ORIGINAL RESEARCH

Early postoperative complications associated with perforation peritonitis at a tertiary teaching hospital in Lusaka, Zambia: A prospective, observational study

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Abstract

Background

Perforation peritonitis is a common surgical emergency seen by surgeons and remains a life-threatening condition with high morbidity and mortality. This study aimed to determine the site of perforation and the postoperative complications of perforation peritonitis.

Methods

This prospective, observational study was conducted at the Department of Surgery, University Teaching Hospital in Lusaka, Zambia, from July 2018 through March 2019. All consecutively admitted patients aged ≥18 years undergoing emergency exploratory laparotomy for nontraumatic perforation peritonitis were included in the study.

Results

One hundred patients participated in the study (77 men, 23 women), and the mean age was 37.24 (range, 18-78 years). The main site of perforation was the stomach in 49 patients (49%), the small bowel in 40 (40%), the colon in 8 (8%), both small bowel and colon in 1 (1%), urinary bladder in 1 (1%), and unidentified site in 1 (1%). The postoperative outcomes included anastomotic leakage (9%), wound dehiscence (3%), and relaparotomy (17%). The frequencies of unfavourable outcomes (anastomotic leakage, relaparotomy, and death) were highest in association with stomach perforations, followed by ileal perforations. The stomach was significantly prone to anastomotic leakage (P=0.008). The mortality rate was 36%.

Conclusions

The stomach was the leading site of perforation. The commonest postoperative outcome was relaparotomy. Perforation peritonitis is associated with a high mortality rate.

Keywords: perforation peritonitis, emergency laparotomy, mortality, Zambia

Introduction

Perforation peritonitis is among the commonest surgical emergencies.[1] Associated aetiologic factors include perforated peptic ulceration, infective causes, trauma, anastomotic disruption, intestinal ischaemia, and abdominal surgery.[2] Such perforations result in generalized peritonitis and sepsis and are associated with high morbidity and mortality.[3],[4]

The intra-abdominal organs that can perforate include the gallbladder, extrahepatic biliary tree, urinary bladder, stomach, duodenum, jejunum, ileum, appendix, caecum, and colon.[2],[5] The leading sites of perforation vary by geographic location.[6]

Factors, such as advanced age, late presentation, delay in the treatment, septicaemia, comorbidity, cause of intestinal perforation, and intra-abdominal pus volume, contribute to high mortality and postoperative complication rates.[1],[7]

Complications of perforation peritonitis include electrolyte imbalance, abdominal collection, intra-abdominal abscess formation, wound infection, enterocutaneous

fistula formation, respiratory failure, sepsis, septic shock, and thrombotic episodes due to prolonged inpatient management.[3],[4],[8] This study investigated outcomes with reference to anastomotic leakage, wound dehiscence, relaparotomy, and mortality.

In Zambia, at the University Teaching Hospital (UTH), 1 in 5 emergency abdominal operations is performed as part of the management of perforation peritonitis.[9] Furthermore, emergency abdominal procedures are associated with high rates of unfavourable postoperative outcomes,[10] with mortality rates associated with peritonitis from gastric perforation as high as 37%.[11] At UTH, a cross-sectional study determined that 85% of laparotomies were performed as emergency cases and that about 20% of all abdominal operations were performed to treat perforation peritonitis.[9] Additionally, a 1-year surgical audit found peritonitis to be the second commonest cause of death at UTH's Main Intensive Care Unit (ICU).[12] Although the mortality rate for gastric perforation is known, no UTH references are available regarding outcomes associated with anastomotic leakage, wound dehiscence, and relaparotomy at first admission. The postoperative outcomes of intestinal perforation peritonitis have not been established at UTH. Even though a rapid diagnostic test for identifying ileal tuberculosis in the context of ileal perforation has been investigated at UTH, there remains no published evidence regarding associated postoperative outcomes.[13]

This study aimed to determine the outcomes of perforation peritonitis by anatomical site at the Department of Surgery, UTH, regardless of the preoperative factors, which often are unclear and could contribute to morbidity and mortality. Knowledge of the outcomes associated with emergency laparotomy for perforation peritonitis will aid in surgical decision-making.

Methods

This prospective, observational study was conducted at UTH's Department of Surgery in Lusaka, Zambia, from July 2018 through March 2019. The study included all consecutively admitted patients aged ≥18 years undergoing emergency laparotomy for nontraumatic perforation peritonitis diagnosed preoperatively or intraoperatively. The management of perforation peritonitis followed the standard surgical procedure of fluid resuscitation, intravenous antibiotics, and laparotomy with peritoneal lavage. Tissue biopsies of the perforation margins were obtained for histopathologic diagnoses, and the results were subsequently made available to the units in charge of the patient for appropriate management. The outcomes, assessed by clinical observation within 30 postoperative days, were prospectively captured. There was no loss to follow-up during the 30-day study, and all patients were reviewed and followed up in the surgical outpatient clinic, except for those who died within the 30-day period.

Patients with peritonitis due to appendiceal perforation were excluded.

The sample size of 100 was calculated using the formula, $N=z^2p(1-p)/e^2$, where 'N' is the minimum sample size required, 'z' is the z-score corresponding to the desired confidence level (a z-score of 1.96 corresponds to a 95% confidence level), 'p' is the estimated proportion of the population with the characteristic of interest, '1−p' is the proportion of the population without the characteristic of interest, and 'e' is the tolerable margin of error.

Data were collected using a data collection tool and included age, sex, indication, site of perforation, and postoperative outcome (anastomotic leakage, wound dehiscence, relaparotomy, or death).

Statistical analysis

Statistical analysis was performed using SPSS Statistics for Windows, version 20.0 (IBM Corp., Armonk, NY, USA). Statistical significance was defined by $P<0.05$ and 95% confidence intervals. Continuous data are presented as mean ± standard deviation and range. Proportions were used for categorical data and tested for significance using the chi-square test. Outcomes (dead/alive or complicated/uncomplicated), as dependent variables, had their significance determined using the chi-square test. Pearson correlation and regression analyses were also conducted.

Ethical considerations

This study was granted ethical approval by ERES Converge (Ref: No.2018-Jun-010), a private institutional review board registered by the Registrar of Societies in Lusaka, Zambia. UTH administration also approved the study. Written informed consent was obtained from all patients.

Results

During the study period, there were 415 emergency laparotomies performed; of these, 125 laparotomies (30.1%) were performed for nontraumatic perforation peritonitis. There were 100 eligible participants included in the study: 77 men (77%) and 23 women (23%). The mean age was 37.24±14.12 (range, 18-78 years), and 57% of patients were between 18 and 37 years old. The mean age among men was 37.38±13.32 (range, 19-72 years), while that among women was 36.78±16.84 (range, 18-78 years) (Table 1). The preoperative indication for abdominal surgery for the majority of patients (79%) was peritonitis, and 9 patients had peritonitis with complications. For 18 patients, the preoperative bedside diagnosis was intestinal obstruction (unknown cause, n=13; mechanical obstruction, n=3; and paralytic ileus, n=2) (Table 2).

Site of perforation

The sites of perforation were as follows: stomach (49%), ileum (36%), colon (8%), duodenum (3%), jejunum (1%), both ileum and colon (1%), urinary bladder (1%), and unidentified site (1%) (Table 3). Gastric, duodenal, jejunal, ileal, colonic, and urinary bladder perforations were observed in men, whereas gastric, ileal, and colonic perforations were observed in women ($P=0.0498$). Of 49 gastric perforations, 41 (83.67%) were anterior on the pyloric antrum, and 7 (14.29%) were found on the anterior aspect of the body of the stomach; another perforation (2.04%) involved both the anterior and posterior walls.

Table 1. Demographic data and hospital stay

Variable	Women	Men	Total n (%)
Age group, years			
18-37	15	42	57 (57.0)
38-57	5	30	35 (35.0)
58-78	3	5	8 (8.0)
Total	**23 (23.0)**	**77 (77.0)**	**100 (100)**
Age, mean ± SD, years	36.78 ± 16.84	37.38 ± 13.32	37.2 ± 14.1
Age range, years	18-78	19-72	18-78
Hospital stay, mean ± SD (range), years			9.5 ± 6.9 (0-30)

SD, standard deviation

The perforation count (P=0.006) was significantly associated with death; however, there were no significant associations between death and perforation size (P=0.07) or site P=0.204). Perforation size correlated positively with perforation count (Pearson correlation, r=0.345, P=0.01).

Perforation peritonitis outcomes

Of the 64 patients who survived, 11 (17.19%) developed complications (anastomotic leakage, wound dehiscence, and relaparotomy). Of the remaining 36 patients who died, 8 had developed complications (n=2 with anastomotic leakage only, n=4 with leakage plus relaparotomy, and n=2 with no leakage but relaparotomy). The frequency of anastomotic leakage was higher among patients who died than among those who survived and was significantly associated with the size of perforation (P=0.001). Furthermore, there was a significant association between gastric perforation and anastomotic leakage (P<0.05).

The postoperative outcomes included wound dehiscence (3%), anastomotic leakage (9%), and relaparotomy (17%) (Table 4). The mean postoperative interval before anastomotic leak onset was 5.33±1.87 days, while the mean postoperative interval to relaparotomy was 9.94±5.82 days. The various indications for the 17 relaparotomies are shown in Table 5.

Of the 36 patients who died, the causes of death in order of frequency were septic shock, sepsis, acute kidney injury), pneumonia, multiorgan failure, septicaemia, and disseminated intravascular coagulopathy due to upper gastrointestinal bleeding (Table 6).

Hospital stay

Hospital stay durations ranged from 3 hours (death in the ICU) to 30 days (mean of 9.53±6.86 days). Thirty-four patients (34%) required ICU care, and the mean ICU stay was 3.39±2.74 days (range, 3 hours to 10 days). Of these 34 patients admitted to the ICU, 29 patients died (P=0.001). The other 7 deaths were in the surgical ward.

Table 2. Indications for abdominal surgery

Indication	n (%)
Peritonitis	79 (79.0)
Mechanical intestinal obstruction	18 (18.0)
Inguinal hernia with perforation	1 (1.0)
Gastric outlet obstruction	1 (1.0)
Acute appendicitis	1 (1.0)

Table 3. Perforation sites by sex

Perforation site	Women	Men	Total n (%)
Stomach	7	42	49 (49.0)
Ileum	10	26	36 (36.0)
Colon	5	3	8 (8.0)
Jejunum	0	3	3 (3.0)
Duodenum	0	1	1 (1.0)
Both ileum and colon	1	0	1 (1.0)
Urinary bladder	0	1	1 (1.0)
Unidentified	0	1	1 (1.0)

Discussion

Sex

Our study included more men than women who were managed for perforation peritonitis, with a ratio of 3.3:1. The male predominance aligns with published findings from other studies investigating perforation peritonitis.[14]-[17]

Age

Similar to our study, a mean age of 37.8 years was found in a study conducted in India.[4] Nevertheless, perforation peritonitis can occur at any age.[4],[15],[16]

Table 4. Outcomes by perforation site

Outcome	Perforation site						Total n (%)
	Stomach	Duodenum	Jejunum	Ileum	Colon	Others	
Leakage	5	0	0	2	2	0	9 (9.0)
Wound dehiscence	1	0	0	2	0	0	3 (3.0)
Relaparotomy	10	0	0	6	1	0	17 (17.0)
Died	16	1	1	12	3	3	36 (36.0)
Survived	33	0	2	24	5	0	64 (64.0)

Table 5. Indications for relaparotomy

Indication	n (%)
Leakage	6 (6.0)
Wound dehiscence	3 (3.0)
Subphrenic/subhepatic/interloop abscess	3 (3.0)
Intra-abdominal pus collection	1 (1.0)
Postoperative generalized peritonitis	1 (1.0)
Gangrenous stoma/ileostomy	1 (1.0)
Intestinal obstruction (small bowel volvulus and adhesions)	1 (1.0)
Postoperative intestinal obstruction (paralytic ileus)	1 (1.0)
Total	17 (17.0)

Table 6. Causes of death in 36 patientsa

Cause of death	n
Septic shock	19
Sepsis	10
Acute kidney injury	9
Pneumonia	3
Multiorgan failure	2
Septicaemia	1
Disseminated intravascular coagulopathy	1

[a]Some of the patients had >1 possible cause of death.

Site of perforation

The prominent site of gastrointestinal perforation is variable across the globe. At laparotomy, the operator can fail to identify the perforation site if it is small and sealed with fibrin tissue, or the operator may fail to locate the perforation regardless of its associated features. In contrast, perforations can be large, overt, or multiple, making them easily identifiable during exploratory laparotomy. In India, investigators observed that gastroduodenal perforations were the commonest, followed by small bowel perforations and colonic perforations.[17] However, other investigators have found contrasting results. In India and Kenya, the duodenum has been identified as the commonest site of perforation, followed by the ileum and the stomach,[16],[18] while in France, the colon has been shown to be the commonest site,[5] with the appendix being identified as the commonest site in Ibadan, Nigeria.[15] In northeastern Nigeria, the ileum was the commonest site of perforation, followed by perforated peptic ulcer and perforated appendix.[3] There is no single leading site of gastrointestinal perforation documented in the literature, and variation has also been noted within Africa.

Stomach

The majority of gastric perforations were anterior on the pyloric antrum. Our frequent finding of prepyloric perforation sites aligns with previous findings.[19] However, in our study, the rate of 83.67% was higher than the 74% determined by a study conducted at a university hospital in Bangkok, Thailand.[19] Gastric perforations are mostly caused by peptic ulcer disease and gastric cancer; other documented causes include endoscopic instrumentation, trauma, and minimally invasive laparoscopy.[11],[19],[20]

Compared with patients with intestinal perforations, those with gastric perforations had higher frequencies of postoperative anastomotic leakage, relaparotomy, and death. There was a significant association between the stomach as a perforation site and subsequent anastomotic leakage (P=0.008). The mortality rate associated with gastric perforation (32.65%) was slightly lower than the rate (37%) determined by a cross-sectional study conducted at UTH in 2009.[11] The literature has documented rates as low as 9% [19], but the mortality rate for gastric perforation at UTH remains high.

Small intestine

The majority of small bowel perforations were ileal perforations, followed by jejunal and duodenal perforations. Our finding of small bowel perforations usually being solitary aligned with findings from a study conducted in Nigeria,

where small bowel perforations were solitary in 72.2% of patients.[21] Postoperatively, among patients treated for small bowel perforations, the frequencies of anastomotic leakage, wound dehiscence, and relaparotomy did not reach statistical significance. Of 36 patients with ileal perforation, 10 received temporary ileostomies. The literature shows that temporary ileostomies are preferred over primary closure or resection and anastomosis in the contexts of delayed presentation, septic shock, severe abdominal contamination, and delayed surgery.[22] However, ileostomies have been associated with stoma-related complications, such as skin excoriation, gangrene, retraction, and fluid and electrolyte imbalances.[22] Furthermore, the patient must be subjected to another major operation or relaparotomy to reverse or revise the ileostomy.[23]

Several causes of ileal perforation have been investigated, and these include tuberculosis, typhoid, trauma, helminth infestation, intestinal obstruction with gangrenous bowel, and inflammatory conditions.[3],[4],[20],[22],[24] Typhoid has been highlighted as a major precipitant of ileal perforation.[22] In our study, the mortality rate associated with small bowel (mostly ileal) perforation was 35%; other publications report mortality rates associated with ileal perforations ranging between 13.9%[21] and 60%.[24]

Large intestine

Large bowel perforations are infrequent and are associated with severe complications.[25] Colonic perforations, though not as common as small bowel and gastroduodenal perforations, were associated with worse outcomes.[25] The rates of large bowel perforation vary globally, ranging from 1.27% to 32% in our literature review.[5],[17] There are several causes of large bowel perforation, including trauma, colonoscopy, local ischaemia, bowel obstruction, amoebiasis, and colonic ulceration.[4],[20],[25] These are mainly due to colorectal cancer and colonic diverticulitis.[4],[20],[25]

Perforation peritonitis outcomes

Anastomotic leakage

In terms of perforation site, the rates of postoperative repair leakage, relaparotomy, and mortality were highest in association with gastric perforations, followed by ileal perforations. In our study, the anastomotic leakage rate was 9%, which was higher than the rate of 11.5% reported from an analysis of 192 patients treated for nontraumatic small bowel perforation at a tertiary teaching hospital in northern India.[26] Patients with repair leaks were urgently taken back to the operating theatre for relaparotomy. Such patients who had gastrointestinal leakage had poor outcomes, with 6 out of 9 these patients dying. The factors associated with gastrointestinal repair leakage after surgically managed perforation peritonitis include age, sex, comorbidities, intra-abdominal infection, haemodynamic instability, and nutritional status.[6],[26],[27] Surgical factors, such as the surgical technique and suture material, can influence the healing of surgical repairs.[26],[27]

Abdominal wound dehiscence

Our study determined a 3% abdominal wound dehiscence rate, similar to other studies.[27] A study conducted in India determined a wound dehiscence rate of 2.74%.[17] Other investigators have found higher rates of wound dehiscence. A study conducted in Nairobi, Kenya,[16] determined a rate of 18.6%, with abdominal wound dehiscence rates of 9.8% and 20% reported from a retrospective study conducted in Azare, North-East Nigeria[3] and a prospective study conducted at a single surgical unit in India,[18] respectively. Patient-related and surgery-related factors influence abdominal wound dehiscence. These factors include age, sex, obesity, anaemia, malignancy, hypoalbuminaemia, intra-abdominal sepsis, haemodynamic instability, wound infection, abdominal surgery, emergency surgery, and suture material.[27]-[29] Wound dehiscence has been associated with prolonged hospitalization because patients require subsequent wound closure.[28],[29]

Relaparotomy

Among patients who required relaparotomy, the majority (82.35%) underwent the second operation within 14 days of the initial laparotomy. Investigators in Ibadan, Nigeria, determined a relaparotomy rate of 8.4%.[15] Repair leakage was the leading reason for relaparotomy in our study, followed by wound dehiscence. Anastomotic leakage was previously shown to account for 60% of relaparotomies at UTH.[9] The same study found a mortality rate of 40% associated with relaparotomy. Other indications for relaparotomy include postoperative intestinal obstruction, tertiary peritonitis, and bleeding.[9] Patients with perforation peritonitis are at risk of intra-abdominal pus collection, abscess formation, and postoperative peritonitis, all of which interfere with recovery and wound healing.[20] In our study, relaparotomy could have been precipitated by a failure to adequately lavage the contaminated peritoneum or failure of a given patient's immune system to clear the initial intra-abdominal infection, consequently warranting a relaparotomy to carry out peritoneal lavage/drainage. Patients also underwent relaparotomy for ileostomy reversal and as part of the management of intestinal obstruction. Patients who developed complications or underwent relaparotomies consequently have longer hospital stays.[30]

Mortality

The ICU mortality rate in our study was 85.29%. In the ICU, 6 patients died within hours of surgery. Of the 36 patients who died, 8 had anastomotic leaks and underwent relaparotomies. A higher perforation count was associated with a higher mortality rate. The high mortality in our study could be attributable to late patient presentation and patients presenting with complications, such as hypovolaemia, anaemia, and acute kidney injury. Patients with acute kidney injury had no access to haemodialysis, an intervention that could have changed the recovery course and outcomes. Furthermore, the presence of sepsis and multiorgan failure among patients treated for perforation peritonitis could also have influenced the outcomes. At the time of death, some

patients had multiple possible causes of death; of these, septic shock was the most common. In a study conducted in Harare, Zimbabwe, septic shock requiring inotropic support was the commonest cause of death.[31] A study conducted in India found septicaemia to be the commonest cause of death.[32] The overall mortality rate in our study was relatively high in comparison to the rates reported in the articles in our literature review. Elsewhere in India, mortality rates of 5.7% and 8.2% were determined.[17],[18] In Nairobi, Kenya, a prospective, cross-sectional study involving 70 patients found an overall mortality rate of 12.9%.[16]

Postoperative hospital stay

Thirty-four patients (34%) were admitted to the ICU, with this rate being much higher than the 6.5% found in Nigeria and the 11% found in a study conducted in the United Kingdom.[10],[15] The high number of patients requiring ICU care could be attributable to patients presenting in advanced septic states or presenting late with complications. Most of our patients were admitted to the ICU because their postoperative clinical condition necessitated close monitoring and organ support.

Limitations

The emergency laparotomies were performed by various surgeons, and this could have confounded our findings. However, all surgeons, including this study's principal investigator, were fourth-year registrars and had comparable levels of experience and expertise.

The study did not aim to measure the time elapsed from perforation to surgery, and this information was never captured. However, we recognize that the interval before hospital admission following an intra-abdominal visceral perforation could impact patient outcomes. Furthermore, histopathologic diagnosis can guide clinical management. Though the histopathology results were not available during the study period, they were subsequently sent to the relevant departments to guide ongoing patient follow-up and management.

Finally, late presentation due to distance, lack of funds, or transport could have been confounding factors.

Conclusions

The main site of intra-abdominal organ perforation was the stomach. The commonest postoperative outcome, among those specifically investigated, was relaparotomy. The mortality rate associated with perforation peritonitis was high.

Recommendations

Further studies should investigate the duration of symptoms and signs before hospital admission, as illness severity could affect postoperative outcomes. Long-term, prospective research with larger sample sizes should be conducted. Additionally, outcomes of perforation peritonitis could be better understood by considering the histopathologic features of surgical biopsies. Ideally, such results would be processed and reported promptly to enhance clinical decision-making as well as inform research efforts.

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