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Perforated Peptic Ulcer: Main Factors of Morbidity and Mortality

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Abstract. It is well stated in the literature that medical treatment for peptic ulcer is based on a combination of proton pump inhibitors (PPIs) and antibiotics to eradicate *Helicobacter pylori*. This treatment is associated with a high rate of immediate success and a low rate of recurrence at 12 months, although it is not effective in all patients. Peptic ulcer (PU) perforation is a serious problem that leads to high complication and mortality rates. Surgical treatment, with its various possibilities, constitutes the ideal treatment. Surgical intervention in these cases, however, can be directed to treating the perforation alone, or it can offer definitive treatment of the ulcer itself. With the hope of establishing why such complications and mortality were seen in the patients in our hospital population, we gathered the facts about PU perforations and the types of surgery performed. We studied 210 consecutive patients (150 men, 60 women) who had undergone surgery at our hospital because of perforation between January 1, 1990 and December 31, 2000. The patients' median age was 53.0 ± 20.6 years (men 47.7 ± 17.3 years; women 66.3 ± 22.0 years). Altogether, 86 patients had significant associated illnesses, 62 were admitted more than 24 hours after the perforation, and 25 were admitted in shock. We performed resections in 10 patients; 88 patients were treated by suturing the perforation with or without a patch of epiploon; and 112 underwent a troncular vagotomy with drainage (VT + Dr). A total of 21 patients died (10%). Significant risk factors that led to complications were identified by statistical studies. They were a perforation that had been present more than 24 hours, the coexistence of significant associated illnesses, and resection surgery. The significant risk factors that led to death were the presence of shock at admission, the coexistence of significant illnesses, and resection surgery. There was no statistically significant difference concerning morbidity and mortality between simple closure of the perforation and definitive surgery (VT + Dr).

Introduction of H_2-blockers and proton pump inhibitors (PPIs) in clinical practice and more precise knowledge about peptic ulcer physiopathology that the studies of *Helicobacter pylori* brought us during the 1990s provides patients with a high probability of cure and a low rate of recurrence for the middle term, as shown by a well conducted trial. These facts made medical treatment of PU disease preferable to elective surgical treatment, whose dominant role has remained unchanged when ulcer disease complications are in question [1, 2]. This fact applies to treatment of the perforated PU, whose incidence has remained stable or has slightly declined during the second half of the twentieth century [3]. Today, however, some claim that we are being faced with a higher rate of elderly people affected by this complication.

The best surgical option for these patients is still in question. Simple closure, regardless of whether protected with an epiploon patch, continues to be the preferred option for many surgeons. It is the easiest, quickest, safest operation, and it can be applied to all situations by every surgeon; moreover, it can be complemented later with an effective medical treatment that should include eradication of *H. pylori*. Other groups support the role of definitive surgery, stating that this treatment, when indicated, does not increase the morbidity or mortality due to the perforation. The purpose of this study was to investigate the factors associated with the patients, the perforations, and the operations performed. We then related these factors to the postoperative complications and the mortality of the patients.

Materials and Methods

Patients

A series of 210 consecutive patients with PU perforation associated with peritonitis who required emergency surgery between January 1, 1990 and December 31, 2000 were included in this study. All patients in whom a definitive histologic diagnosis revealed or confirmed the presence of a malignant lesion in the stomach were excluded. After the initial diagnosis and the usual reanimation measures (correcting the hydric, metabolic, and acid-base preexisting imbalances, nasogastric intubation and aspiration, intravenous antibiotics) the patients underwent surgical treatment.

At admission, complaints attributable to previous ulcerous disease; chronic ingestion of nonsteroidal antiinflammatory drugs (NSAIDs), aspirin, corticosteroids, or immunosuppressants; alcohol ingestion and smoking habits; evolution of the acute episode (hours); and the patient's vital signs were recorded. Altogether, 124 patients had no associated pathology, and 86 were afflicted with co-morbidities. Table 1 summarizes the clinical characteristics of the patients.

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Table 1. Patients' clinical features.

No. of patients	210	%
Age (years), mean ± SD	53.1 ± 20.6	
Male	47.7 ± 17.3	
Female	66.3 ± 22.0	
Sex		
Male	150	71.5
Female	60	28.5
Dyspepsia > 3 months	122	58.0
NSAIDs and steroid therapy	33	15.7
Delayed presentation (> 24 hours)	62	29.5
Shock on admission	25	11.9
Location		
Pyloroduodenal	172	82.0
Gastric	38	18.0
Medical illness	86	40.9
Cardiovascular	34	
Respiratory	20	
Renal	11	
Multiple arthroses	9	
Diabetes mellitus	8	
Hepatic cirrhosis	6	
Rheumatoid arthritis	3	

NSAIDS: nonsteroidal antiinflammatory drugs.

Table 2. Postoperative complications.

Complication	No.	%
Respiratory infection	24	11.4
Wound infection	12	5.7
Wound dehiscence	11	5.2
Suture leakage	7	3.3
Abdominal abscess	7	3.3
Peritonitis	7	3.3
Sepsis	6	2.8
Cardiovascular	6	2.8
Renal failure	3	1.4
Hepatic failure	2	0.95

Table 3. Causes of mortality.

Cause of death	No. of patients	%
Sepsis	10	4.8
Respiratory failure	4	2.0
Myocardial infarction	2	1.0
Heart failure	1	0.5
Apoplexy	1	0.5
Unknown	3	1.5
Total	21	10.0

Surgical Technique

The exact location of the perforation was confirmed by the surgeon in the operating room. A total of 172 patients had pyloric ($n = 88$) or bulbar ($n = 84$) perforations and were categorized as having a duodenal ulcer (DU) perforation; 38 patients had a gastric ulcer (GU) perforation.

In 88 patients (35 with a GU) closure of the perforation was performed with or without an epiploon patch; 112 patients underwent troncular vagotomy with a drainage operation (Weinberg or Finney pyloroplasty or gastrojejunostomy) (VT + Dr); and 10 patients underwent subtotal gastrectomy or vagotomy with antrectomy**.** Each operation was the surgeon's preference for the individual patient.

All GUs were biopsied during surgery. Treatment of the associated peritonitis consisted of mechanical cleansing of the peritoneal cavity with saline in large quantities (> 3000 ml). Subhepatic drainage was optional and was rarely used; when it was used, it was mainly during resection surgery.

Assessment Criteria

Treatment delay denotes the duration of time from the appearance of the perforation to the start of the operation. The time of perforation (i.e., the start of acute symptoms) was determined by personal interview, from case notes, or from hospital records; the beginning of the operation was obtained from the anesthesia record. The criteria used refer to the postoperative complications (intraabdominal and general) and the surgical mortality (i.e., death occurring within 4 weeks after surgery or during the hospitalization). All information related to the preoperative evaluation, surgery performed, and its complications were confirmed during personal interviews conducted by one of three of the authors (C.N., A.S.S., or J.N.S) . The data have been prospectively recorded since 1990 in a database created with this purpose (Access for Windows) and stored in a personal computer.

Statistical Analysis

The data analysis was performed with the SPSS9.0 program. The frequencies of the used variables (sex, age, pulse and blood pressure at admission, alcohol ingestion, smoking and drug habits, significant co-morbidities, localization of the perforation, duration and type of surgery performed) were compared by the χ^2 test with Yates correction or by Fisher's exact test. The association between variables and the morbidity and mortality was estimated by the odds ratio (OR) calculation and 95% confidence intervals (CI).

When univariate analysis of factors showed significant differences ($p < 0.05$) we calculated the adjusted OR by a multivariate logistic regression model.

Results

A total of 88 patients (33 with a perforated GU) underwent simple closure (covered with a patch of epiploon in 53). Another 122 underwent definitive surgical treatment, which included 10 resection procedures and 112 troncular vagotomies plus drainage operations.

Morbidity affected 37 (42.5%) of the patients in the simple closure group and 31 (25.4%) of those in whom definitive surgery was performed. Some patients experienced more than one complication.

Altogether, 21 patients (10%) died as a consequence of the operation: 15 (17.2%) after simple closure and 6 (4.9%) after definitive surgery (3 after VT + Dr and 3 after resection surgery). Tables 2 and 3 show the causes of morbidity and mortality in our patients.

As shown in Table 4, the variables with statistical significance that led to morbidity were age, pulse and blood pressure at admission, associated illnesses, perforation evolution, and type of surgery performed. The logistic regression analysis (Table 5) adjusted each of the variables to the others with significant OR found that only a perforation evolution longer than 24 hours, associated illnesses, and resection surgery were significant risks (Table 6). The variables

Table 4. Relation between morbidity and other variables.[a]

Variable	Patients		χ^2	p
	Number	%		
Sex				
Male	150	31.8	0.36	0.55
Female	60	36.1		
Age (years)				
≤ 50	105	14.6	34.82	< 0.001
50-69	45	45.5		
≥ 70	60	57.6		
BP at admission (mmHg)				
≥ 100	163	30.1	4.72	0.03
< 100	25	52.0		
Pulse at admission (beats/minute)				
< 100	129	30.2	4.86	0.03
≥ 100	36	50.0		
Alcohol consumption				
No	36	38.29	0.45	0.50
Yes	83	32.5		
Smoking habit				
No	41	31.7	0.25	0.62
Yes	84	27.4		
NSAID use				
No	46	26.1	1.76	0.18
Yes	35	40.0		
Comorbidities				
No	126	16.7	37.55	< 0.001
Yes	86	57.0		
Evolution of perforation (hours)				
≤ 24	139	20.9	29.3	< 0.001
> 24	62	59.7		
Operation				
TV + Dr	112	20.5	22.03	< 0.001
Suture	88	43.2		
Resection	10	80.0		
Ulcer type				
Gastric	38	42.1	1.67	0.20
Duodenal	172			

TV + Dr, troncular vagotomy plus drainage operation; BP: blood pressure.

[a]Number of operations observed and percent complications.

Table 5. Univariate logistic regression: odds ratio and confidence intervals at 95% (dependent variable: morbidity).

Variable	OR	95% CI
Age (years)		
< 50	1.00	2.18–10.96
50–69	4.89	3.76–16.92
≥ 70	7.97	
BP at admission (mmHg)		
≥ 100	1.00	1.07–5.91
< 100	2.52	
Pulse at admission (beats/minute)		
< 100	1.00	1.09–4.91
≥ 100	2.31	
Comorbidities		
No	1.00	3.51–12.48
Yes	6.62	
Evolution of perforation (hours)		
≤ 24	1.00	2.92–10.77
> 24	5.61	
Operation		
TV + Dr	1.00	1.58–5.48
Suture	2.94	3.08–77.89
Resection	15.48	

Table 6. Multivariate logistic regression: adjusted odds ratio and CI at 95% (dependent variable: morbidity).

Variable	OR	95% CI
Age (years)		
≤ 50	1.00	0.99–7.70
50–69	2.76	0.97–7.12
≥ 70	2.62	
BP at admission (mmHg)		
≥ 100	1.00	0.51–.4.71
< 100	1.55	
Comorbidity		
No	1.00	1.87–9.87
Yes	4.30	
Evolution of perforation (hours)		
≤ 24	1.00	1.83–9.70
> 24	4.21	
Operation		
TV + Dr	1.00	0.41–2.31
Suture	0.98	3.43–140.59
Resection	21.95	

with statistical significance that led to mortality are the same as those that led to morbidity (Table 7). They were blood pressure < 100 mmHg at admission, associated illnesses, and resection surgery (Tables 8, 9).

Discussion

As in other centers, we have verified over the last few years a marked decrease in the number of patients with uncomplicated PU subjected to elective surgery. This has come about since the introduction of H_2-blockers and PPIs to clinical practice, complemented by the eradication of *H. pylori*. This decline, however, was not associated with a decrease in the number of patients admitted with PU perforation, similar to reports from other centers [1, 2, 4].

A total of 62 patients presented to our surgical department with a perforated ulcer that had been present more than 24 hours. In fact, 26 of the patients had had their perforated ulcers more than 48 hours). They are taken into account in Table 1 as delayed presentations. Explanations for such delays are that, first, the patients find it difficult to see their family doctors because they live in extremely rural, backwoods areas. Second, our hospital receives patients referred by smaller hospitals, some of them located 100 km away, which delays the patient's presentation at our institution. A third explanation is the advanced age of these patients. The average age of patients who have had perforations of > 24 to < 47 hours of evolution is 58.38 ± 22.77 years, the age of those with perforations of > 48 hours' evolution is 69.96 ± 17.51 years.

It has been noted in the literature that there is an increasing number of elderly persons affected by this problem [4, 5], although we did not see a significant number of elderly patients in our series. In contrast to other reports that have indicated an increasing number of female patients affected by the disease over the past few years [6, 7], we had a male/female ratio of 2.5:1.0.

What we did observe was a clear difference in the mean age relative to the appearance of this PU complication between men (47.7 ± 17.3 years) and women (66.3 ± 22.0 years), for which we have no convincing explanation.

Only 33 (15.7%) of our patients were taking NSAIDs at the time of the perforation. There were clinical data suggesting the existence of previous PU disease in 122 patients, which may explain the high rate of patients submitted to definitive surgery.

Table 7. Relation between mortality and other variables.

Variable	Patients		χ^2	p
	No.	% Dead		
Sex				
Male	150	7.3	5.67	0.02
Female	60	19.7		
Age (years)				
≤ 50	105	1.0	29.32	< 0.001
50-69	45	11.4		
≥ 70	60	28.8		
BP at admission (mmHg)				
≥ 100	163	5.5	15.40	< 0.001
< 100	25	32.0		
Pulse at admission (beats/minute)				
< 100	129	6.2	4.48	0.03
≥ 100	36	19.4		
Alcohol consumption				
No	36	8.3	0.43	0.51
Yes	83	3.6		
Smoking habit				
No	41	7.9	1.71	0.19
Yes	84	1.2		
NSAID use				
No	46	4.3	0.06	0.81
Yes	35	5.7		
Comorbidity				
No	124	2.4	20.92	< 0.001
Yes	86	23.3		
Evolution of perforation (hours)				
≤ 24	139	3.6	18.07	< 0.001
> 24	62	24.2		
Operation				
TV + Dr	112	2.7	16.90	< 0.001
Suture	88	18.2		
Resection	10	30.0		
Ulcer type				
Gastric	38	13.2	0.08	0.78
Duodenal	172	10.6		

Table 8. Univariate logistic regression: odds ratio and CI at 95% (dependent variable: mortality).

Variable	OR	95% CI
Sex		
Male	1.00	1.29–7.52
Female	3.12	
Age (years)		
≤ 50	1.00	1.48–115.45
50-69	13.07	5.32–320.06
≥ 70	41.27	
BP at admission (mmHg)		
≥ 100	1.00	2.75–23.62
< 100	8.05	
Pulse at admission (beats/minute)		
< 100	1.00	
≥ 100	3.65	1.22–10.88
Comorbidity		
No	1.00	3.56–43.33
Yes	12.42	
Evolution of perforation (hours)		
≤ 24	1.00	2.95–24.82
> 24	8.55	
Operation		
TV + Dr	1.00	2.27–28.70
Suture	8.07	2.64–91.70
Resection	15.57	

Table 9. Multivariate logistic regression: adjusted odds ratio and CI at 95% (dependent variable: mortality).

Variable	OR	95% CI
Sex		
Male	1.00	0.08–1.72
Female	0.37	
Age (years)		
≤ 50	1.00	0.16–33.73
50–69	2.35	0.55–78.84
≥ 70	6.59	
BP at admission (mmHg)		
≥ 100	1.00	1.53–34.52
< 100	7.26	
Comorbidity		
No	1.00	1.67–195.58
Yes	18.06	
Evolution of perforation (hours)		
≤ 24	1.00	0.74–13.59
> 24	3.18	
Operation		
TV + Dr	1.00	0.33–15.91
Suture	2.31	1.10–227.12
Resection	15.79	

For decades the literature has reported conflicting data concerning the impact of the evolution of the perforation (in hours) in terms of surgical mortality. In series with large numbers of patients [8, 9] it became clear that as the therapeutic delay increased so did the mortality rate. Recent studies have expressed some doubt about this supposition [10, 11]. Our analysis indicated that the critical point at which the therapeutic delay becomes significant is 24 hours after the perforation occurs.

The data we obtained shows that the risk of mortality and morbidity is statistically significant ($p < 0.001$) when the patient is submitted to surgery with a perforation that is more than 24 hours old, although this theory is not supported by the multivariate analysis regarding mortality.

Another factor frequently noted in the literature regarding surgical mortality is the coexistence of significant co-morbidities. This factor was also found to be important in our series. The risk of morbidity was six times higher and the risk of mortality twelve times higher when we compared patients with or without associated co-morbidities.

The factors mentioned above are in agreement with the analysis reported by Boey et al. [12]. They claimed that postoperative mortality is influenced by the presence of shock at admission or by an interval between the perforation and treatment of more than 24 hours.

Our analysis confirmed that the presence of shock at admission (BP maximum < 100 mmHg) was a determining factor in the patient's final prognosis.

Surgical treatment for a perforated PU is, in our opinion, the correct therapeutic option depending on the patient's clinical condition. A conservative approach (Taylor's method) should be used only in exceptional situations. Even during laparotomy it is possible to mistake a perforated PU for a perforated tumor.

During the same period we observed 10 gastric cancer perforations. Closing the perforation was the only possible procedure for six patients with unresectable disease. Two underwent a type R2 resection for advanced disease, and two were operated on with a diagnosis of "benign disease." All of these patients were excluded from the study.

An issue that remains under discussion is the appropriate surgical option (simple closure or definitive surgery) in view of the fact that medical treatment today is so effective. In our patients a study of the impact of the surgical procedure on their mortality revealed that their survival was clearly affected by resection surgery. The risks of simple closure of the perforation versus VT + Dr were the same. This finding agrees with our recommendations, primarily in situations where there are no risk factors and we are operating on an "old" perforated PU, where definitive treatment of the disease does not increase the possibility of morbidity and mortality. We do not advise the use of resection surgery for a GU perforation, with or without troncular vagotomy, as it is associated with a high risk of mortality. The mortality in our series, which seems to have occurred particularly in patients in whom closure of the perforation was performed (15/88 patients), was 10%. Lower [13, 14] and higher [15, 16] values have been reported in the English-language literature, probably reflecting the different characteristics of the populations treated in other hospitals. The high mortality rate for the simple closure group is probably due to the choices made for these patients when they are exposed to surgery. For instance, surgeons tend to shorten the operating time for patients at high risk. This group includes elderly patients, usually with cardiovascular disease, in whom the diagnosis is often late and peritonitis is of accentuated gravity. Here the cause of death is usually persistent sepsis or pulmonary failure, expressed as multiorgan failure.

Some have stated that GU perforation is associated with higher mortality [17] than DU perforation. This was not observed in our series, where we found no statistical difference ($p = 0.78$) between the mortality rates for GU (13.2%) and DU (10.6%).

The improved prognosis for perforated PUs is associated with effective prophylaxis of NSAIDs ulcers, whose incidence has been rising worldwide with the increased consumption of these drugs and the earlier diagnosis, especially in elderly people. On the other hand, if data from other centers can be applied to our hospital, in the future we may be operating on older patients more often than we are today, making this task a difficult one [18] .

We believe that minimally invasive surgery can help decrease the mortality associated with perforated PUs, but it is not yet clear if this assumption will have an impact on mortality in the near future.

Résumé. Se nos jours, il est bien indiqué dans la littérature que le traitement de choix médical de la maladie ulcéreuse est basé sur l'association d'inhibiteurs de la pompe à protons (IPP) et des antibiotiques pour l'éradication d'*Helicobacter pylori*. Ce traitement a un taux élevé de succès immédiats et un taux de récidive relativment bas à 12 mois, bien qu'ill ne soit pas efficace chez tous les patients. La perforation d'ulcère (PU) est une complication sérieuse qui peut se voir pendant la maladie ulcéreuse et qui, même aujourd'hui, est associée à une morbidité et mortalité élevées. Le traitement chirurgical, avec ses variations, constitue le traitement idéal de cette complication, et alors, on a le choix entre le traitement simple de la perforation (suture) ou le traitement définitif de la maladie ulcéreuse. Dans cette série de 210 patients consécutifs (150 hommes et 60 femmes) opérés dans le département de chirurgie de notre Hôpital pour PU entre 01/01/1990 et 31/12/2000, nous avons cherché à identifier les facteurs de risque (en rapport avec le patient, la complication qu'est la perforation, et le type de chirurgie) déterminants pour la morbidité et la mortalité. La médiane d'âge des patients a été de 53 ± 20.6 ans (hommes: 47.7 ± 17.3; femmes: 66.3 ± 22.0), 86 patients avaient une co-morbidité, 62 ont été admis plus de 24 heures aprés la perforation et 25 en état de choc. Nous avons réalisé une résection chez 10 patients, une suture de la perforation, avec ou sans épiploplastie, chez 88, et une vagotomie tronculaire + procédé de drainage (V.T. + Dr.) chez 112 patients. Vingt et un patients sont décédés (10%). Les facteurs de risque de morbidité identifiés par notre étude étaient une perforation de plus de 24 heures, la co-existence de tares et la résection chirurgicale; ceux de la mortalité étaient la présence de choc à l'admission, la co-existence de tares et la résection chirurgicale. En ce qui concernait la morbidité ou la mortalité, on n'a pas trouvé de différence significative entre la suture simple et la chirurgie définitive.

Resumen. En la actualidad, el tratamiento medico estándar de la úlcera péptica conlleva la administración de inhibidores de la bomba de protones (PPI) asociada a antibióticos con objeto de erradicar al *Helicobacter pylori*. Este tratamiento proporciona un alto porcentaje de curaciones inmediatas con escasas recidivas a los 12 meses; sin embargo no es eficaz en todos los pacientes. La perforación de la úlcera péptica (P.U.) es, incluso en la actualidad, una grave complicación pues cursa con elevadas tasas de morbi-mortalidad. La cirugía con sus dintintas técnicas constituye el tratamiento ideal para esta complicación; puede limitarse a tratar exclusivamente la perforación o bien abordar el tratamiento definitivo de la enfermedad ulcerosa. Con objecto de determinar, en nuestro Hospital, las características del paciente, la incidencia de la perforación y la influencia del tipo de cirugía realizada sobre la morbi-mortalidad, hemos estudiado una serie de 210 pacientes (150 hombres y 60 mujeres) ingresados en nuestro departamento de cirugía entre 01/01/1990 y 31/12/2000 por perforación de P.U. La edad media fue de 53 ± 20.6 años (en hombres: 47.7 ± 17.3; en mujeres: 66.3 ± 22). 86 pacientes tenían sensación de enfermedad grave; 62 ingresaron con una perforación de más de 24 horas de evolución; 25 lo hicieron en estado de shock. En 10 pacientes se efectuó una resección gástrica, 88 fueron tratados mediante sutura de la perforación con o sin epiploplastia; en 112 se realizó una vagotomía troncular y operación de descarga (VT + Dr.) Murieron 21 pacientes (10%). El estudio estadístico reveló que los factores más importantes determinantes de morbilidad fueron: perforación de más de 24 horas, coexistencia con sensación de enfermedad grave y la cirugía resectiva. Por lo que a la mortalidad se refiere, los factores más importantes fueron: estado de shock al ingreso, sensación de enfermedad grave y tratamiento resectivo. No se registró diferencia alguna, por lo que a la morbi-mortalidad se refiere, entre la simple sutura de la perforación y el tratamiento quirúrgico definitivo de la enfermedad (V.T. + Dr.).

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