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## ORIGINAL RESEARCH ARTICLES

### Surgical outcomes for perforated peptic ulcer: A prospective case series at an academic hospital in Monrovia, Liberia



#### *Les résultats chirurgicaux de l'ulcère gastroduodénal perforé: Série de cas prospective en hôpital universitaire à Monrovia, Liberia*

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**Introduction:** The incidence of perforated peptic ulcer remains high in low and middle-income countries. Mortality can be significant, and early surgical management with careful evaluation of pre-operative risk factors is essential. The purpose of this study was to describe the clinical outcomes of surgical treatment for perforated peptic ulcer disease in Liberia and to explore risk factors for adverse outcomes.

**Methods:** This study prospectively examined 20 consecutive patients undergoing primary closure with omental patch for perforated pre-pyloric or duodenal peptic ulcer at the John F. Kennedy Medical Centre (JFKMC) in Monrovia, Liberia from May 2009 to March 2010. Pre-operative information was captured in a questionnaire. Risk factors were assessed for univariate and multivariate associations with in-hospital mortality.

**Results:** Median age was 33 years and 85% were males. A majority of the patients (70%) had a history of gastritis and antacid use. Median time from beginning of symptoms to surgery was 4.5 days. Over-all in-hospital mortality following surgical therapy for perforated peptic ulcer disease was 35%. Median length of stay among survivors was 16 days, and death occurred at median 1 day after admission. Long symptom duration and age > 30 years of age were significantly associated with in-hospital mortality on univariate ( $\beta = 2.60$  [0.18–5.03],  $p = 0.035$ ) and multivariate testing ( $\beta = 2.95$  [0.02–5.88],  $p = 0.049$ ).

**Conclusion:** Peptic ulcer disease and its treatment represent a potentially substantial source of morbidity and mortality in limited-resource settings. In this case series, surgical treatment for perforated peptic ulcer disease carried a high mortality, and the results highlight the potential for public health systems strengthening to prevent poor health outcomes. Peptic ulcer disease in low- and middle-income countries presents unique epidemiology and treatment challenges that may differ significantly from evidence-based guidelines in high-income countries.

**Introduction:** L'incidence de l'ulcère gastroduodénal perforé reste élevée dans les pays à faible et moyen revenu. La mortalité peut être élevée, et la prise en charge chirurgicale précoce, associée à une évaluation soignée des facteurs de risque préopératoires, est essentielle. L'objectif de cette étude était de décrire les résultats cliniques du traitement chirurgical des ulcères gastroduodénaux perforés au Liberia et d'étudier les facteurs de risque associés aux issues défavorables.

**Méthodes:** Cette étude s'est penchée prospectivement sur 20 patients consécutifs subissant une fermeture primaire avec patch épiploïque pour traiter l'ulcère prépylorique ou gastroduodénal perforé au Centre médical John F. Kennedy (JFKMC) à Monrovia, au Liberia, de mai 2009 à mars 2010. Les informations préopératoires ont été saisies dans un questionnaire. Les facteurs de risque ont été évalués à des fins d'associations univariées et multivariées avec la mortalité hospitalière.

**Résultats:** L'âge médian était 33 ans et 85% de l'échantillon était composé d'hommes. Une majorité de patients (70%) avait des antécédents de gastrite et avait eu recours aux antiacides. Le temps moyen entre l'apparition des symptômes et l'opération était de 4,5 jours. Le taux global de mortalité hospitalière suite à une opération pour ulcère gastroduodénal perforé s'élevait à 35%. La durée moyenne de séjour des survivants était de 16 jours, et les décès survenaient en moyenne un jour après d'admission. Des symptômes sur une longue durée et un âge supérieur à 30 ans étaient significativement associés à la mortalité hospitalière dans les tests univariés ( $\beta = 2,60$  [0,18–5,03],  $p = 0,035$ ) et multivariés ( $\beta = 2,95$  [0,02–5,88],  $p = 0,049$ ).

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**Conclusion:** L'ulcère gastroduodénal et son traitement représentent une source de morbidité et de mortalité substantielle potentielle dans des environnements caractérisés par des ressources limitées. Dans cette série de cas, le traitement chirurgical de l'ulcère gastroduodénal perforé était associé à une forte mortalité, et les résultats mettent en avant le potentiel de renforcement des systèmes de santé publique afin d'éviter des issues défavorables en termes de santé. Les ulcères gastroduodénaux dans les pays à faible et moyen revenu présentent des défis uniques sur le plan épidémiologique et thérapeutique susceptibles de différer dans une large mesure des directives scientifiquement fondées disponibles dans les pays à revenu élevé.

## African relevance

- Approximately 2 billion people world-wide do not have access to safe surgical services.
- Most African national health systems do not sufficiently provide emergency surgical services.
- Mortality from emergency surgery is high in part due to late presentation.
- Peptic ulcer presents country-specific epidemiology and treatment challenges.

## Introduction

The worldwide incidence of peptic ulcer disease has decreased in recent years,<sup>1</sup> largely due to the advent of improved endoscopic diagnostics, introduction of proton pump inhibitors (PPIs), and attention to *Helicobacter pylori* eradication.<sup>2</sup> Still, peptic ulcer disease remains a significant health and economic burden in low- and middle-income countries (LMICs).<sup>3,4</sup> LMICs are often characterized by high prevalence of untreated *H. pylori* infection and concomitant environmental exposures such as NSAIDs or aspirin.<sup>5</sup> Additionally, inadequate access to surgical and anesthesia care can prove devastating in complex and perforated peptic ulcer disease, which affects 7–10/100,000.<sup>5</sup> Overall mortality from perforated peptic ulcer has been reported at 9% and as high as 22% in LMICs,<sup>4,6</sup> even though early surgical management can be life-saving. Careful evaluation of pre-operative risk factors is imperative to guide appropriate clinical management. Thus, data from individual LMICs about epidemiology of disease and outcomes are critical to inform such practices.

At the tertiary referral hospital in Monrovia, Liberia, where this study took place, we observed that a considerable proportion of patients with acute abdomen were diagnosed with gastric perforation. The nature and behavior of clinical disease seem to be unique, and to our knowledge no study has been performed on gastric perforation in Liberia. This study aimed to prospectively determine the clinical outcomes after surgical treatment for peptic ulcer disease and to explore in-hospital mortality risk factors. We hypothesized that delayed presentation to the hospital would have a negative impact on survival.

## Methods

In this prospective case-series analysis, we evaluated all 20 patients presenting to the surgical department of J.F.K Medical Centre, Monrovia, Liberia with acute abdomen from March 2009 to March 2010, who underwent exploratory laparotomies and were found to have perforated pre-pyloric or duodenal peptic ulcer. Patients were identified, consented, and interviewed prior to surgical intervention. Factors considered in the pre-operative questionnaire included: employment

status, income and family responsibility, history of smoking, history of alcohol use, history of gastritis, antacid use, diet history, date of onset of the illness and date reporting to the hospital (data supplement: structured questionnaire). The interviewer was the first author, a general practitioner with over eighteen years of experience in general surgery.

Peptic ulcer perforations were suspected based on medical history and clinical signs, and the patients often presented after having been treated in smaller community hospitals or health centres until they significantly deteriorated. Many of the patients presented with a history of dyspepsia and antacid use, and they could typically tell almost the exact time of onset of the pain with subsequent and gradually increasing symptoms of peritonitis. Medical history and physical examination were not able to distinguish perforated peptic ulcer from differential diagnoses such as typhoid perforation, ruptured appendix and other causes of bowel perforations and peritonitis, and these patients were excluded from further analysis at the point of surgery. After a mid-line laparotomy, the patients with peptic ulcer perforation underwent gastrorrhaphy with omental patch, without placement of intra-abdominal drain. Antibiotics were prescribed on average 3–5 days after the operation. HIV-status was negative for all included patients. Anesthesia was usually provided by nurse-anesthetists.

We used Chi-square test to analyze binary data, and Mann–Whitney *U* for ordinal data. Select risk factors were also dichotomized and assessed for associations with in-hospital mortality by multivariate logistic regression. Long symptom duration was defined as more than 4 days between onset of illness and surgery. The data were analyzed using the IBM SPSS v.19.1 (Chicago, IL). The study was approved by the JFK hospital direction, and by the Institutional Review Board of Boston Children's Hospital for the Harvard Program in Global Surgery and Social Change.

## Results

20 patients were treated over the course of the study period. Demographics and clinical details of patients operated for perforated peptic ulcer are presented in Table 1. The median age of patients was 33 years [interquartile range 26–46]. Most patients were male (85%) and reported a history of gastritis and antacid use (70%). All patients underwent operations within 24 h after presentation to the hospital, and the median time from initial symptoms to surgery was 4.5 days [interquartile range 4–6]. Overall mortality was 7/20 (35%), and median time to death was 1 day after presentation [interquartile range 0–4]. Median length of stay among survivors was 16 days [interquartile range 11–29]. Three sample clinical vignettes are given in Fig. 1.

Long symptom duration and age > 30 years of age were significantly associated with higher in-hospital mortality ( $p = 0.02$ ). However, non-survivors did not differ compared to survivors in terms of median age (39 years. vs. 28 years.,

**Table 1** Demographics and clinical parameters of patients with perforated peptic ulcer.

|   | <i>n</i> |                         |
|---|----------|-------------------------|
| Age (years)                                     | 20       | 33 [26–46] <sup>a</sup> |
| <i>Gender</i>                                   |          |                         |
| Female  | 3        | 15%                     |
| Male  | 17       | 85%                     |
| <i>Marital status</i>                           |          |                         |
| Unmarried                                       | 10       | 50%                     |
| Married   | 9        | 45%                     |
| Divorced  | 1        | 5%                      |
| <i>Employment</i>                               |          |                         |
| Unemployed                                      | 11       | 55%                     |
| <i>History</i>                                  |          |                         |
| History of gastritis                            | 14       | 70%                     |
| Previous antacids                               | 14       | 70%                     |
| Smoking   | 11       | 55%                     |
| Alcohol   | 16       | 80%                     |
| < 2 meals/day                                   | 2        | 10%                     |
| <i>Blood group</i>                              |          |                         |
| A   | 0        | 0%                      |
| B   | 4        | 21%                     |
| AB  | 1        | 5%                      |
| O   | 14       | 74%                     |
| Rh +  | 15       | 88% <sup>b</sup>        |
| Mortality                                       | 7        | 35%                     |
| <i>Duration</i>                                 |          |                         |
| Symptom debut (days preop)                      |          | 4.5 [4–6] <sup>a</sup>  |
| Length of stay (days)                           |          | 16 [11–29] <sup>a</sup> |
| Mortality (days postop)                         |          | 1 [0–4] <sup>a</sup>    |
| <sup>a</sup> Median with [interquartile range]. |          |                         |
| <sup>b</sup> <i>n</i> = 17.                     |          |                         |

$p = 0.07$ ), gender (71% male vs. 92% male,  $p = 0.27$ ), median duration of symptoms (4 days [3–6] vs. 5 days [5–6],  $p = 0.08$ ), previous history of dyspepsia, marital status, employment

status, blood group, or alcohol, and tobacco consumption (Table 2).

Long symptom duration and age > 30 years of age were also significantly associated with in-hospital mortality on univariate ( $\beta = 2.60$  [0.18–5.03],  $p = 0.035$ ) and multivariate testing ( $\beta = 2.95$  [0.02–5.88],  $p = 0.049$ ), compared to short symptom duration and younger age (Table 3).

## Discussion

This study indicates that long symptom duration and older age are significant risk factors associated with in-hospital mortality after surgical treatment for perforated peptic ulcer disease. The results highlight the considerable risks involved with surgical care in low- and middle-income countries, and the fact that any national health system for surgery must include not only safe anesthesia and operative capacity, but also prevention and timely referrals. The high proportion of patients of the male sex (85%) and with a history of gastritis (70%) implies that focused education and preventive efforts in this population could likely mitigate the incidence of perforated peptic ulcer.

In LMICs there are numerous hurdles for patients with surgical needs, ranging from cultural perceptions of healthcare, travel distance and direct and hidden patient costs, to shortage of operating rooms, safe anesthesia, sterilization capacity, surgical instruments, and surgeons.<sup>7</sup> Some of the treatment delays seen in this study may have been caused by beliefs in traditional treatments,<sup>8</sup> the lack of trained manpower in smaller clinics to properly diagnose and refer this condition,<sup>9</sup> and inadequate finances to pay hospital bills.<sup>10</sup> Delays in care likely increase also the incidence and severity of postoperative complications, such as high rate of sepsis and metabolic derangement.

One reason for the decrease in peptic ulcer disease in high-income countries is the increased understanding of ulcer disease, the dissemination of this information to the public, and a widespread adoption of proton pump inhibitor use among primary caregivers. Access to primary treatment and the

## Clinical presentations

1. K: 52 years old male admitted at 5:45 am. Physical findings: axillary temperature 99.7° F, respiratory rate 38/minute, Pulse rate 116 beats/minute, BP 118/60 mmHg. He was tachypneic, tachycardic, febrile, and with moderate abdominal distention with tenderness. He was dehydrated, septic and lethargic, bowel sounds were absent, rectum was empty, hemoglobin 8 gm/dL. Electrolyte analysis could not be done. He was resuscitated with Lactated Ringers solution to correct assumed fluid and electrolytes imbalances, a unit of blood was transfused, and metronidazole and ceftriaxone were infused at admission and immediately prior to surgery. He underwent surgery from 5:05 pm to 8:25 pm, twelve hours after hospital presentation.
2. Q: 35 years old female admitted at 9:44 am. Physical findings at presentation: axillary temperature 102° F, respiratory rate 28 cycles /minute, pulse 114 beats/minute, BP 130/90mmHg. She was tachypneic, tachycardic, febrile, septic, mild abdominal distention with tenderness, dehydrated and lethargic; and bowel sounds were absent. She underwent surgery at 8: 25 pm, almost eleven hours after hospital presentation.
3. F: 48 years old male admitted at 6am. He came in with abdominal pains and distention, tenderness, fever, fast respirations, septic and fast heartbeat. He underwent surgery at 4pm, ten hours after admission. He died in the immediate post-operative period despite prolonged aggressive resuscitation with blood, IV fluids, antibiotics and oxygen.

**Figure 1** Sample vignettes: Initials, age, and timing of patients have been modified to protect patient integrity.

**Table 2** Risk factors for in-hospital mortality.

|                                      | Survival |            | Mortality |            | <i>p</i> -value |
|--------------------------------------|----------|------------|-----------|------------|-----------------|
|                                      | <i>n</i> |            | <i>n</i>  |            |                 |
| Age                                  |          |            |           |            |                 |
| Median age <sup>a</sup>              | 13       | 28 [25–40] | 7         | 39 [36–49] | 0.07            |
| Age < 30 years                       | 9/13     | 69%        | 1/7       | 14%        |                 |
| Age > 30 years                       | 4/13     | 31%        | 6/7       | 86%        | 0.02            |
| Female gender                        | 1/13     | 8%         | 2/7       | 29%        | 0.27            |
| Days of symptoms before surgery      |          |            |           |            |                 |
| Median days of symptoms <sup>a</sup> | 13       | 4 [3–6]    | 7         | 5 [5–6]    | 0.08            |
| Symptom duration < 4 days            | 9/13     | 69%        | 1/7       | 14%        |                 |
| Symptom duration > 4 days            | 4/13     | 31%        | 6/7       | 86%        | 0.02            |
| Marital status                       |          |            |           |            |                 |
| Unmarried                            | 7/13     | 54%        | 3/7       | 43%        |                 |
| Married                              | 6/13     | 46%        | 3/7       | 43%        |                 |
| Divorced                             | 0/13     | 0%         | 1/7       | 14%        | 0.37            |
| Unemployed                           | 7/13     | 54%        | 4/7       | 55%        | 1.0             |
| History of gastritis                 | 10/13    | 77%        | 4/7       | 57%        | 0.61            |
| Smoking                              | 8/13     | 38%        | 4/7       | 57%        | 0.64            |
| Alcohol                              | 11/13    | 85%        | 5/7       | 71%        | 0.59            |
| < 2 meal per day                     | 2/13     | 15%        | 0/7       | 0%         | 0.51            |
| Rh +                                 | 11/13    | 92%        | 4/7       | 80%        | 0.52            |
| ABO                                  |          |            |           |            |                 |
| A                                    | 0        | 0%         | 0         | 0%         |                 |
| B                                    | 2/13     | 17%        | 2/7       | 29%        |                 |
| AB                                   | 1/13     | 8%         | 0/7       | 0%         |                 |
| O                                    | 9/13     | 75%        | 5/7       | 71%        | 0.64            |

<sup>a</sup> Median [interquartile range].

**Table 3** Risk-factors for in-hospital mortality, univariate and multivariate regression.

|                           | $\beta$ | [95% CI]    | <i>p</i> -Value |
|---------------------------|---------|-------------|-----------------|
| <i>Univariate</i>         |         |             |                 |
| Age > 30 years            | 2.60    | [0.18–5.03] | 0.035           |
| Symptom duration > 4 days | 2.60    | [0.18–5.03] | 0.035           |
| <i>Multivariate</i>       |         |             |                 |
| Age > 30 years            | 2.95    | [0.02–5.88] | 0.049           |
| Symptom duration > 4 days | 2.95    | [0.02–5.88] | 0.049           |

incidence of peptic ulcers and peptic ulcer perforations are also likely influenced by socioeconomic factors, particularly in limited-resource settings.

Our findings are congruent with what has been demonstrated in other low-income setting studies examining peptic ulcer disease. Lohsiriwat and colleagues presented a series of 152 patients (78% male, average age 52 years)<sup>6</sup> wherein complication rate was 30% and overall mortality rate was 9%. The authors noted that the presence of modifiable risk factors and late stage of presentation contributed to higher mortality in this population. Ohene-Yeboah and colleagues prospectively examined patients from January 1998 to June 2004. Similarly in this study, more males were affected by a ratio of about 3 to 1, with median age of 55 years. There were 244 gastric and 87 duodenal perforations giving a ratio of 2.8 to 1. Most of these perforations were associated with the intake of NSAIDs (47.7%). The overall mortality was 22.1%. Age

and mortality were higher for duodenal ulcers. Dakubo and colleagues examined a total of 326 cases treated for peptic ulcer perforation, including 267 males and 59 females, with mean age of about 41 years (range 4–87 years). There was a strong association with consumption of ulcerogenic substances (67%). More than half of all patients (54%) reported to the hospital after 24 h. Post-operative complications occurred in 19%, and overall mortality was 11%. Age > 60 years, alcohol intake and resectional surgery were factors significantly associated with post-operative mortality.

Two known risk factors for peptic ulcer disease were left unaccounted for in our study: *H. pylori* infection and ulcerogenic substance intake. *H. pylori* infection has been identified in 65–70% of patients with perforated peptic ulcer,<sup>11</sup> which is significantly lower than the 90–100% prevalence among patients with non-complicated disease,<sup>11</sup> and notably higher than the 23% prevalence among NSAID users with perforation.<sup>12</sup> During the time of our study, culture results and in-depth diagnostics of patient comorbidities were commonly unavailable. Therefore as a representative limitation of many facilities in LMICs, we were therefore not able to detect *H. pylori*, and also many of our patients could not afford the cost of *H. pylori* eradication therapy or proton-pump inhibitors. Furthermore, it should be noted that discharge sometimes is postponed until the patient or their family can pay the hospital bill. However, financial reasons did not influence the measurement of length of stay reported in this study, the length of stay reflected the period during which the patient was still undergoing treatment, which means that this outcome was not confounded by issues related to poverty and socioeconomic

status of the patient and his or her social network. The time between admission and surgery was not prospectively collected, and since this information was not available upon retrospective review of the medical files we were not able to evaluate the trade-off between emergent surgery and preoperative resuscitation. Similarly, the rates of post-operative complications such as bleeding, protracted pain, infection, and wound dehiscence were not prospectively recorded and were not comprehensively available upon retrospective review. These missing data points considerably limit the granularity and generalizability of our conclusions. Lack of patient education and burdensome financial costs associated with obtaining health care represent two substantial barriers to adequate post-operative follow-up that warrant further study. In Liberia, as in many low-income settings, poor patient follow-up is multifactorial.

Despite the proven cost-effectiveness of surgical services in low- and middle-income countries,<sup>13</sup> currently an approximate 2 billion people world-wide do not have access to surgery.<sup>14</sup> The World Bank recently emphasized the global maldistribution of surgical providers, lack of surgical infrastructure and detrimental out-of-pocket payment for surgery, and the World Health Assembly may in 2015 vote for a resolution toward universal access to safe affordable surgery and anesthesia with financial protection.<sup>15</sup> Liberia is a country where the scarcity of surgical and anesthesia infrastructure and care personnel has been particularly well documented.<sup>14–17</sup>

As the only tertiary academic medical facility in Liberia, our institution hopes to establish a culture of data collection and analysis, as well as of outcomes monitoring through studies such as this and other prospective studies in the future. Ultimately, these data will help inform clinical practice to provide improvements in surgical quality and healthcare outcomes for all Liberians. Our results help to establish a baseline understanding of the impact of surgery for peptic ulcer disease within our community. Bringing surgical disease out of the OR and directly into the public health system strengthening arena will highlight the importance of education and primary prevention from a health system standpoint.

## Conclusion

Mortality from peptic ulcer disease remains high in low- and middle-income countries, and early surgical management can be life saving. Timely referrals and treatment of modifiable risk factors may prevent late-stage complications, though access to treatments and longitudinal care remains a significant challenge. Future studies should take into consideration the use of NSAIDs and the presence of *H. pylori*, and the role of primary and secondary prevention.

## Contributions

J.F.M. conceptualized and designed the study, collected prospectively the data, interpreted the results, helped draft the manuscript, and approved the final manuscript as submitted. C.D.H. interpreted the results, critically reviewed the manuscript, and approved the final manuscript as submitted. P.B.P. interpreted the results, helped drafting the manuscript, and approved the final manuscript as submitted. T.E.C.

interpreted the results, helped drafting the manuscript, and approved the final manuscript as submitted. S.A.K. interpreted the results, critically reviewed the manuscript, and approved the final manuscript as submitted. T.Y.J. interpreted the results, critically reviewed the manuscript, and approved the final manuscript as submitted. M.K. interpreted the results, critically reviewed the manuscript, and approved the final manuscript as submitted. J.G.M. interpreted the results, critically reviewed the manuscript, and approved the final manuscript as submitted. L.E.H. analyzed and interpreted data, helped drafting the manuscript, and approved the final manuscript as submitted.

## Conflict of interest

The authors declare no conflict of interest.

## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.afjem.2014.11.002>.

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