Risk Stratification in Perforated Duodenal Ulcers

A Prospective Validation of Predictive Factors

JOHN BOEY, M.D., F.A.C.S. SAMUEL K. Y. CHOI, F.R.C.S.E. A. POON, F.R.C.S.E., F.R.A.C.S. T. T. ALAGARATNAM, F.R.C.S., F.R.C.S.E.

From the Department of Surgery, University of Hong Kong, Queen Mary Hospital, Hong Kong

In order to validate a previously derived set of risk factors, 259 consecutive patients who had simple closure or definitive operation for perforated duodenal ulcers were studied prospectively. Major medical illness, preoperative shock, and longstanding perforation (more than 24 hours) correctly predicted the outcome in 93.8% of patients. Most importantly, 16 patients (6.2%) who died after operation could be identified (no false-negative error). The mortality rate increased progressively with increasing numbers of risk factors: 0%, 10%, 45.5%, and 100% in patients with none, one, two, and all three risk factors, respectively. These findings underscore the importance of patient selection and the feasibility of a risk grading system in guiding surgical management. Definitive surgery can be done safely in good-risk patients. Simple closure is preferable in those patients with uncomplicated perforations if any risk factor is present. Truncal vagotomy and drainage may be required if there is coexisting bleeding or stenosis. Nonoperative treatment deserves re-evaluation in patients with all three risk factors because of their uniformly dismal outcome after operation.

PERFORATED DUODENAL ULCERS result in an operative mortality rate of about 6% (Table 1).[1-24] Yet, this risk has not deterred surgeons from using immediate definitive surgery in their treatment. Even more crucial than recognizing patients who may relapse after closure alone is the problem of identifying those patients in whom definitive surgery entails an inordinate risk. We previously determined prognostic risk factors in 213 patients who had surgery for perforated ulcers.[24] Concurrent medical illnesses, preoperative shock, and a longstanding perforation were found to be independent clinical features related to postoperative deaths. Because such an analysis may apply only to the patient population from which they were derived, these findings needed to be validated in a separate series of patients. In this study, we prospectively evaluated the usefulness of these three risk factors in guiding the surgical management of patients with perforated duodenal ulcers.

Supported by grants from the University and Medical Faculty Research Grants Committee, University of Hong Kong.

Reprint requests: John Boey, M.D., Department of Surgery, University of Hong Kong, Queen Mary Hospital, Hong Kong.

Submitted for publication: May 28, 1986.

Patients and Methods

We studied 259 consecutive patients who had surgery for perforated duodenal ulcers from August 1981–February 1984. Their mean age was 51.3 ± 17.8 years. The ratio of males to females was 3.6:1. Surgery was performed an average of 11.8 hours (range: 2–120 hours) after the onset of perforation. A comparison of these patients with the 213 patients in our preceding study is given in Table 2. The two groups were basically comparable except for slightly fewer patients in the current series who had gross peritoneal contamination as defined previously.[24]

Risk Score and Predicted Survival

A value of 1 was assigned for each independent risk factor (severe medical illness, preoperative shock, and longstanding perforation) that was present in a patient. Because we avoid definitive surgery in perforations exceeding 24 hours, this cut-off limit was selected to define a longstanding perforation. The risk score of each patient represented the sum total of risk factors present in the patient.

The outcome of each patient was predicted from the discriminant function (stepwise analysis by the generalized distance method of Rao[25]) obtained in the earlier study:

$$\text{Discriminant value} = 3.40\,(\text{medical illness}) + 3.12\,(\text{shock}) + 0.68\,(>24\,\text{hrs}) - 0.53$$

The mean discriminant value was −0.23 among the survivors and +5.29 in those who died. The standardized

discriminant coefficients were 0.69, 0.56, and 0.23 for medical illness, shock, and long-standing duration, respectively.

A separate discriminant function with 48 hours as the cut-off limit to define a long-standing perforation was also evaluated in a similar manner.

The same surgical policy and operative techniques as that of the initial study[24] were used. Proximal gastric vagotomy with closure was the preferred definitive procedure. Truncal vagotomy with pyloroplasty was used only if there was concomitant pyloric stenosis, bleeding, or previous ulcer surgery. Simple closure was performed in 183 patients, 45 of whom had one or more risk factors. Vagotomy and drainage was done in 12 patients, including four patients who had one or two risk factors and coexisting bleeding or pyloric stenosis. None of the 64 patients who had proximal gastric vagotomy had any risk factors. The distribution of risk factors is shown in Table 3. The inclusion of patients who had definitive surgery in the analysis is based on the assumption that the operative risks of a more extensive procedure is at least equivalent to that of closure alone.

Statistical analysis was done by the corrected chi-square test, the Fisher exact test, the unpaired Student's t-test, and the Mann–Whitney rank sum test for nonparametric data.[26] Ninety-five per cent confidence limits were determined for binomially distributed variables. The level of statistical significance was 5%.

TABLE 1. *Operative Mortality Rates of Perforated Duodenal Ulcers in Recent Studies*

			Simple Closure		Definitive Operation	
	N	Overall Mortality (%)	N	No. of Deaths (%)	N	No. of Deaths (%)
Pierandozzi[1]	75	1.3	—	—	75	1 (1.3)
Hamilton[2]	80	5.0	44	4 (9.1)	36	0 (0)
Maynard[3]	83	8.4	34	7 (20.6)	49	0 (0)
Mark[4]	71	9.9	52	7 (13.5)	19	0 (0)
Smith[5]	96	3.1	33	2 (6.1)	63	1 (1.6)
Donaldson[6]	352	8.0	300	27 (9.0)	52	1 (1.9)
Booth[7]	344	2.9	332	10 (3.0)	12	0 (0)
Wangensteen[8]	126	4.0	89	5 (5.6)	37	0 (0)
Greco[9]	155	5.8	143	8 (5.6)	12	1 (8.3)
Sawyers[10]	360	5.6	254	17 (6.7)	106	3 (2.8)
Coutsoftides[11]	132	6.8	109	7 (6.4)	23	2 (8.7)
Gray[12]	176	6.3	77	10 (13.0)	99	1 (1.0)
Griffin[13]	174	7.5	122	8 (6.6)	52	5 (9.6)
Jordan[14]	157	5.7	40	8 (20.0)	117	1 (0.8)
Sawyers[15]	21	0	—	—	21	0 (0)
Kay[16]	162	4.3	57	4 (7.0)	105	3 (2.9)
Playforth[17]	161	5.0	161	8 (5.0)	—	—
Baekgaard[18]	112	2.7	112	3 (2.7)	—	—
Donovan[19]	52	7.7	14	4 (28.6)	38	0 (0)
Kirkpatrick[20]	184	6.5	137	9 (6.6)	47	3 (6.4)
Ferraz[21]	20	0	—	—	20	0 (0)
Jordan[22]	109	13.8	37	15 (40.5)	72	0 (0)
Wara[23]	161	9.9	90	13 (14.4)	71	3 (4.2)
Boey*[24]	472	5.3	322	23 (7.1)	150	2 (1.3)
Total	3835	5.9	2559	199 (7.8)	1276	27 (2.1)

* Results from both current study and previous study.

TABLE 2. *Comparison of Perforated Duodenal Ulcer Patients in Two Consecutive Studies*

	First Study[24] (N = 213)	Current Study (N = 259)	p
Men, % patients	85.4	78.8	NS†
Age, mean (±SD) years	49.0 (17.7)	51.3 (17.8)	NS*
Duration of perforation, median, hours	12.3	11.8	NS‡
over 24 hours, % patients	16.9	13.5	NS†
over 48 hours, % patients	7.5	5.8	NS†
Gross peritoneal contamination, % patients	10.8	5.4	0.05†
Shock, % patients	5.2	5.4	NS†
Other major illness, % patients	7.5	10.4	NS†
Chronic ulcer symptoms median, months	18.2	24.3	NS‡
Previous ulcer surgery, % patients	3.3	3.1	NS†
Definitive surgery, % patients	34.7	29.3	NS†
Risk score, median	0.1	0.1	NS‡
Morbidity rate, % patients	12.7	14.3	NS†
Mortality rate, % patients	4.2	6.2	NS†

NS Not significant.
* Unpaired Student's t-test.
† Corrected chi-square test.
‡ Mann–Whitney test.

Results

Mortality and Morbidity Rates

Of the 16 hospital deaths (6.2%), all but two occurred after simple closure. Nine patients died of chest infections and respiratory failure, three patients died of fulminant abdominal sepsis, two patients died of postoperative myocardial infarctions, one patient died of heart failure, and one patient died of a massive stroke. Four patients had perforations in the hospital while being treated for medical conditions, and three patients had advanced underlying malignancies.

The overall morbidity rate was 14.3% (Table 4). Respiratory problems predominated, and many patients died after prolonged mechanical ventilation. Intra-abdominal

TABLE 3. *Distribution of Risk Scores*

Operation	No. of Patients				
	Risk Score				
	0	1	2	3	Total
Closure only	138	27	10	8	183
Vagotomy and drainage	8	3	1	—	12
Proximal gastric vagotomy and closure	64	—	—	—	64
Total	210	30	11	8	259

sepsis occurred in eight patients who had established abscesses. Seven patients (2.7%) had superficial wound infections despite the routine use of prophylactic antibiotics. Five patients were re-examined in the early postoperative period because of a bleeding ulcer, suspected abscess (only a small sterile fluid collection was found), small bowel obstruction, or wound dehiscence (two patients).

Prediction of Operative Outcome

The practical application of these three risk factors is shown by the progressive rise in mortality rate with increasing numbers of risk factors (Table 5). The median risk score of the 32 patients predicted to die was 1.8, whereas that of the 16 patients who died was 2.5. None of the 210 patients without any risk factor died after operation even though 72 patients had an immediate definitive operation.

The close correlation between the calculated discriminant values and the final outcome of the 259 patients is illustrated in Figure 1. Good separation of the two groups was observed with the most overlap occurring among patients with discriminant values between 2.87 and 3.55. There was a consistent tendency for patients to survive even though they were predicted to die.

The discriminant function had an accuracy rate of 93.8% and a sensitivity rate of 100% for predicting the 16 patients who died after operation. However, there was a false-positive error rate of 50% among the 32 patients predicted to die.

TABLE 4. *Postoperative Complications in 37 Patients*

	No. of Patients
Pneumonia	10
Respiratory failure	13
Cardiac problems	13
Intra-abdominal abscess	8
Gastrointestinal bleeding	4
Wound infection	13
Wound dehiscence	3
Total	64

TABLE 5. *Correlation between Mortality Rate and Risk Scores*

Operation	No. of Patients	Mortality Rate (%)				
		Risk Score				
		0	1	2	3	Total
Closure only	183	0	7.4	40.0	100	7.7
Vagotomy and drainage	12	0	33.3	100	—	16.7
Proximal gastric vagotomy and closure	64	0	—	—	—	0
Total	259	0	10.0	45.5	100	6.2

For the 472 consecutive patients from both series, the discriminant function had an overall accuracy rate of 93.9%. There was a 100% sensitivity rate for predicting the 25 postoperative deaths. The false-positive error rate was 52.8% among the 53 patients predicted to die.

The second discriminant function that used 48 hours as the cut-off limit to define a longstanding perforation had an accuracy rate of 94.6%. However, the sensitivity rate fell to 93.8% (15 of 16 deaths), and the false-positive error rate was still 46.4%.

Discussion

Recent mortality figures for perforated duodenal ulcers range from 2.7–13.8% (Table 1). This disparity probably reflects varying proportions of poor-risk patients in individual series. Patients must be grouped into different risk categories before surgical results can be meaningfully compared. Thus far, the lack of a uniform risk grading system has thwarted a methodical appraisal of the comparative safety of definitive surgery.

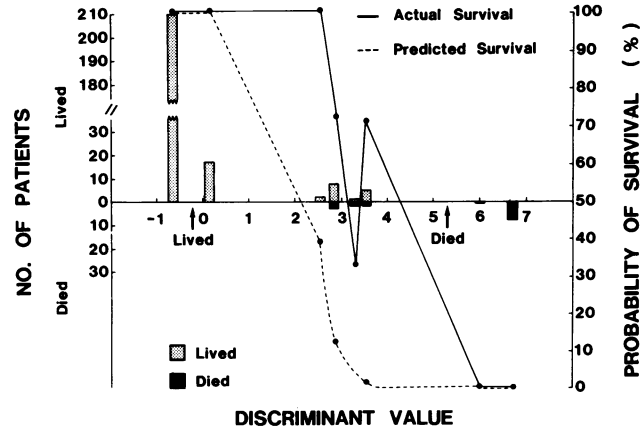

FIG. 1. Correlation between predicted and actual outcome of patients with perforated duodenal ulcers. The predicted probability of survival (broken lines) is based on the discriminant function derived from the 213 patients in the initial series. The actual survival rate (solid lines) is based on the 259 patients in the current series. The arrows indicate the group mean discriminant values for the surviving and dead patients.

This study reaffirms the value of three independent variables—severe medical illness, preoperative shock, and longstanding perforations—in identifying high-risk patients with perforated ulcers. These variables can be readily determined by clinical assessment alone, and can serve as a guide in surgical management. The previously derived discriminant function that incorporated these risk factors was validated by its successful prediction of all 16 patients who died in this second prospective series. An accuracy rate of 93.9% was attained in the combined series of 472 consecutive patients. All 25 patients (5.3%) who died were recognized before operation as poor-risk patients (no false-negative errors). Twenty-eight of 53 patients (52.8%) who were predicted to die survived. From a clinical perspective, this false-positive error rate is acceptable and does not detract seriously from the value of this predictive discriminant function. The high error rate largely reflects the general definitions used for the shock and medical illness variables. A more refined grading system of these risk factors and the addition of other individually significant variables[24] might reduce this error rate. However, this would complicate the risk scoring system, yet not enhance the primary objective of identifying patients in whom definitive surgery is inadvisable.

The time limit beyond which definitive surgery is likely to be hazardous is ill-defined. The higher incidence of heavy bacterial proliferation and worse prognosis indicate 48 hours as the maximum limit.[24,27] On the other hand, 12 hours or less[3,28] appears stringent, and would curtail the number of patients who are eligible for definitive surgery. Slightly more high-risk patients could be distinguished by the discriminant function using 24 hours rather than 48 hours as the cut-off limit. Because of the greater propensity for peritoneal contamination and the relatively few patients treated more than a day after perforation, we usually avoid definitive surgery when more than 24 hours have elapsed.

Risk stratification of patients with perforated ulcers should facilitate their management and improve survival rates. Most patients (80% in this study) are otherwise healthy individuals free of any risk factors. Among the 472 patients, all 381 patients defined as good-risk patients (no risk factor present) survived regardless of whether simple closure or definitve sugery was performed. In these patients, the prevention of relapse should be a secondary but relevant consideration. That none of 143 patients who were defined as good-risk patients died after definitive surgery attests to the importance and feasibility of patient selection. Similar encouraging reports by Sawyers and Herrington,[10,15] Ferraz,[21] Jordan,[14,23] and others[1–6,12,13,19,20,22] corroborate the safety of immediate definitive operations in selected patients. These reports belie the contention that definitive surgery invariably jeopardizes the safety of patients. The 95% confidence limits for operative mortality rates after simple closure and definitive operation among our 381 good-risk patients were 0–1.4% and 0–2.3%, respectively. Such a minute difference in mortality rate is likely to defy substantiation by a controlled study. For comparison, even with suboptimal risk patients included, the 2.1% collective mortality rate after definitive operation (Table 1) falls within these estimates. These findings strongly suggest that the mortality rate of definitive surgery in well-chosen patients is unlikely to exceed that of closure alone.[23,29] In addition, the morbidity rate of definitive surgery should be measured against that of an operation performed for relapse after closure. Some disadvantages of curative surgery are further offset by the dangers of an emergency operation for bleeding or reperforation after simple closure.[23] Most surgeons confine definitive surgery to fit patients who are prone to relapse. To date, a chronic ulcer is the single most reliable criterion that characterizes these patients.[9,16,30–32]

Approximately 15% of our patients had or two risk factors. Their higher cumulative mortality rate (45% with two risk factors) makes simple closure a more prudent choice. An exception arises if there is a concurrent ulcer complication that necessitates definitive surgery. This applies particularly to coexisting posterior ("kissing") ulcers that often bleed after operation.[33] Both deaths that occurred after definitive surgery were in patients with ischemic heart disease who had concomitant pyloric stenosis or bleeding that precluded simple closure. In general, truncal vagotomy and pyloroplasty (or gastrojejunostomy) is the most expedient choice in such patients.

The excellent results achieved by surgical intervention in patients at good risk justifiably casts routine nonoperative treatment in disfavor. However, 14 patients (3%) in this combined series had all three risk factors and were moribund at presentation. All but one patient died (92.9% mortality rate), accounting for half of all postoperative deaths. This very high mortality rate disputes the merits of even simple closure for these patients. Nonoperative treatment has been variably effective in several reports[4,6–9,16,19,20,22,34]; however, because patient selection criteria were not uniform or unspecified, the indications for this modality of treatment are rather imprecise. We concur with Jordan[23] and others[6,7] that conservative management warrants reassessment in poor-risk individuals. By measuring prognostic factors, nonoperative treatment can be allocated to a clearly defined high-risk group. Nevertheless, its efficacy still must be clarified, as a fatal result may be inevitable regardless of treatment.

Calculating discriminant values to predict the outcome of a patient is impractical and unnecessary. Indeed, the fact that half of the patients predicted to die actually survived with appropriate management argues against such a rigid clinical application. It is sufficient to be aware that the presence of any risk factor increases the operative haz-

ards. The relative importance of these three predictive factors can be gauged by the value of their individual standardized discriminant coefficients. In this study, major medical illnesses and preoperative shock each confer approximately three times the amount of risk as a long-standing perforation. However, in clinical practice it would be cumbersome to weight these risk factors as any one of them should already interdict definitive surgery. Moreover, although these three factors had the most predictive value, other individually significant varibles such as gross peritoneal contamination and old age should not be ignored when considering definitive surgery. Adopting a standard risk scoring system should provide a more systematic approach in the management of perforated ulcers. This is especially pertinent as definitive surgery is increasingly advocated in its treatment.

Acknowledgments

The kind assistance of Ms. Kelly L. M. Wong, B.Sc., is gratefully acknowledged. Computer facilities were made available through the courtesy of the Centre for Computer Studies and Applications, University of Hong Kong.

References

1. Pierandozzi JS, Hinshaw DR, Stafford CE. Vagotomy and pyloroplasty for acute perforated duodenal ulcer: a report of seventy-five cases. Am J Surg 1960; 100:245–250.
2. Hamilton JE, Harbrecht PJ. Growing indications for vagotomy in perforated peptic ulcer. Surg Gynecol Obstet 1967; 125:61–64.
3. Maynard A deL, Froix CJL, Oropeza G. Gastroduodenal perforation. Arch Surg 1968; 97:96–104.
4. Mark JBD. Factors influencing the treatment of perforated duodenal ulcer. Surg Gynecol Obstet 1969; 129:325–330.
5. Smith L, Beehan PJ. Definitive operations for perforated duodenal ulcers. Surg Gynecol Obstet 1969; 129:465–469.
6. Donaldson GA, Jarrett F. Perforated gastroduodenal ulcer disease at the Massachusetts General Hospital from 1952 to 1970. Am J Surg 1970; 120:306–311.
7. Booth RAD, Williams JA. Mortality of duodenal ulcer treated by simple suture. Br J Surg 1971; 58:42–44.
8. Wangensteen SL, Wray RC, Golden GT. Perforated duodenal ulcer. Am J Surg 1972; 123:538–542.
9. Greco RS, Cahow CE. Alternatives in the management of acute perforated duodenal ulcer. Am J Surg 1974; 127:109–114.
10. Sawyers JL, Herrington JL Jr, Mulherin JL Jr, et al. Acute perforated duodenal ulcer. Arch Surg 1975; 110:527–530.
11. Coutsoftides T, Himal HS. Perforated gastroduodenal ulcers. Am J Surg 1976; 132:575–576.
12. Gray JG, Roberts AK. Definitive emergency treatment of perforated duodenal ulcer. Surg Gynecol Obstet 1976; 143:890–894.
13. Griffin GE, Organ CH Jr. The natural history of the perforated duodenal ulcer treated by suture plication. Ann Surg 1976; 183:382–385.
14. Jordan PH Jr, Korompai FL. Evolvement of a new treatment for perforated duodenal ulcer. Surg Gynecol Obstet 1976; 142:391–395.
15. Sawyers JL, Herrington JL Jr. Perforated duodenal ulcer managed by proximal gastric vagotomy and suture plication. Ann Surg 1977; 185:656–660.
16. Kay PH, Moore KTH, Clark RG. The treatment of perforated duodenal ulcer. Br J Surg 1978; 65:801–803.
17. Playforth MJ, McMahon MJ. The indications for simple closure of perforated duodenal ulcers. Br J Surg 1978; 65:699–701.
18. Baekgaard N, Lawaetz O, Poulsen PE. Simple closure or definitive surgery for perforated duodenal ulcer. Scand J Gastroenterol 1979; 14:17–20.
19. Donovan AJ, Vinson TL, Maulsby GO, Gewin JR. Selective treatment of duodenal ulcer with perforation. Ann Surg 1979; 189: 627–636.
20. Kirkpatrick JR, Bouwman DL. A logical solution to the perforated ulcer controversy. Surg Gynecol Obstet 1980; 150:683–686.
21. Ferraz EM, Filho HAF, Bacelar TS, et al. Proximal gastric vagotomy in stenosed or perforated duodenal ulcer. Br J Surg 1981; 68: 452–454.
22. Wara P, Kristensen ES, Sorensen FH, et al. The value of parietal cell vagotomy compraed to simple closure in a selective approach to perforated duodenal ulcer. Operative morbidity and recurrence rate. Acta Chir Scand 1983; 149:585–589.
23. Jordan PH Jr. Proximal gastric vagotomy without drainage for treatment of perforated duodenal ulcer. Gastroenterology 1982; 83:179–183.
24. Boey J, Wong J, Ong GB. A prospective study of operative risk factors in perforated duodenal ulcers. Ann Surg 1982; 195:265–269.
25. Klecka WR. Discriminant analysis. *In* Nie NH, Hull CH, Jenkins JG, et al., eds. SPSS: Statistical Package for the Social Sciences. New York: McGraw-Hill, 1975; 434–467.
26. Siegel S. Nonparametric Statistics for the Behavioral Sciences. New York: McGraw-Hill, 1956; 95–127.
27. Boey J, Wong J, Ong GB. Bacteria and septic complications in patients with perforated duodenal ulcers. Am J Surg 1982; 143: 635–639.
28. Nemanich GJ, Nicoloff DM. Perforated duodenal ulcer: long-term followup. Surgery 1970; 67:727–734.
29. Jordan GL, DeBakey ME, Duncan JM Jr. Surgical management of perforated peptic ulcer. Ann Surg 1974; 179:628–633.
30. Boey J, Lee NW, Wong J, Ong GB. Perforations in acute duodenal ulcers. Surg Gynecol Obstet 1982; 155:193–196.
31. Illingworth CFW, Scott LDW, Jamieson RA. Progress after perforated peptic ulcer. Br Med J 1946; 1:787–790.
32. Dean ACB, Clark CG, Sinclair-Gieben AH. The late prognosis of perforated duodenal ulcers. Gut 1962; 3:60–64.
33. Stabile BE, Hardy HJ, Passaro E Jr. "Kissing" duodenal ulcers. Arch Surg 1979; 114:1153–1156.
34. Kristensen ES. Conservative treatment of 155 cases of perforated peptic ulcer. Acta Chir Scand 1980; 146:189–193.