

Adverse Operative Risk Factors for Perforated Peptic Ulcer

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Abstract

Introduction: Mortality from perforated peptic ulcer still remains high as a result of more perforations in the elderly who are generally more ill. We conducted this retrospective study to determine the adverse operative risk factors for perforated peptic ulcers. **Materials and Methods:** Two hundred and six consecutive patients operated for perforated peptic ulcers from 1 January 1993 to 31 December 1997 were reviewed. **Results:** Majority (n = 194) of the patients had perforations at the pyloroduodenal region and the remaining 10 patients had perforated benign gastric ulcers. The median age at surgery was 58 years (range 18 to 91 years). Forty-four patients (21.4%) were more than 70 years old. The 30-day operative mortality rate was 10.7% (n = 22). Advanced age (>70 years), female gender, concurrent major medical illness, perforation developed while hospitalised for other medical illnesses, prolonged perforation (>24 hours) and preoperative hypotension (systolic blood pressure <90mmHg) were indicators for operative mortality by univariate analysis. By logistic regression analysis, only concurrent major medical illness, prolonged perforation and preoperative hypotension were independent adverse risk factors. The operative mortality rate for patients with 0, 1, 2 and 3 independent adverse risk factors were 0%, 11%, 30% and 88%, respectively. **Conclusions:** As concurrent medical illness is a non-modifiable factor and preoperative hypotension is usually resulting from treatment delay and inadequate resuscitation, emphasis should place on shortening the time to surgery as well as prompt resuscitation.

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Key words: Mortality, Perforated peptic ulcer, Poor risk factors, Preoperative hypotension, Prolonged perforation

Introduction

Although there has been a significant decline in elective surgery for peptic ulcer disease with the introduction of H-2 blocker, the incidence of peptic ulcer perforation has remained relatively unchanged over the years.¹⁻⁴ The mortality rate from perforated peptic ulcer remains high as more perforations occur in the elderly who are generally more ill.²⁻⁹ Locally, few studies have addressed the issue of perforated peptic ulcer and its surgical outcome.⁹⁻¹² Our aim was to evaluate the adverse operative risk factors for perforated peptic ulcers.

Materials and Methods

The records of all patients who underwent surgery for perforated peptic ulcer from 1 January 1993 to 31 December 1997 at the Singapore General Hospital were reviewed retrospectively.

Patients' profiles and associated major medical illnesses were recorded. Preoperative chest X-rays were performed

for all patients to look for presence of pneumoperitoneum. They all received intravenous antibiotics and either H2 antagonist or proton pump inhibitors. Nasogastric tube was inserted to decompress the stomach and minimise spillage. Active fluid resuscitation was commenced immediately and surgery was carried out as soon as patients were adequately resuscitated and haemodynamically stable.

Preoperative shock was defined as systolic blood pressure of less than 90 mmHg. The duration of perforation was measured from the time of onset of acute abdominal pain to the time of surgery. Major medical illnesses were defined as illnesses requiring long-term medication for at least 3 months. Operative morbidity and mortality were defined as postoperative complications and death within 30 days of surgery. Statistical analysis was done using computer statistical software—SPSS version 7.5 and Epistat. Univariate analysis was performed by chi-square test or by Fisher's exact test for small numbers. Independent adverse

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risk factors were calculated with logistic regression analysis. *P* values less than 0.05 were taken to be significant.

Results

There were 206 consecutive patients (158 males and 48 females) over the 5-year study period. Majority of these patients were Chinese (*n* = 173, 84%), with Malays (6.3%), Indians (4.4%) and other races (5.3%) contributing the rest. The median age at surgery was 58 years with a range of 18 to 91 years. Forty-four patients (21.4%) were 70 years or older. Almost 40% of the patients had at least one or more major medical illnesses (Table I). Sixty-four patients (31.1%) were chronic cigarette smokers, 42 patients (20.4%) and 5 patients (2.4%) were on non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids, respectively. Documentation of *Helicobacter pylori* (*H. pylori*) infection was incomplete and thus not analysed in this study. Eighteen patients had perforation while hospitalised for unrelated medical problems.

Nineteen patients (9.2%) experienced hypotensive shock prior to surgery. The median duration of perforation before surgery was 14 hours. Thirty-eight patients (18.5%) had long-standing perforation (more than 24 hours). Thirty-one patients (15.0%) were operated based on clinical signs of peritonitis without radiological evidence of pneumoperitoneum. Majority of the patients (*n* = 194, 94.2%) had perforation at the anterior part of pyloroduodenal region. Ten patients had perforated benign gastric ulcers. The remaining 2 patients had perforated peptic ulcers at the second part of the duodenum and the posterior surface of the first part of the duodenum, respectively. Types of surgical procedures are shown in Table II.

There were 22 (10.7%) postoperative deaths in this study. Table III shows the results of univariate analysis performed to identify factors that potentially affected mortality. Advanced age (more than 70 years old), female gender, major medical illnesses, preoperative shock, long-standing perforation (>24 hours) and perforation that

developed while hospitalised for unrelated medical problems were significantly associated with increased risk of death. Using logistic regression analysis, the same variables were examined for their independent effect in predicting mortality (Table IV). It showed that only major medical illness [relative risk (RR) 6.91, 95% confidence interval (95% CI) 1.33 to 35.71, *P* = 0.021], preoperative shock [RR 7.12, 95% CI 1.98 to 25.57, *P* = 0.003] and long-standing perforation [RR 6.18, 95% CI 1.84 to 20.69, *P* = 0.003] were independent adverse risk factors for mortality. Using the independent adverse risk factors to predict mortality, none of the 109 patients without any adverse risk factors died after surgery, giving 100% sensitivity. The mortality rates for patients with 0, 1, 2 and 3 adverse risk factors were 0%, 11%, 30% and 88%, respectively (Table V).

Discussion

Operative mortality for perforated peptic ulcer has declined significantly since the introduction of antibiotics.⁴

TABLE II: TYPES OF SURGERY

	No. of patients (%)
Omental patch repair	152 (73.8)
Truncal vagotomy and drainage	46 (22.3)
Partial gastrectomy	6 (2.9)
Ulcerectomy	1 (0.5)
Roux-en Y jejunoduodenostomy	1 (0.5)

TABLE III: UNIVARIATE ANALYSIS OF FACTORS POTENTIALLY AFFECTING MORTALITY

Variable	<i>P</i> value
Patient profile	
a) age (>70 years)	0.002
b) sex (female)	0.013
Major medical illness	<0.001
a) hypertension (<i>P</i> = 0.030)	
b) diabetes (<i>P</i> = 0.003)	
c) cardiac (<i>P</i> = 0.019)	
d) respiratory (<i>P</i> = 0.010)	
e) renal failure (<i>P</i> = 0.018)	
f) cancer (<i>P</i> = 0.553)	
g) others (<i>P</i> = 0.013)	
Predisposing ulcerogenic factor	
a) NSAIDs	0.278
b) corticosteroids	0.089
c) on chemotherapy	0.366
Preoperative shock	<0.001
Long-standing perforation (>24 hours)	<0.001
Perforation during hospital stay	0.001
Site of perforation	0.290

NSAIDs: non-steroidal anti-inflammatory drugs

TABLE I: MAJOR MEDICAL ILLNESS

Major medical illness	No. of patients (%)
Hypertension	33 (16.0)
Diabetes mellitus	26 (12.6)
Cardiac	22 (10.7)
Respiratory	20 (9.7)
Underlying malignancy	17 (8.3)
Chronic renal failure	6 (2.9)
Others e.g. CVA, SLE etc	11 (5.3)
No medical illness	129 (62.6)
One medical illness	36 (17.5)
Two medical illnesses	26 (12.6)
Three or more medical illnesses	15 (7.3)

CVA: cardiovascular accident; SLE: systemic lupus erythematosus

TABLE IV: LOGISTIC REGRESSION ANALYSIS OF FACTORS POTENTIALLY AFFECTING MORTALITY

Variable	Relative risk	CI	P value
Age (>70 years)	1.29	0.38 - 4.38	0.68
Sex (female)	1.49	0.45 - 4.91	0.51
Major medical illness	6.91	1.33 - 35.71	0.02
Perforation during hospital stay	2.70	0.69 - 10.65	0.16
Preoperative shock	7.12	1.98 - 25.57	<0.01
Perforation (>24 hours)	6.18	1.84 - 20.69	<0.01

TABLE V: COMPARISON OF MORTALITY RATES AND RISK FACTORS

Risk factors	No. of patients	No. of death (%)
0	109	0 (0)
1	62	7 (11)
2	27	8 (30)
3	8	7 (88)

This trend is however reversed recently and a slightly higher mortality rate has been observed in the last decade. This is attributed to a rising trend of perforation in the elderly patients who are more ill.^{2,4} The mortality rate remains high today, ranging from 24% to 47%.⁵⁻⁸ Our study showed a significantly higher mortality rate for patients older than 70 years (25% versus 7%, $P = 0.02$). This was, however, not borne out in the multivariate analysis suggesting that age by itself was not the main contributing factor of mortality. We found that concurrent major medical illnesses, preoperative shock and perforation more than 24 hours were 3 independent adverse risk factors. The presence of 3 independent adverse risk factors at the time of diagnosis predicted mortality rate of 88%.

In a prospective study to evaluate operative risk factors for perforated duodenal ulcers by Boey et al^{13,14} from Hong Kong, similar 3 independent adverse risk factors were identified. A scoring system based on the findings was proposed to predict the mortality rate. The authors argued that a definitive ulcer surgery in the form of vagotomy or gastrectomy should be performed on all good-risk patients (no adverse risk factor) as simple closure would result in recurrent ulceration in up to 42%.^{15,16} The above studies were, however, conducted before the introduction of proton-pump inhibitors and discovery of *H. pylori*. The incidence of relapse after surgical closure of perforation were reduced significantly with the widespread use of H-2 blockers and more so after the introduction of proton-pump inhibitors.^{17,18} In addition, the discovery of *H. pylori* as the main causative agent in peptic ulcer disease and perforation represents a therapeutic landmark.¹⁹⁻²¹ Eradication of *H. pylori* has been proven to be effective in hastening ulcer healing and preventing recurrence.^{22,23} This has prompted some surgeons

to advocate a move away from acid-reductive surgery to simple closure with subsequent anti-*H. pylori* treatment for all patients.^{20,24} Whether this approach can replace the conventional definitive ulcer surgery remains to be determined because the cause of perforation in a proportion of patients was related to NSAIDs consumption rather than *H. pylori* infection. A randomised controlled trial would be difficult today in view of ethical issue involved in the treatment of *H. pylori* positive patients.

The operative mortality rate of 10.7% in our series is comparable with most recent large studies.^{5-9,13,14,25} Majority of the deaths (15 out of 22) occurred when there were 2 or more adverse risk factors. Patients with perforation who are elderly and severely ill at presentation often pose therapeutic dilemma to clinicians. Identification of risk factors may thus help in the selection of therapeutic approach. The very dismal surgical outcome of patients with 3 adverse risk factors (mortality rate = 88%) may prompt one to initiate alternative non-operative treatment although poor results may be expected regardless of modes of treatment for this group of patients.^{13,14}

Efforts to improve surgical outcome for perforated ulcers should focus on reducing the independent adverse risk factors. As concurrent medical illness is a non-modifiable factor and preoperative shock is usually resulting from treatment delay and inadequate resuscitation, emphasis should place on shortening the time to surgery as well as prompt resuscitation. Svanes et al²⁶ reported that there was a proportional increase in mortality with increase treatment delay. The increase in mortality became accelerated when the delay exceeded 12 hours. The authors calculated that a delay of more than 24 hours would increase the mortality by 7- to 8-fold. This is further compounded by recent trend of widespread use of NSAIDs which had been implicated in the occurrence of silent perforation in elderly, adding to diagnostic difficulty and treatment delay.²⁷ Thus, increased awareness of this surgical emergency especially in high risk patients should be repeatedly instilled in all medical personnels so that treatment delay can be minimised.

REFERENCES

1. Stabile B E, Passaro E Jr. Duodenal ulcer: A disease in evolution. *Curr Probl Surg* 1984; 21:6-17.
2. Walt R, Katschinski B, Logan R, Ashley J, Langman M. Rising frequency of ulcer perforation in elderly people in the United Kingdom. *Lancet* 1986; 3:489-92.
3. Agrez M V, Henry D A, Senthilvelan S, Duggan J M. Changing trends in perforated peptic ulcer during the past 45 years. *Aust N Z J Surg* 1992; 62:338-43.
4. Svanes C, Salvesen H, Stangeland L, Svanes K, Soreide O. Perforated peptic ulcer over 56 years: time trends in patients and disease

- characteristics. *Gut* 1993; 34:1666-71.
5. Irvin T T. Mortality and perforated peptic ulcer: a case for risk stratification in elderly patients. *Br J Surg* 1989; 76:215-8.
 6. O'Riordain D S, O'Dwyer P J, O'Higgins N J. Perforated duodenal ulcer in elderly patients. *J R Coll Surg Edinb* 1990; 35:93-4.
 7. Lena G M, Blomgren M D. Perforated peptic ulcer: long-term results after simple closure in the elderly. *World J Surg* 1997; 21:412-5.
 8. Ball A B S, Thomas P A, Evans S J. Operative mortality after perforated peptic ulcer. *Br J Surg* 1989; 76:521-2.
 9. Kum C K, Chong Y S, Koo C C, Rauff A. Elderly patients with perforated peptic ulcers: factors affecting morbidity and mortality. *J R Coll Surg Edinb* 1993; 38:344-7.
 10. Kang J Y. Peptic ulcer surgery in Singapore, 1951-80, with particular reference to racial difference in incidence. *Aust N Z J Med* 1985; 15:604-8.
 11. Kang J Y. Mortality from peptic ulcer in Singapore 1938-80. *Singapore Med J* 1983; 24:333-6.
 12. Kang J Y. Some observation on the epidemiology of peptic ulcer disease in Singapore. *Singapore Med J* 1992; 33:468-71.
 13. Boey J, Wong J, Ong G B. A prospective study of operative risk factors in perforated duodenal ulcers. *Ann Surg* 1982; 195:265-9.
 14. Boey J, Choi S M K, Alagaratnam T T, Poon A. Risk stratification in perforated duodenal ulcers: a prospective validation of predictive factors. *Ann Surg* 1987; 205:22-6.
 15. Raimes S A, Delvin H B. Perforated duodenal ulcer [editorial]. *Br J Surg* 1987; 74:81-2.
 16. Bornman P C, Theodorou N A, Jeffery P C. Simple closure of perforated duodenal ulcer: a prospective evaluation of a conservative management policy. *Br J Surg* 1990; 77:73-5.
 17. Macintyre I M, Miller A. Impact of H-2 receptor antagonists on the outcome of treatment perforated duodenal ulcer. *J R Coll Surg Edinb* 1990; 35:348-52.
 18. Hermansson M, Stael von Holstein C, Ziling T. Peptic ulcer perforation before and after the introduction of H-2 receptor blockers and proton pump inhibitors. *Scand J Gastroenterol* 1997; 32:523-9.
 19. Marshall B J, Warren J R. Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. *Lancet* 1984; i:1311-5.
 20. Sebastian M, Chandran V P, Elashal Y I M, Sim A J W. *Helicobacter pylori* infection in perforated peptic ulcer disease. *Br J Surg* 1995; 82:360-2.
 21. Ng E K W, Chung S C S, Sung J J Y, Lam Y H, Lee D W H, Lau J Y W, et al. High prevalence of *Helicobacter pylori* infection in duodenal ulcer perforation not caused by non-steroidal anti-inflammatory drugs. *Br J Surg* 1996; 83:1779-81.
 22. Graham D Y, Lew G M, Klein P D, Evan D G, Evan D J Jr, Saeed Z A, et al. Effect of treatment of *Helicobacter pylori* infection on the long-term recurrence of gastric or duodenal ulcer. A randomised controlled study. *Ann Intern Med* 1992; 116:705-8.
 23. Marshall B J, Goodwin C S, Warren J R, Murray R, Blincow E D, Blackbourn S J, et al. Prospective double-blind trial of duodenal ulcer relapse after eradication of *Campylobacter pylori*. *Lancet* 1988; ii: 1437-42.
 24. Corvera C U, Kirkwood S K. Recent advances: General surgery. *BMJ* 1997; 315:586-9.
 25. Evans J P, Smith R. Predicting poor outcome in perforated peptic ulcer disease. *Aust N Z J Surg* 1997; 67:792-5.
 26. Svanes C, Lie R T, Svanes K, Lie S A, Soreide O. Adverse effects of delayed treatment for perforated peptic ulcer. *Ann Surg* 1994; 220: 168-75.
 27. Collier D St J, Pain J A. Non-steroidal anti-inflammatory drugs and peptic ulcer perforation. *Gut* 1985; 26:359-63.