East African Medical Journal Vol. 81 No. 12 December 2004
EVALUATION OF RISK FACTORS FOR MORTALITY IN PERFORATED PEPTIC ULCER IN ANKARA NUMUNE TEACHING HOSPITAL, ANKARA, TURKEY
N. Ozalp, MD, B. Zulfikaroglu, MD, I. Bilgic, MD and M. Koc, MD, Associate Professor of Surgery, Department of Surgery, Ankara Numune Teaching and Research Hospital, Ankara 06100, Turkey

Request for reprints to: Dr. B. Zulfikaroglu, Department of Surgery, Ankara Numune Teaching and Research Hospital, Ankara 06100, Turkey

EVALUATION OF RISK FACTORS FOR MORTALITY IN PERFORATED PEPTIC ULCER IN ANKARA NUMUNE TEACHING HOSPITAL, ANKARA, TURKEY

N. OZALP, B. ZULFIKAROGLU, I. BILGIC and M. KOC

ABSTRACT

Objective: **To assess the risk factor that influence mortality from perforated peptic ulcer.**
Design: **Retrospective study.**
Setting: **Ankara Numune Teaching and Research Hospital, Ankara, Turkey.**
Subjects: **A total of 342 patients with perforated peptic ulcer disease were identified from April 1997 to January 2004. Data for the patients were extracted from the hospital records, operative notes and clinic charts.**
Main outcome measures: **Age, sex, coexisting medical illness, use of non-steroidal anti-inflammatory drugs (NSAID) or steroids, preoperative shock, delay in treatment location of ulcer size, type of operation time, albumin concentration postoperative complications, postoperative hospitals stay and mortality results for all patients were obtained.**
Results: **Patients were aged from 17 to 80 years (mean 63 years, median 68 years) there were 210 males and 132 females. The mortality rate was 8.8% (30/342), and 62 patients had postoperative complications. Multivariate analysis showed that co-existing medical illness, preoperative shock, delay in treatment and low albumin concentrations were independent risk factors that significantly contributed to mortality.**
Conclusion: **This study confirms co-existing medical illness, preoperative shock, delay in treatment and low albumin concentration as significant risk factors that increase mortality in patients with perforated peptic ulcers. These factors could serve as a guide to opine the risk and to improve the outcome in patients with perforated peptic ulcer. Mortality could be reduced by preventing delay in diagnosis and treatment for any co-existing medical illness and providing appropriate nutrition support.**

INTRODUCTION

Over the past two decades various authors have reported a decrease in the prevalence of uncomplicated gastroduodenal peptic ulcer fundamentally due to the introduction of new pharmacological agents that allow a more efficient control of the outbreaks of the disease(1). Elective surgery for peptic ulcer disease has decreased considerably since the introduction of H_2 receptor antagonists. Today most symptoms are adequately managed by medications. On the other hand, it is also well known that the number of acute surgical procedures performed on patients with complicated peptic ulcer has remained unchanged(2). The incidence of perforated peptic ulcer has been nearly constant over the past 50 years, but the median age of the patients has increased from 41 to 62(3). So, patients requiring surgery are at a high-risk and thus incur a high surgical mortality(4).

The aim of the present study was to review our experience in the treatment of perforated peptic ulcer disease and determine the risk factors that contribute to operative mortality and morbidity.

MATERIALS AND METHODS

This retrospective review involved patients operated on for perforated peptic ulcers from April 1997 to January 2004 at the Ankara Numune Teaching and Research Hospital, Ankara, Turkey. A total of 342 patients were recruited. Data for the patients were extracted from the hospital records, operative notes and clinic charts. Patients with clinical or radiologic signs of perforated peptic ulcers were excluded. We obtained the age, sex, co-existing medical illness, use of non-steroidal anti-inflammatory drugs (NSAIDs) or steroids, preoperative shock, delay in treatment, location of ulcer size, type of operation, operating time, albumin concentration, postoperative complications, postoperative hospital stay, and mortality results of all patients.

Preoperative shock was defined as preoperative systolic blood pressure of less than 100mm Hg. Co-existing medical illnesses included the cardio-respiratory disease, renal failure, diabetes mellitus, hepatic precoma, or any other organ failure. Delay in treatment denoted time from perforation to the start of the operation. Time of perforation (start of acute symptoms) was given in the case notes. Either simple closure or definitive surgery included truncal vagotomy and gastric resection, or vagotomy with a drainage procedure

was performed. The following complications were of particular interest: wound infection, prolonged ileus, intra-abdominal complications abscess and leakage. Operative mortality was defined as death during hospitalization or within 30 days of operation.

After closure of the perforation, thorough peritoneal lavage with warm normal saline (minimum 3 litres) was performed before closure of the abdominal incision in every case. Intravenous antibiotics were given at induction of anaesthesia and were continued for five days or until the fever had settled for more than one day. A nasogastric tube was inserted routinely and suction continued postoperatively until ileus resolved. The albumin concentration was checked the day after the operation. Fisher's exact test, the Mann-Whitney U test, and stepwise logistic regression were used for statistical analysis. A probability of $p < 0.05$ was accepted as significant.

RESULTS

A total of 342 consecutive patients with perforated peptic ulcer disease from April 1997 to January 2004 were identified. All the patients were treated surgically. The age of the patients ranged from 17 to 80 years (mean 63 years, median 68 years); there were 210 males and 132 females. Among all the patients 82% had pneumoperitoneum on initial evaluation. Fifty-eight patients (17%) had abdominal radiographs that were within normal limits and perforated ulcer was recognised during laparotomy, three patients free air demonstrated CT scanning. At the time of operation, twenty patients (5.8%) were receiving steroids, and forty nine (14%) were receiving NSAIDs.

Twenty seven patients were in shock preoperatively. Univariate analysis showed that preoperative shock was an independent risk factor that significantly contributed to mortality (Table 1).

The median delay in treatment was 21 hours (range 4 hours to 9 days). Patients were operated on within 6 hours, there were no deaths perioperatively and those on more than 48 hours after perforation had a significantly higher mortality risk. Univariate analysis also showed that coexisting medical illness and low albumin concentrations were independent risk factors that significantly contributed to mortality.

The location of the ulcer and median operating time were not related to the mortality and morbidity. The median operating time was 106 minutes and most of the perforations were in duodenum bulb and the prepylorus. The median size of the ulcers was 5mm. Size of the ulcer was not related to the mortality. However, the ulcer was significantly larger in the patients with morbidity. Simple closure was carried out in 322 patients, and definitive procedure was carried out in 20 patients. The mortality and morbidity rates of different procedures showed no statistically significant difference.

The median postoperative hospital stay was 6 days. Complications, however, prolonged hospitalisation to a median of 16 days (range 4 to 71 days). Seventy three complications developed postoperatively in 62 patients (18.1%) including the thirty who died (Table 2). Respiratory problems predominated, and many patients died after mechanical ventilation. Co-existing medical illness, delay in treatment and ulcer size were significantly related to postoperative morbidity.

Table 1

Risk factors related to hospital mortality and morbidity

Clinical parameter	Mortality			Morbidity		
	Lived	Died	P-value	None	Present	P-value
No.	321	30		280	62	
Male, per cent of patients	0.61	0.68	ns	0.61	0.60	ns
Age (mean ±SD years)	62.7±16.5	64.8±12.4	ns	61.9±11.3	62.2±12.7	ns
Preoperative shock (%)	10.2	62.5	<0.001	7.8	54.5	<0.001
Coexisting medical illness (%)	18	75	<0.001	14.7	57.5	<0.001
Delay in treatment (Median, hours)	16.4	54.8	<0.001	11.9	38.4	<0.001
Ulcer size (Median, mm)	5.7	4.8	ns	5.6	11.2	<0.005
Type of operative, No. of patients (%)						
Definitive procedures	18 (90%)	2 (10%)	ns	16 (80%)	4 (20%)	ns
Simple closure	294 (91.3%)	28 (8.7%)		264 (82%)	58 (18%)	
Operating time (Median minutes)	105.0	118.5	ns	102.5	108.3	ns
Albumin concentration (Mean±SD years)	29±5	20 ± 4	<0.001	31±4	21±4	<0.001
Postoperative hospital stay (Median, days)	6.2	5.9	ns	5.8	16.1	ns
NSAID use, No. of patients (%)	42 (13.4%)	7 (23.3%)	ns	38 (13.5%)	11 (17.7%)	ns
Steroid use, (No. of patients, %)	18 (5.8%)	2 (6.6%)	ns	15 (5.3%)	5 (8%)	ns

Table 2

Postoperative complications

No. of patients	62
Total complications	73
Pulmonary	28
Pneumonia	15
Adults respiratory distress syndrome	6
Pneumothorax	2
Pulmonary oedema	5
Wounded related	24
Infection	17
Dehiscence	7
Intra-abdominal abscess	11
Pancreatitis	2
Multisystem organ	6
Cardiac	2

Eleven patients were re-explored in the early postoperative period because of a suspected abscess (two patients), small bowel obstruction (two patients), and wound dehiscence (seven patients). Thirty patients (8.8%) died. Fifteen patients died of pneumonia and respiratory failure, eight patients died of fulminant abdominal sepsis, six patients died of multiorgan failure, and one patient died of postoperative myocardial infractions. Co-existing medical illness, preoperative shock, delay in treatment and low albumin concentrations were independent risk factors that significantly contributed to mortality.

DISCUSSION

Peptic ulcer disease has been recognised as a medically treatable and possibly curable illness(4). Since the introduction of potent drugs for the control of gastric acidity, the number of elective operations for peptic ulcer has declined. The discovery of *H.pylori* as a cause of duodenal ulcer disease means that a large proportion of the disease is potentially curable with antibiotics(4).

However, the incidence of perforation was not affected, and may even have increased (5-8). Unfortunately, the mortality among patients with perforated peptic ulcer has increased, despite advances in preoperative care(3). Svanes and Salvesen(3) reported that the patients were older and had more coexisting medical illness, and treatment was delayed longer during the recent decade than in the past(3). The present series, with its mortality rate of 8.8% is comparable with other recent series that reported mortality rates of 4 to 30% (4,9,10).

Previous studies reported that old age was a risk factor in perforated peptic ulcer(11,12), but we have not found this to be significant in our study. The apparent significance of old age reported in other studies may have arisen from an indirect association with independent risk factors. It was not age by itself, but the fact that older patients had more severe medical problems, delayed treatment longer, and poor nutritional condition that resulted in the higher mortality. When co-morbidities and nutritional status were controlled for, age did not emerge as an independent risk factor. Our data indicates that the co-existing medical condition of the patients, defined herein by the number of medical conditions present prior to the acute emergency condition of the perforated ulcer, was the most powerful predictor of morbidity and mortality. Preoperative hypertension was also associated with both complications and mortality.

The optimal surgical treatment for perforated peptic ulcer has been controversial(9,10,11,13). Hamby and Zweng(11) reported no difference in postoperative complications, mortality and short-term results between simple closure and a definitive procedure, but the definitive operation had better long term results and protected many patients from recurrent ulceration. These authors supported the definitive operation at the time of perforation over simple closure. In the present series, mortality was 8.7% (28/322) among the patients treated by simple closure and 10% (2/20) among those who had a definitive procedure. The operation type did not seem to be the risk factor, and statistical analysis confirmed this.

Most surgeons chose simple closure over a definitive procedure for high risk patients with perforated peptic ulcer (4,9,10,13). Simple repair has been the most commonly performed procedure since its popularization by Graham in 1937(14). However, long-term follow-up of patients who underwent simple repairs reveals a high incidence of ulcer relapse. In 1984, Marshall(15) discovered *Helicobacter pylori* accounted for most cases of peptic ulcer(16), and *H. pylori* was a curable infection(16). Thus, with the discovery of *H. pylori* in the pathogenesis of duodenal ulcer, simple closure alone with anti-*Helicobacter* therapy is effective for most cases of perforated peptic ulcer(13). Ng *et al.* (13) reported that after *H. pylori* eradication and without maintenance acid-suppression agents, 95% of patients remained ulcer free at one year follow-up. Their remission rate is similar to those previously reported in uncomplicated ulcers after *H. pylori* eradication(17) and is comparable to that achieved by immediate proximal gastric vagotomy or gastrectomy were annoying problems after definitive procedures(20).

We therefore suggest that simple closure combined with treatment against *H. pylori* would be the optimal strategy with good short- term and long term results in patients with perforated peptic ulcers, except for those with poor local conditions. Using multivariate data analysis, we have shown that a patient's likelihood of adverse outcome after operation for perforated peptic ulcer is independent of operative procedure and can be predicted using four preoperative factors: coexisting medical illness, delay in treatment, shock, and low albumin concentration.

In conclusion, this study confirms coexisting medical illness, preoperative shock, delay in treatment, and low albumin concentration as significant risk factors that increase mortality in patients with perforated peptic ulcers. These factors could serve as a guide to opine the risk and to improve the outcome in patients with perforated peptic ulcer. Mortality could be reduced by preventing delay in diagnosis and treatment, treating for any coexisting medical illness, and providing appropriate nutrition support. Once a perforation has occurred, timely diagnosis and management are necessary.

REFERENCES

1. Sanchez-Bueno, F. Marin, P. Rios, A. *et al.* Has the incidence of perforated peptic ulcer decreased over the last decade. *Dig. Surg.* 2001; **18:**444-448.
2. Makeka, J., Laitinene, S. L. and Kairalouma, M.I. Complication of peptic ulcer disease before and after the introduction of H_2 receptor antagonists. *Hepatogastroenterology.* 1992; **39:**144-148.
3. Svanes, C., Salvenesn, H., Stangeland, L., Svanes, K. and Soreide, O. Perforated peptic ulcer over 56 years. Time trends in patients and disease characteristics. *Gut.* 1993; **34:**166-1671.
4. Towfigh, S., Chandler, C., Hines, O.J. and McFadden, D.W. Outcomes from peptic ulcer surgery have not benefited from advances in medical therapy. *Amer. J. Surg.* 2002; **68:**385-389.
5. Scheeres, D.E., Dekryger, L.L. and Dean, R.E. Surgical treatment of peptic ulcer disease before and after introduction of H_2 blockers. *Amer. J. Surg.* 1987; **7:**392-395.
6. Mckay, A.J. and McArdle, C.S. Cimetidine and perforated peptic ulcer. *Brit. J. Surg.* 1982; **69:**319-321.
7. Watkins, R.M., Dennison, A.R. and Collin, J. What has happened to perforated peptic ulcer? *Brit. J. Surg.* 1984; **71:**774-780.
8. Hendry, W.S., Valerio, D. and Kyle, J. Perforated peptic ulcer in North East Scotland. 1972-1981. *J. R. Coll. Surg. Edinb.* 1984; **29:**69-73.
9. Chou, N.H., Mok, K.T. Chang, H. *et al.* Risk factors of mortality in perforated peptic ulcer. *Eur. J. Surg.* 2000; **166:**149-153.
10. Blomgren, L.G.M. Perforated peptic ulcer. Long term results after simple closure in the elderly. *World. J. Surg.* 1997; **21:**412-415.
11. Hamby, L.S., Zweng, T.N. and Strodel, W.E. Perforated gastric and duodenal ulcers. An analysis of prognostic factor. *Amer. J. Surg.* 1993; **59:**319-324.
12. Bodner, B. Harrington, M.E. and Kim, U. A multifactorial analysis of mortality and morbidity in perforated peptic ulcer disease. *Surg. Gynecol. Obstet.* 1990; **171:**315-320.
13. Ng, E.K., Lam, Y.H., Sung, J.J. *et al.* Eradication of *Helicobactor pylori* prevents recurrence of ulcer after simple closure of duodenal ulcer perforation. *Ann. Surg.* 2000; **231:**153-158.
14. Graham, R.R. The treatment of perforated duodenal ulcers. *Surg. Gynecol. Obstet.* 1937; **64:**235.
15. Marshall, B.J. and Warren, J.R. Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. *Lancet.* 1984; **1:**1311-1314.
16. Tokunaga, Y. Hata, K. Ryo, J. Kitaoka, A., Tohuka, A. and Ohrumi, K. Density of *Helicobacter pylori* infection in patients with peptic ulcer perforation. *J. Amer. Coll. Surg.* 1998; **186:**659-663.
17. Van der Hulst, R.W., Rauws, E.A., Koycu, B. *et al.* Prevention of ulcer recurrence after eradication of *Helicobacter pylori*. A prospective long term follow up study. *Gastroenterol.* 1997; **113:**1082-1086.
18. Jordan, P.H. and Thornby, J. Perforated pyloroduodenal ulcers. Long term results with omental patch closure and parietal call vagotomy. *Ann. Surg.* 1995; **221:**479-488.
19. Hay, J.M., Lacaine, F. and Kohlmann, G. Immediate definitive surgery for perforated duodenal ulcer does not increase operative mortality. A prospective controlled trial. *World. J. Surg.* 1998; **12:**705-709.
20. Tovey, F.I. Godfery, J.E. and Lewin, M.R. A gastrectomy population. 25-30 years. *Postgrad. Med. J.* 1990; **66:**450-456.