

Significant factors associated with fatal outcome in emergency open surgery for perforated peptic ulcer

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This paper is dedicated to the memory of Prof. Francesco Paccione, Head of the Department of Surgery who died prematurely in 1996.

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Abstract

AIM: To evaluate the main factors associated with mortality in patients undergoing surgery for perforated peptic ulcer referred to an academic department of general surgery in a large southern Italian city.

METHODS: One hundred and forty-nine consecutive patients (M:F ratio=110:39, mean age 52 yrs, range 16-95) with peptic ulcer disease were investigated for clinical history (including age, sex, previous history of peptic ulcer, associated diseases, delayed abdominal surgery, ulcer site, operation type, shock on admission, postoperative general complications, and intra-abdominal and/or wound infections), serum analyses and radiological findings.

RESULTS: The overall mortality rate was 4.0 %. Among all factors, an age above 65 years, one or more associated diseases, delayed abdominal surgery, shock on admission, postoperative abdominal complications and/or wound infections, were significantly associated (χ^2) with increased mortality in patients undergoing surgery ($0.0001 < P < 0.03$).

CONCLUSION: Factors such as concomitant diseases, shock on admission, delayed surgery, and postoperative abdominal and wound infections are significantly associated with fatal outcomes and need careful evaluation within the general workup of patients admitted for perforated peptic ulcer.

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INTRODUCTION

There has been a marked decrease in elective surgery for peptic

ulcer disease (PUD) following introduction of medical therapies including H₂-receptor antagonists, and more recently proton pump inhibitors with or without antibiotics for *H. pylori* eradication. By contrast, the number of acute complications *e.g.* ulcer perforation and bleeding requiring emergency surgery, have remained quantitatively constant^[1,2]. Peptic ulcer perforation is a serious complication which affects almost 10 % of PUD patients. Overall, PUD accounts for more than 70 % of mortality associated with the disease^[3,4]. Several potential predicting factors for perforation have been evaluated in the literature, including use of ulcerogenic drugs (*e.g.* steroids, NSAIDs, immunosuppressive agents, *etc.*), and the development of an acute, rather than chronic peptic ulcer^[5-8].

In this paper, we studied the main factors associated with mortality in a large number of patients undergoing surgery for perforated peptic ulcers (PPU) in a large referral academic hospital in southern Italy.

MATERIALS AND METHODS

Patients

The study population comprised 149 consecutive patients with an established intra-operative final diagnosis of PUD referred for emergency surgery to the 1st Department of General Surgery of the University of Bari. Bari is the main city of a province of about 1 500 000 inhabitants in the south-eastern coast of Italy. During a time spanning from 1988 to 1997 all patients were treated exclusively by open surgical approach, as agreed by all staff members. Since then, additional patients have been treated also by laparoscopy for PPU, but due to the scant number of cases, they were not included in the present analysis. Overall, there were 39 females and 110 males (mean age 52 years, range 16-95). The diagnosis of gastrointestinal ulcers was based on clinical features, blood tests, routine laboratory tests, and radiological findings (*i.e.* plain abdominal X-ray in all cases and abdominal CT scan in 87 % of patients). Invariably, the definitive diagnosis of PPU was obtained at surgery. The time between presumed perforation and surgery was considered delayed if longer than 12 h. The following factors were analysed: age >65 years, sex, previous ulcer history, associated medical diseases, delayed operation, site of ulcer, type of operation, shock on admission, postoperative general complications, postoperative intra-abdominal and/or wound infections.

Surgical procedure

An open surgical approach was performed leading to a non definitive operation (*i.e.* ulcer excision and suture with or without pyloroplasty) in 120 patients (80.5 %) and to definitive operations (*i.e.* Billroth II resection) in 29 patients (19.5 %). The decision to perform one or the other type of surgery depended on several known factors including location and extent of lesions, feasibility of a safe non-definitive surgery, presence or absence of anaesthesiological risk factors, and surgeon's attitude. No truncal or selective vagotomies were performed. All operations were performed by the same surgical staff whose colleagues were well trained in gastrointestinal surgery.

Statistical analysis

All calculations were performed with the *NCSS 2001* statistical software (Kaysville, UT, USA). The chi-square test was used to compare proportions. A two-tailed probability (*P*) value of less than 0.05 was considered statistically significant^[9,10].

RESULTS

The time between perforation and surgery was delayed in 51 patients (34.2 %), 79 patients (53.0 %) had associated diseases which are listed in Table 1. Cardiovascular, chronic obstructive pulmonary diseases and diabetes mellitus were the most frequently (over 65 %) associated conditions. A previous history of PUD was found in 53 (35.6 %) patients and 9 (6.0 %) were shocked on admission. Gastric and duodenal ulcers were perforated in 23 (15.4 %) and 126 (84.6 %) patients, respectively.

Table 1 Associated diseases in study group

Cardiovascular disease	27
Diabetes mellitus	20
Chronic obstructive pulmonary disease	19
Impaired liver function	8
Renal failure	7
Coagulation disorders	6
Cerebrovascular disease	4
Neurological disease (others)	3
Malignancy	2
Thyroid disease	1
Gallstones	1
Acute pancreatitis	1
Total	99

Types of postoperative complications are reported in Table 2. The most frequent events were due to general, rather than abdominal complications or wound infections.

Table 2 Postoperative complications

General	
Cardiac	7
Respiratory	7
Sepsis	7
Renal	5
Mental disorders	2
Ictus	1
Deep venous thrombosis	1
Total	30
Abdominal	
Abscess	6
Bleeding	2
Stenosis	2
Total	10
Wound infections	8
Total	48

The analysis of factors associated with mortality is depicted in Table 3. Of the 149 patients, 6 died yielding an overall mortality rate of 4.0 %. The presence of one or more associated diseases, delay in surgical approach, shock on admission, postoperative abdominal complications (6 dehiscence/abscess, 2 bleedings, 2 stenosis) and the postoperative wound infections were all significantly ($0.0001 < P < 0.04$) associated with increased mortality in patients undergoing surgery for PPU. By contrast, age, sex, previous history and site of peptic ulcer, type of surgical treatment and the development of postoperative general complications were not associated with increased mortality.

Table 3 Analysis of factors associated with mortality in 149 patients undergoing surgery for perforated peptic ulcer

	<i>n</i>	Mortality (%)	<i>P</i> value
Male:Female	110:39	3.6 vs. 5.1	NS
Age (<65: >65 years)	63:86	1.6 vs. 5.8	NS
Previous ulcer history (yes:no)	53:96	5.7 vs. 3.1	NS
Associated disease (yes:no)	79:70	7.6 vs. 0.0	0.02
Delayed operations (yes:no)	41:108	9.8 vs. 1.9	0.04
Site (duodenal:gastric)	126:23	3.1 vs. 8.7	NS
Operation type (non definitive:definitive)	120:29	2.5 vs. 10.3	NS
Shock on admission (yes : no)*	9:140	55.6 vs. 0.7	0.0001
Postop. general complications (yes:no)	30:119	6.7 vs. 3.4	NS
Postop. abdominal complications (yes:no)*	10:139	50.0 vs. 0.7	0.0001
Postoperative wound infections (yes:no)*	8:141	37.5 vs. 2.1	0.0001

Data analyzed by χ^2 test and *Fisher's exact test.

DISCUSSION

Several factors might contribute to increased postoperative mortality in patients with PPU. Perforation has been found to be a major complication of PUD with a mortality rate ranging from 6 % to 31 %^[6-8, 11-20].

Age of patients with PPU has been gradually increasing over the last years^[21-23]. In this series, an age >65 years tended to be associated with increased mortality. This finding is in line with other studies in which older patients frequently had associated diseases, or they were more on NSAIDs treatment^[8,16,22]. It should be also noted that the mean age of patients from this series was considerably lower than that from patients included in different studies. Thus, such differences might account for the markedly lower overall mortality rate (4.0 %), as compared to other series^[6-8, 11-20].

In accord with others^[19, 23], we could not find that male sex was associated with a greater mortality rate. Also, there was no significant difference in mortality rate between gastric or duodenal ulcer and in patients with or without previous ulcer history. Apparently, these findings were at variance with those from two other studies^[13, 24] reporting a higher mortality rate in gastric peptic ulcer than in duodenal peptic ulcer and in acute peptic ulcer than in chronic peptic ulcer. Such apparent discrepancies might be explained by the characteristics of patients included in the study, and/or by different age or different surgical procedures^[16,18].

This study confirmed the previous observations^[5,8,15,25-28] that shock on admission and delayed operation were both associated with a greater mortality rate.

Despite the fact that surgery remains the choice of treatment for PPU, the type of procedure in emergency is still debated. In some series definitive surgery had lower rates of recurrence and mortality than non definitive surgery^[16,18,19,29,30]. Otherwise, non-definitive surgery was more frequently performed in patients admitted with more risk factors than definitive surgery, and this might explain the higher mortality rate of such studies. Moreover, diffusion of the laparoscopic approach to PPU with less surgical trauma and less metabolic and physiological disturbances, has determined an increase of non definitive surgical procedures performed by simple closures^[3,20,22,31]. In the present study, there was no difference in mortality rate between definitive (*i.e.* Billroth II resection) or non-definitive (*i.e.* ulcer excision and suture with or without pyloroplasty)

surgical procedure.

It has been reported that mortality rate increased progressively with increasing numbers of risk factors^[6,8]. Indeed, the mortality rate was 0 % and 7.6 % in the group of patients without and with associated diseases, respectively. In the present study cardiovascular, chronic obstructive pulmonary diseases and diabetes mellitus were the most frequent concomitant diseases. Besides, 6 patients developing a postoperative abscess had a previous history of chronic obstructive pulmonary disease. A possible explanation for such an outcome could be the reduced tissue oxygenation resulting in damage of post-surgical wound healing process. This possibility was supported by recent studies from our group at the intestinal level in both experimental and clinical conditions^[32-36].

We also observed that in patients developing postoperative abdominal complications (*i.e.* 6 abscesses, 2 bleedings, and 2 stenosis) and wound infections, the mortality rate was significantly higher ($P=0.0001$) than those without abdominal complications. We would like to explain that such a striking difference was due to the development of a generalized sepsis in the group of patients with intra-abdominal abscess. Indeed, 83.3 % (*i.e.* 5/6) of patients with dehiscence and abdominal abscess, died in the postoperative period, otherwise, in this group with postoperative complications, the appearance of stenosis or bleeding was not associated with a higher mortality rate. In our experience the presence of wound infection appeared to be a predictive factor for mortality. A careful analysis of the 3 patients who died of wound infection, however, revealed that the cause of exitus was septicaemia complicating an abdominal abscess. By contrast, postoperative general complications did not influence the prognosis of patients with PPU.

In conclusion, concomitant diseases, shock on admission, delayed surgery, and postoperative abdominal and wound infections are factors significantly associated with fatal outcomes in patients undergoing emergency surgery for perforated peptic ulcer. Older age tends to fulfill a similar trend. Thus, such factors need to be carefully taken into account during the general workup of patients admitted for PPU.

REFERENCES

- Christensen A, Bousfield R, Christiansen J. Incidence of perforated and bleeding peptic ulcers before and after the introduction of H₂-receptor antagonist. *Ann Surg* 1988; **207**: 4-6
- Bliss DW, Stabile BE. The impact of ulcerogenic drugs on surgery for the treatment of peptic ulcer disease. *Arch Surg* 1991; **126**: 609-612
- Lau WL, Leung KL, Kwong KH, Davey IC, Robertson C, Dawson JJ, Chung SC, Li AK. A randomised study comparing laparoscopic versus open repair of perforated peptic ulcer using suture or sutureless technique. *Ann Surg* 1996; **224**: 131-138
- Svanes C, Salvesen H, Stangeland L, Svanes K, Soreide O. Perforated peptic ulcer over 56 year. Time trends in patients and disease characteristics. *Gut* 1993; **34**: 1666-1671
- Boey J, Wong J, Ong GB. A prospective study of operative risk factors in perforated duodenal ulcers. *Ann Surg* 1982; **195**: 265-269
- Boey J, Choi SKY, Alagaratnam TT, Poon A. Risk stratification in perforated duodenal ulcers. *Ann Surg* 1987; **205**: 22-26
- Boey J, Wong J. Perforated duodenal ulcers. *World J Surg* 1987; **11**: 319-324
- Evans JP, Smith R. Predicting poor outcome in perforated peptic ulcer disease. *Aust N Z J Surg* 1997; **67**: 792-795
- Armitage P, Berry G. Statistical methods in medical research. *Blackwell Scientific Publ* 1994
- Dawson B, Trapp RG. Basic & Clinical Biostatistics. New York: McGraw-Hill 2001
- Gunshefsky L, Flancbaum L, Brolin R, Frankel A. Changing pattern in perforated peptic ulcer disease. *Am Surg* 1990; **56**: 270-274
- Greiser WB, Bruner BW, Shamoun JM, Jurkovich GJ, Ferrara JJ. Factors affecting mortality in patients operated upon for complications of peptic ulcer disease. *Am Surg* 1989; **55**: 7-11
- Hodnett RM, Gonzalez F, Lee WC, Nance FC, Deboisblanc R. The need for definitive therapy in the management of the perforated gastric ulcers. Review of 202 cases. *Ann Surg* 1989; **209**: 36-39
- Horowitz J, Kukora JS, Ritchie WP Jr. All perforated ulcers are not alike. *Ann Surg* 1989; **209**: 693-697
- Irvin TT. Mortality and perforated peptic ulcer: a case for risk stratification in elderly patients. *Br J Surg* 1989; **76**: 215-218
- Suter M. Surgical treatment of perforated peptic ulcer. Is there a need for a change? *Acta Chir Belg* 1993; **93**: 83-87
- Lee FY, Leung KL, Lai BS, Ng SS, Dexter S, Lau WY. Predicting mortality and morbidity of patients operated on for perforated peptic ulcers. *Arch Surg* 2001; **139**: 90-94
- Blomgren LGM. Perforated peptic ulcer: long-term results after simple closure in the elderly. *World J Surg* 1997; **21**: 412-415
- Sillakivi T, Lang A, Tein A, Peetsalu A. Evaluation of risk factors for mortality in surgically treated perforated peptic ulcer. *Hepatogastroenterology* 2000; **47**: 1765-1768
- Michelet I, Agresta F. Perforated peptic ulcer: laparoscopic approach. *Eur J Surg* 2000; **166**: 405-408
- Svanes C, Salvesen H, Stangeland L, Svanes K, Soreide O. Perforated peptic ulcer over 56 years. Time trend in patients and disease characteristics. *Gut* 1993; **34**: 1666-1671
- Cocks JR. Perforated peptic ulcer - the changing scene. *Dig Dis* 1992; **10**: 10-16
- 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
- McGee GS, Sawyers JL. Perforated gastric ulcers. *Arch Surg* 1987; **122**: 555-561
- Hamby LS, Zweng TN, Strodel WE. Perforated gastric and duodenal ulcer: an analysis of prognostic factors. *Am Surg* 1993; **59**: 319-324
- Mattingly SS, Ram MD, Griffin WO Jr. Factors influencing morbidity and mortality in perforated duodenal ulcer. *Am Surg* 1980; **46**: 61-66
- McIntosh JH, Berman K, Holliday FM, Byth K, Chapman R, Piper DW. Some factors associated with mortality in perforated peptic ulcer: a case control study. *J Gastroenterol Hepatol* 1996; **11**: 82-87
- Wakayama T, Ishizaki Y, Mitsusada M, Takahashi S, Wada T, Fukushima Y, Hattori H, Okuyama T, Funatsu H. Risk factors influencing the short-term results of gastroduodenal perforation. *Surg Today* 1994; **24**: 681-687
- Jordan PH, Thornby J. Perforated pyloroduodenal ulcers. Long-term results with omental patch closure and parietal cell vagotomy. *Ann Surg* 1995; **221**: 479-488
- Robles R, Parrilla P, Lujan JA, Torralba JA, Cifuentes J, Liron R, Pinero A. Short note: long-term follow-up of bilateral truncal vagotomy and pyloroplasty for perforated duodenal ulcer. *Br J Surg* 1995; **82**: 665
- Matsuda M, Nishiyama M, Hanai T, Saeki K, Watanabe T. Laparoscopic omental patch repair for perforated peptic ulcer. *Ann Surg* 1995; **221**: 336-240
- Testini M, Scacco S, Loiotila L, Regina G, Vergari R, Papa F, Paccione F. Comparison of oxidative phosphorylation in the small vs. large bowel anastomosis. *Eur Surg Res* 1998; **30**: 1-7
- Testini M, Piccinni G. Wound healing of intestinal anastomosis after digestive surgery under septic condition. *World J Surg* 1999; **23**: 1315-1316
- Testini M, Margari A, Amoroso M, Lissidini G, Bonomo GM. Le deiscenze nelle anastomosi colo-rettali: fattori di rischio. *Ann Ital Chir* 2000; **71**: 433-440
- Testini M, Piccinni G, Amoroso M, Di Venere B, Nicolardi V, Bonomo GM. Chronic obstructive pulmonary disease and failure of large bowel anastomosis. *It J Coloproctol* 2000; **3**: 91-94
- Testini M, Portincasa P, Scacco S, Piccinni G, Minerva F, Lissidini G, Papa F, Loiotila L, Bonomo GM, Palasciano G. Contractility *in vitro* and mitochondrial response in small and large anastomosed rabbit bowel. *World J Surg* 2002; **26**: 493-498