibration, and a p-value of <0.05 was considered statistically significant.

Results

A total of 128 patients were included. The mean age was 47.8±16.3 years (range 18-82 years), and 108 (84.4%) were male. Ninety-seven (75.8%) perforations were duodenal and 31 (24.2%) were gastric.

Symptoms had been present for more than 24 hours in 46 (35.9%) patients, 22 (17.2%) presented with preoperative shock, and 33 (25.8%) were classified as ASA III-IV. Serum albumin was <3.0 g/dL in 42 (32.8%) patients.

Open surgery was performed in 116 (90.6%) and laparoscopy in 12 (9.4%); 117 (91.4%) underwent closure with an omental patch, 5 (3.9%) underwent primary closure without a patch, and 6 (4.7%) required distal gastric resection. Fifty-one patients (39.8%) developed at least one postoperative complication. Compared with patients without complications, those with morbidity were older (56.4±15.2 vs 42.1±14.2 years; $p<0.001$) and more frequently had symptom duration >24 hours (56.9% vs 22.1%; $p<0.001$), preoperative shock (33.3% vs 6.5%; $p<0.001$), comorbidity (45.1% vs 16.9%; $p<0.001$), ASA class III-IV (43.1% vs 14.3%; $p<0.001$), hypoalbuminemia (54.9% vs 18.2%; $p<0.001$), perforation size >1 cm (39.2% vs 14.3%; $p=0.001$), and Boey score ≥2 (41.2% vs 7.8%; $p<0.001$).

Table 1: Baseline and operative characteristics according to occurrence of postoperative complications

Characteristic	Complication (n=51)	No complication (n=77)	p value
Age, years, mean±SD	56.4±15.2	42.1±14.2	<0.001
Male sex, n (%)	41 (80.4)	67 (87.0)	0.312
Symptoms >24 h, n (%)	29 (56.9)	17 (22.1)	<0.001
Preoperative shock, n (%)	17 (33.3)	5 (6.5)	<0.001
Any major comorbidity, n (%)	23 (45.1)	13 (16.9)	<0.001
ASA class III-IV, n (%)	22 (43.1)	11 (14.3)	<0.001
Serum albumin <3.0 g/dL, n (%)	28 (54.9)	14 (18.2)	<0.001
Perforation size >1 cm, n (%)	20 (39.2)	11 (14.3)	0.001
Gastric perforation, n (%)	17 (33.3)	14 (18.2)	0.049
Boey score ≥2, n (%)	21 (41.2)	6 (7.8)	<0.001

The most frequent complication was surgical-site infection in 23 (18.0%) patients, followed by pulmonary complications in 18 (14.1%), postoperative sepsis in 12 (9.4%), prolonged ileus in 10 (7.8%), wound dehiscence in 9 (7.0%), intra-abdominal collection in 8 (6.3%), acute kidney injury in 7 (5.5%), and repair-site leak in 6 (4.7%). Seventeen patients (13.3%) experienced Clavien-Dindo grade III-V morbidity. Seven (5.5%) required reoperation, most commonly for leak or uncontrolled intra-abdominal sepsis. Eight patients (6.3%) died within 30 days. The median hospital stay was significantly longer among patients with complications than among those without complications (14 days [IQR 11-21] vs 7 days [IQR 6-9]; $p<0.001$).

Table 2: Spectrum and severity of 30-day postoperative complications (N=128)

Postoperative outcome	n (%)	Typical time of detection
Any postoperative complication	51 (39.8)	Within 30 days
Surgical-site infection	23 (18.0)	Postoperative days 4-10
Pulmonary complication	18 (14.1)	Postoperative days 2-7
Postoperative sepsis	12 (9.4)	Postoperative days 2-9
Prolonged ileus >5 days	10 (7.8)	After postoperative day 5
Wound dehiscence	9 (7.0)	Postoperative days 6-14
Intra-abdominal collection	8 (6.3)	Postoperative days 5-15
Acute kidney injury	7 (5.5)	Postoperative days 1-5
Repair-site leak	6 (4.7)	Postoperative days 3-10
Clavien-Dindo grade III-V	17 (13.3)	Within 30 days
Reoperation	7 (5.5)	Within 30 days
30-day mortality	8 (6.3)	Within 30 days

In the multivariable logistic regression model, symptom duration >24 hours, preoperative shock, and serum albumin <3.0 g/dL remained independently associated with postoperative morbidity.

Age ≥60 years also retained a significant association. Perforation size >1 cm and ASA III-IV showed increased point estimates but did not remain statistically significant after adjustment for correlated physiological variables.

The final model demonstrated acceptable calibration (Hosmer-Lemeshow p=0.680) and explained 42% of the variation in postoperative morbidity by Nagelkerke R^2.

Table 3: Multivariable predictors of postoperative morbidity

Predictor	Adjusted odds ratio	95% CI	p value
Age ≥60 years	2.41	1.03-5.66	0.043
Symptoms >24 h	3.18	1.38-7.34	0.007
Preoperative shock	4.26	1.41-12.89	0.010
Serum albumin <3.0 g/dL	2.89	1.22-6.86	0.016
Perforation size >1 cm	2.36	0.96-5.83	0.062
ASA class III-IV	2.21	0.89-5.47	0.087

Discussion

In the present prospective study, we found that about 1/5 of the patients who underwent emergency surgery for PPU developed a postoperative complication, and 13.3% of patients suffered from major Clavien-Dindo grade III-V morbidity. Surgical-site infection, pulmonary complications, sepsis, prolonged ileus, wound dehiscence, intra-abdominal collection, and repair-site leak were the most common events. These results confirm that successful closure of the perforation does not stop the acute disease process and that the severity and duration of the peritoneal contamination and the physiological reserve of the patient are significant factors in postoperative outcome.

The observed morbidity rate of 39.8% is clinically reasonable and similar to the wide range of values reported in the literature. Kocer et al. found that age, delay to presentation, shock, and comorbidity were key factors in morbidity and mortality following perforation, which is in keeping with the multifactorial nature of postoperative risk [9]. The present findings build upon this idea by showing that delay, shock, and low albumin were individually associated with complications after adjustment. The pattern indicates that factors other than the anatomical perforation, such as modifiable system-level factors and preoperative physiological status, may play as important a role as the perforation itself.

There has been a long history of risk stratification to identify patients requiring more aggressive perioperative management. The PULP score was created to predict the risk of death following PPU, and includes the following parameters: age, comorbidity, shock, delayed presentation, laboratory abnormalities and ASA status [10]. Further population-based analysis revealed that the PULP and ASA scores provided better prediction of mortality than the Boey score, and that hypoalbuminemia was a particularly strong individual predictor [11]. A Boey score ≥2 was strongly associated with complications on univariable analysis and age, shock, delay and hypoalbuminemia had greater independent explanatory value in the multivariable model in the present cohort.

This is in line with the notion that simple bedside scores are useful for triage but should not be used as a substitute for assessment of individual physiological variables. Saafan et al. investigated the usefulness of the PULP score in predicting 30-

day morbidity following repair of perforated duodenal ulcer, and compared it with Boey and ASA scores [12]. Anbalakan et al. also found that the commonly used models were inadequate and had to be locally validated before the scores could be used for individual prognosis [13]. We found that a pragmatic approach is warranted: the patient who presents with hypotension and albumin less than 3.0 g/dL more than 24 hours after the onset of symptoms should be considered to be at high risk, even if a formal score is not calculated. Early critical-care involvement, invasive hemodynamic monitoring if appropriate, aggressive sepsis management, respiratory optimization, and a decreased threshold for postoperative imaging or intervention in the event of clinical deterioration may be beneficial in such patients.

Leak from repair site was seen in 4.7% of patients and was one of the most serious complications as it often resulted in intra-abdominal sepsis or reoperation. Lund et al. showed that there is significant morbidity associated with postoperative leak after operative PPU repair, and that hypoalbuminemia and duodenal location are significant risk factors [14]. The correlation between low albumin and overall morbidity in our cohort could be due to the ability of albumin to serve as an indicator of chronic disease status and the severity of acute inflammation as well as its role in wound healing. Albumin should not be regarded as a nutritional parameter alone, as it can decrease in systemic inflammation and is an indicator of a vulnerable physiological phenotype that needs more attention.

In this study, open repair was the main surgical procedure performed, as it was typically the procedure performed in the emergency setting, with generalized contamination, hemodynamic instability and varying availability of advanced emergency laparoscopy.

Randomized trials have been pooled together and demonstrated that laparoscopic repair may have a beneficial effect on surgical-site infection, nasogastric tube duration and postoperative pain in selected patients, while major outcomes are similar to those of open repair [15]. The randomized LAMA trial also proved the feasibility of laparoscopic repair, but highlighted the need for proper patient selection and surgical skill [16]. This study was not designed to compare approaches and the small laparoscopic subgroup did not allow for adjusted comparisons. As such, the present results should be considered as risk factor data and not as evidence for a particular access route.

In univariable analysis, perforation size was associated with morbidity, and had a clinically significant, but not statistically significant, adjusted odds ratio. Large defects are technically more difficult, can be found in friable tissue and can be a risk for failure of repair. Wang et al. reported that the leakage rate was higher for perforations ≥25 mm after omental patch repair, suggesting that great care should be taken when operating on very large perforations [17]. In the case of perforated gastric ulcers, the question of whether to undertake a patch repair or resection is individual, and there is no clear mortality benefit for either approach in a systematic review by Zhu et al. [18] that identified significant selection bias in the evidence available. These data can be helpful in tailoring the operation to the quality of tissue, size, location, suspicion of malignancy, contamination, and patient stability, and not using a single procedure for all perforations.

Postoperative decision making is also crucial as unnecessary testing could be counterproductive. Jayaraman et al. showed that routine postoperative contrast imaging was not effective in reliably identifying clinically significant leaks and was linked to increased hospital stay [19]. Leaks and collections were investigated in our cohort based on clinical triggers including persistent tachycardia, fever, abdominal findings, bilious drain output, leukocytosis, or failure of expected recovery. This selective approach is based on the principle that postoperative imaging should be used to solve a clinical problem and not replace frequent bedside evaluation.

The mortality rate of 6.3% in this cohort was lower than some population based series but clinically significant. The variations between studies may be due to age distribution, delay in referral, comorbidity, access to intensive care, and case mix. In a tertiary care experience from Tanzania, Chalya et al. found significant morbidity and mortality, and highlighted delayed presentation as a significant negative factor [20]. This observation is consistent across health systems, indicating that minimizing prehospital and in-hospital delay is one of the most actionable targets to improve PPU outcomes.

The advantages of the present study are that prospective data were collected, consecutive patients were recruited, the 30-day outcomes were predefined, the complications were structured and graded, and the multivariable analysis included clinically relevant risk factors.

There are, however, some caveats that must be noted. This was an observational study in a single center with a moderate number of patients and the number of deaths and leaks was too small to develop separate strong prediction models for these two outcomes. Surgical approach and procedure were not randomized and treatment selection was influenced by disease severity and surgeon judgment. Long-term outcome of ulcer recurrence or H. pylori status was not assessed systematically since the study was focused on early postoperative morbidity. It would be helpful to have external validation in larger multicenter cohorts. The overall results suggest that the complications following PPU are not random events. They tend to be grouped in patients with long duration of contamination, shock, advanced age and poor physiological or nutritional reserve. A care pathway which will reduce time to perforation source control, identify high-risk patients early and will incorporate surgical, anaesthetic, critical-care, respiratory and nutritional management is likely to be more effective than focusing solely on the method of perforation closure.

Conclusion

The postoperative morbidity rate in patients who were operated on for peptic ulcer perforation was 39.8%, the most common causes of which were surgical-site infection, pulmonary complications, sepsis, wound complications and intra-abdominal morbidity. Patients at high risk were identified independently as having a delay of more than 24 hours, preoperative shock, hypoalbuminemia, and age ≥60 years. Intensified peri-operative monitoring of physiologically vulnerable patients and early source control can help minimise avoidable complications and enhance short-term outcomes.

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