International Surgery Journal
Vats R et al. Int Surg J. 2018 May;5(5):1702-1707
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: http://dx.doi.org/10.18203/2349-2902.isj20181418

Original Research Article

The outcome of surgery for perforated peptic ulcer in modern times

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Received: 08 March 2018
Accepted: 23 March 2018

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ABSTRACT

Background: A laparotomy for peritonitis due to perforated peptic ulcer is one of the commonest emergency operations done by a general surgeon and is still associated with a marked mortality and morbidity. The aim was to assess the current mortality and morbidity in patients operated for perforated peptic ulcer and to identify the factors associated with increased mortality in these patients.
Methods: All adult patients operated for perforated peptic ulcer over a period of one year were included in this prospective observational study. The demographics, clinical presentation, pre-operative laboratory parameters, operative findings, operation done, and the outcomes were noted in pre-designed proforma. Mortality and morbidity was assessed and factors relating to increased mortality were determined using standard statistical tests of significance such as Chi square test and the student's t test.
Results: 55 patients underwent laparotomy for perforated peptic ulcer (23 gastric and 32 duodenal perforations). There were 53 males and only 2 females in the group. Their mean age was 44 years. The mortality was 16% (9/55) and morbidity was 25% (14/55). Complications were encountered in 14 patients, most commonly surgical site infection in 13% cases, entero-cutaneous fistula occurred in 3 patients and one of them expired despite re-exploration due to persistent sepsis. The other two patients survived, and fistula healed spontaneously. The operative procedure done was Graham's patch or it's modification. Only 2 patients had antrectomy with Billroth II reconstruction.
Conclusions: Despite the advances in management of critically ill patients, the mortality (16%) and morbidity (25%) for this common surgical emergency remains high and is unchanged over the last half century. Presence of comorbidities and low serum albumin are associated with an increased risk of adverse outcome.

Keywords: Mortality, Peptic ulcer perforation, Peritonitis

INTRODUCTION

Peritonitis due to perforated peptic ulcer (PPU) is one of the commonest surgical emergencies attended by a general surgeon. Perforation is an acute life-threatening complication of peptic ulcer disease. In most cases it requires urgent surgical management and is associated with a high rate of mortality and morbidity.[1] Nowadays surgery for PPU, after initial resuscitation, consists of laparotomy/laparoscopy with peritoneal lavage and closure of perforation with or without omental patch. Cellan-Jones in 1929 and Graham in 1937 described their techniques of closure of perforation and reported a mortality rate of 17%.[2,3] The addition of definitive acid reducing procedures after repair of PPU although popular in mid and late twentieth century has been made redundant after the introduction of proton pump inhibitors.[4] Despite the passage of time and improvements in care of critically ill patients, PPU still has a substantial mortality.[5]

This study was done in order to evaluate the outcomes of surgery for PPU and to assess various factors that increase the risk of adverse outcomes.

METHODS

This prospective observational study was conducted at Himalayan Institute of Medical Sciences, Swami Ram Himalayan University, Dehradun over a period of 12 months. It is a tertiary care referral centre for the Garhwal division of Uttarakhand and neighbouring districts of western Uttar Pradesh. Adult patients who underwent exploratory laparotomy for peritonitis due to peptic ulcer perforation were included.

The University Ethics committee had granted permission for the study. Patients who on laparotomy were found to have perforation other than peptic ulcer, were less than 18 years of age or left against medical advice from hospital were excluded. A pre-designed proforma was used to record the demographics, clinical presentation, pre-operative laboratory parameters, operative findings, surgical procedure done and the outcomes. The data was entered in SPSS software version 20.

Mortality and morbidity was assessed in terms of percentages and factors relating to increased mortality were determined using standard statistical tests of significance such as Chi square test, Fisher's exact test and the Student's t test. A p value less than 0.05 was considered statistically significant.

RESULTS

During the study period 55 patients undergoing laparotomy for peritonitis were found to have perforated peptic ulcer. They underwent repair of perforation and were included in this study. There were 53 males and only 2 females. PPU is found to occur mostly in fourth and fifth decade of life (Table 1).

Table 1: Age distribution of patients with PPU and correlation with mortality.

Age groups	Mortality				P value
	No		Yes		
	Frequency	%	Frequency	%	
20-30	9	19.6	0	0.0	0.444
31-40	10	21.7	2	22.2	
41-50	14	30.4	2	22.2	
51-60	7	15.3	3	33.4	
>60	6	13.0	2	22.2	
Total	46	100	9	100	

The oldest patient in the study was aged 72 and survived the surgery. All patients had a laparotomy with peritoneal lavage. The perforation was repaired by Graham's or modified Graham's method in 38 cases and suture repair of perforation without omentopexy in 15 cases. The perforations were repaired with vicryl or silk suture depending upon the choice of the operating surgeon. Definitive procedure (antrectomy with truncal vagotmy and Billroth II reconstruction) was done in only 2 patients with a large size of perforation.

There were 9 deaths resulting in a mortality rate of 16 %. The cause of mortality in most of these patients was sepsis with multi organ dysfunction and most of these patients expired within 48 hours post-operatively. In one patient the initial recovery was satisfactory however this patient developed an entero-cutaneous fistula that was re-explored and again developed a leak. This patient succumbed to septic complications in the third week.

Table 2: Location of PPU and correlation with mortality.

Site of perforation	Mortality				P Value
	No		Yes		
	F	%	F	%	
Duodenal	29	63.1	3	33.3	0.108
Gastric	17	36.9	6	66.7	
Total	46	100	9	100	

32 patients had duodenal perforations, all located in the anterior wall of first part of duodenum and 23 had gastric perforations, of which 20 were located in the antrum (pre-pyloric) and 3 were located in the anterior wall of body along the lesser curvature of stomach. Amongst the 23 gastric perforations there were 6 deaths (26%) and out of the 32 duodenal perforations there were 3 deaths (9%). This seems to suggest that mortality is higher for patients with gastric ulcer perforation however the difference is not statistically significant (Table 2).

Table 3: Morbidity in patients operated for PPU (n = 55).

Complications	Number of events (14 patients)*
Surgical site infections	10
Duodeno-cutaneous fistula	2
Pleural effusion	6
Paralytic ileus	2

*some of the patients had multiple complications

The dimensions of perforation were assessed intra-operatively. Mostly the perforations were of size between 0.5-1 cm. There were 2 giant ulcers (>2 cm) located in the gastric antrum. Both of these antral ulcers were repaired by resection. One of them succumbed to sepsis. No saddle perforation or posteriorly located ulcer was encountered in this study. Among the 12 perforations of size < 0.5 cm, 3 were difficult to identify as they were almost pin- point dimension and were covered by pus flakes or adjacent viscera. The size of perforation had no correlation with mortality. Complications were encountered in 14 patients in this study (Table 3).

Some of the patients had multiple complications. The most frequent complication noted as expected was surgical site infection in 13 % cases. Breakdown of perforation repair with ensuing entero-cutaneous fistula occurred in 3 patients (5%) and one of them expired

despite re-exploration due to persistent sepsis. The other two patients survived, and fistula healed spontaneously.

Table 4: Co-relation of various co-morbidities with mortality in PPU (n = 55).

Co-morbidities	Mortality				P value
	No (46)		Yes (9)		
	F	%	F	%	
COPD	3	6.5	2	22.2	0.184
DM	5	10.9	6	66.7	0.001
HTN	1	2.2	3	33.3	0.012
Others	3	6.5	1	11.1	0.522

Correlation of mortality with various parameters was assessed. A positive history of chronic NSAIDs intake was present in 33 patients and steroid use in 4 however there was no correlation between ingestion of NSAIDs or steroid with mortality. Most of these patients were smokers (49/55) and had a history of alcohol ingestion (36/55) but this did not increase the risk of mortality. Among the pre-existing co-morbid conditions, diabetes and hypertension confer an increased risk of mortality in patients with PPU. COPD did not have a positive correlation with postoperative mortality (Table 4).

Table 5: Correlation of mortality with various laboratory parameters in PPU.

Laboratory parameter	Mortality		P Value
	No (n=46)	Yes (n=9)	
	Mean±SD	Mean±SD	
Hb (gm%)	14.17±2.58	13.33±2.13	0.363
TLC (x103/cu.mm)	9.04±4.41	7.76±6.42	0.466
Creatinine (mg/dl)	1.53±0.84	2.09±1.05	0.085
Potassium (mEq/L)	4.41±0.79	4.50±1.29	0.795
Sodium (mEq/L)	136.70±3.26	140.17±2.83	0.004
Albumin (mg/dl)	3.14±0.75	2.04±0.47	<0.001
Bilirubin (mg/dl)	0.82±0.52	1.42±0.65	0.010

On analyzing the laboratory parameters there was significant correlation between low serum albumin, low sodium and raised bilirubin levels with mortality (Table 5).

Surprisingly serum creatinine did not show a statistically significant impact on mortality. A trend towards increase in mortality was noted in patients who presented late to the hospital after the onset of symptoms however this did not reach statistical significance (Table 6).

Once admitted to the hospital all the patients were taken up for surgery within 6 hours after initial resuscitation.

Table 6: Delay in presentation correlated with mortality.

Delay in presentation	Mortality				P Value
	No		Yes		
	F	%	F	%	
Less than 24 hours	14	30.44	0	0	0.11
24-48 hours	15	32.60	3	33.34	
More than 48 hours	17	36.96	6	66.66	
Total	46	100	9	100	

Hypotension on presentation had no correlation with mortality following surgery for PPU. Although 11 patients had hypotension on initial examination they responded to resuscitation and all of them survived except one.

DISCUSSION

Peptic ulcer disease is a very common clinical entity. Effective treatment is now available with the advent of proton pump inhibitors and *H. pylori* eradication therapy. Surgery for intractable ulcer disease is rarely needed. Although the incidence of peptic ulcer disease has decreased over the past decades and the admission rates for this are declining, the epidemiological pattern of the complications, including bleeding and perforation, have changed little. The risk of PPU is 3.8 -14/100000 population/year and the need for emergency surgery for complications of peptic ulcer is fairly constant at 7 % of hospital admissions.[6] Perforation is the most common complication of peptic ulcer and also the most lethal with mortality rates upto 30%.[7,8] Although outcomes from bleeding ulcers have improved with the availability of modern endoscopic techniques, the outcomes of PPU have still remained unchanged.

The mortality of PPU as reported in previous studies is shown in Table 7 and is in double digits in most series (2, 9-23).

The reports from developed nations, where meticulous record keeping, and rigorous follow-up is available, such as Denmark show that the mortality approaches 30% and the reason may possibly be the older age of the patients with more co-morbidities. Some reports, especially from Asia, show a very low mortality rate (24,25). These include a higher proportion of younger patients without co-existing ailments and many cases operated laparoscopically which may have caused a selection bias. Multiple organ dysfunction is most important cause of mortality in PPU patients. This is also observed in the present study. Adherence to peri-operative sepsis protocol is most important to reduce mortality.[8]

There was an overwhelming preponderance of males in this study. This is similar to the observations of many

other reports of PPU in which almost 80% are males.[22,25] However Saverio D et al from Italy observed that more than half the patients undergoing surgery were females.[26] They were of the opinion that the incidence is more in females due to their longer life expectancy and presence of more co-morbidities leading to a greater use of ulcerogenic medications. PPU is seen commonly in fourth and fifth decade of life in this study. This finding was also noted in the earliest reports from the western world but now the age of afflicted patients is older. From the series in the developing world it is seen that patients are relatively younger.[27,28]

An interesting point noted in this series is the large number of gastric perforations mostly pre-pyloric with an almost equal distribution of duodenal and gastric perforations (1.2:1). Agaba has reported a very high number of pre-pyloric perforations (80%) in a series of 400 patients.[27] This is in sharp contrast to the ratio of duodenal to gastric perforations reported in other studies. Etonyeaku et al from Nigeria reported 10:1, Chalya et al from Tanzania found a 13:1 ratio while Bali et al from India showed a ratio of 5:1.[19,20,28]

The acid reducing procedures (vagotomy/ highly selective vagotomy) are used infrequently and in special circumstances only (e.g. in giant ulcers). In this study vagotomy with drainage procedure was not recquired in any of the PPU patient but 2 patients did undergo antrectomy with vagotomy and Billroth II reconstruction. Rickard et al in a review of surgery for complications of peptic ulcer reported a 60% vagotomy rate from sub-saharan Africa.[23] Seow et al have found a gastric resection rate of 1 in 10 in a series of 599 patients of PPU operated over a period of 8 years.[29] Agaba reported a 2% definite anti-ulcer procedure in a decade long period with 98% patch closure.[27]

Laparoscopic repair of PPU has been reported from many centres. The laparoscopic approach has a lesser rate of wound complications and faster recovery post-surgery, but the major morbidity and mortality remain the same.[30,31] Many of these patients recquire conversion to open surgery. However, with increasing expertise conversion rates are coming down and some dedicated laparoscopic teams are even showing a mortality of 2% in laparoscopic repair.[32] In this study all patients were managed via open approach despite the fact that several of the operating surgeons routinely do laparoscopic surgery in elective cases. This points towards the hesitancy amongst general surgeons to use the laparoscopic approach for PPU repair. In emergency hours, the availability of staff trained to assist in laparoscopic repairs is also an issue.

Some authors have cited the size of perforation as a significant factor in post-operative complications and mortality.[33] Giant ulcers (size more than 3 cm) had a mortality of 50% in comparison with small (5.74%) and large (15.79%) perforations. In the present study only 2 patients were encountered with giant ulcer perforations, out of which 1 patient survived. For the perforations <2 cms. Dimension, the size did not correlate with mortality

Post-operative morbidity following repair of PPU is high and ranges from 17- 63%.[8,26] The most common complication seen in our study is surgical site infection. Wound related problems are also the leading concern reported by other authors.[21,34] There are less surgical site complications in patients undergoing laparoscopic repair for PPU.[30-32] Zimmermann et al concluded that minor morbidity is less in laparoscopic approach but there was no difference in major morbidity or mortality compared to open surgery. Similar views have been put forward by Siow and Mahendran who had a morbidity of 22% in their laparoscopic series. The other frequently seen complications that may have a serious outcome are respiratory and abdominal sepsis (collection). All surgeons dread to see bilio-enteric contents pouring from the drain or surgical wound. The patient is at risk of life and the surgeon has a crisis of confidence with this setback. Leak rates of 2- 8% have been reported after perforation repair.[19,21,22] In the present study the fistula rate was 5%. These unfortunate patients have a 35% chance of mortality.

There are a number of scoring systems for outcome prediction in PPU, yet none appears to be superior and most of them are investigated in isolation.[8] The most frequently used scores are the American Society of Anesthesiologists (ASA) physical status classification system, the Boey score, the peptic ulcer perforation (PULP) score and POMPP score. The last three scores are designed specifically for the prediction of mortality for PPU patients and consider relatively simple data obtained pre-operatively.[18,36,37]

The delay in presentation was observed as one of the most important factors for increased mortality in PPU patients.[2,3] Other investigators have also noted increased risk of death with an increasing interval between perforation and initiation of treatment.[20-23,38] The same has not been observed in this study. The delay in presentation did not have a significant impact on mortality. In an analysis of patients undergoing emergency abdominal surgery in Denmark no significant assosciation between mortality and surgical delay was noticeable.[39] A study of 239 patients of PPU from Turkey found that the duration of symptoms had no effect on mortality.[35]

The blood parameters with a significant impact on mortality were serum albumin, bilirubin and sodium values. This is similar to the study done by Thorsen et al in which they conducted multivariate analysis of factors affecting outcomes. They concluded that hypoalbuminemia is the strongest single predictor of mortality. In the present study the value of serum creatinine was not found statistically significant in relation to mortality in patients of PPU. In the study there

was significant correlation noted in between mortality and associated comorbid conditions namely diabetes and hypertension. This is similar to the study done by Tas et al that co-existing medical illness has a significant role in mortality and morbidity in patients of PPU.[34]

CONCLUSION

The mortality of patients undergoing surgery for PPU was 16% with a morbidity of 25%. The leak rate for perforation repair was 5%. The morbidity most frequently seen is surgical site infection and wound dehiscence. Gastric perforations (pre-pyloric) are being seen in increasing numbers. The operative procedure remains the time-honoured Graham's patch. Laparoscopic repair although reported in literature has not gained widespread acceptance in tackling PPU. From this study it was noted that factors that predispose to mortality in PPU are the presence of co-morbidities and metabolic derangements like hypoalbunemia and hyponatremia. Surprisingly the factors such as age, delay in presentation and serum creatinine traditionally cited as important risk factors for mortality were found not to have any statistical significance in this study. Both morbidity and mortality for PPU as noted is largely similar to studies published over the last century.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Vats R, Rehmani B, Agrawal S. The outcome of surgery for perforated peptic ulcer in modern times. Int Surg J 2018;5:1702-7.