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Morbidity and mortality of perforated peptic gastroduodenal ulcer following emergency surgery

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Abstract *Background:* This study assessed the surgical concept and prognosis of perforated gastroduodenal ulcers. *Patients and methods:* Data from 102 patients who underwent emergency surgery for peptic ulcer perforation were recorded prospectively. To evaluate morbidity and mortality ulcer perforation was classified into three types: type A, solitary peripyloric ulcer located anteriorly in which laparoscopic closure by suture with omentoplasty was treatment of choice and postoperative endoscopic biopsy was mandatory; type B, perforated ulcer with large defect in which excision and suture was necessary; type C, complicated perforated ulcer with destruction of proximal duodenum and penetration into adjacent organs in which resectional surgery was indicated. *Results:* Morbidity and mortality were significantly lower in type A (9%, 4%, respectively) than types B (22%, 20%) and C (34%, 17%). Closure of type A perforation was managed laparoscopically in all cases. Billroth II resection was performed in 75% of type C cases. Age, ASA status, and time of surgery were independent prognostic factors by multivariate analysis, with increased mortality in patients older than 65 years, ASA III and IV, and surgery after 24 h following onset of symptoms. *Conclusions:* Prognosis of perforated ulcer disease is highly correlated with age, comorbid conditions (ASA status), and time of surgery. The proposed classification system helps to determine patients at risk of mortality.

Keywords Gastroduodenal ulcer · Perforation · Surgery · Prognosis

Introduction

As medical treatment including the administration of H_2-receptor antagonists in the 1970s followed by the use of proton-pump inhibitors in the 1980s has substantially been improved, elective surgery for gastroduodenal ulcer disease has been dramatically decreased [1, 2]. However, the incidence of emergency surgery for perforated ulcer has remained relatively unchanged, and potentially increased [3, 4]. Although many retrospective and prospective studies focusing on surgical management including laparoscopic approaches have been published, there is the need for stratifying patients in terms of surgical strategy and risk factors predictive of mortality. Therefore it was the goal of this study to assess surgical concept and prognosis of perforated gastroduodenal ulcer.

Methods

Data collection

Over a period of 5 years (1996–2000) 102 patients (57 women, 45 men) with a mean age of 69 years (range 21–93) underwent emergency surgery for perforated ulcer. Excluded patients were perforated ulcers at the anastomotic site following former ulcer surgery and patients with cancer perforation. Data were prospectively recorded in a computerized registry database including gen-

Table 1 Perforated gastroduodenal ulcer: ulcerogenic agents, age, and ASA status by type (percentages)

	Type A (*n*=23, 22%)	Type B (*n*=50, 49%)	Type C (*n*=29, 29%)
Intake of NSAID and steroids*	30	66	59
H. pylori infection*	44	18	17
Age >65 years*	30	52	48
ASA status III and IV*	35	72	62

* $P<0.05$ type A vs. types B and C (χ^2)

der, patient age, American Society of Anesthesiologists (ASA) status, comorbid conditions (cardiovascular, pulmonary, metabolic, hepatic, renal, or concomitant malignant disease), concomitant immunosuppression (patients after renal transplantation, under chemotherapy or radiation), preoperative risk factors of ulcer disease (nonsteroidal anti-inflammatory drugs, steroids, *Helicobacter pylori* infection, conservative treatment prior to surgery), type of ulcer perforation, sepsis on admission, time of surgery (after onset of symptoms), type of surgery (laparoscopic or open; resectional or nonresectional), severity of peritonitis including microbiological findings (bacterial, fungal), postoperative course on intensive care, morbidity (surgical, septic, and cardiopulmonary) and mortality, among others. Follow-up information was obtained by clinical records.

Classification system and surgical concept

To assess morbidity and mortality objectively following emergency surgery related to ulcer location, severity of defect and type of procedure, gastroduodenal ulcer perforation was classified retrospectively into three types:

- Type A: solitary peripyloric ulcer located anteriorly in which laparoscopic closure by suture with omentoplasty was treatment of choice and postoperative endoscopic biopsy was mandatory to identify treatable *H. pylori* infection and to exclude malignancy (*n*=23)
- Type B: perforated ulcer with large defect in which excision and suture was necessary by open surgery (*n*=50)
- Type C: complicated perforated ulcer with destruction of proximal duodenum and penetration into adjacent organs in which resectional surgery was indicated (*n*=29)

In terms of preoperative risk factors of ulcer disease, patients with ulcerogenic medical treatment (nonsteroidal anti-inflammatory drugs, steroids) were significantly more frequently observed in type B and C ulcer than in type A, while the incidence of *H. pylori* was significantly lower. Also, the proportion of patients with advanced age (>65 years) and ASA status III and IV were significantly more common in types B and C than in type A (Table 1).

Diagnosis and surgery

Diagnosis of suspected gastroduodenal ulcer perforation was made clinically (acute abdomen) and confirmed by radiological examination (free intra-abdominal air). Emergency surgery was indicated if patients had acute abdomen with signs of sepsis or hemodynamic instability. Preoperatively all patients had intravenous antibiotics (mezlocilline plus sulbactame or cefotaxime plus metronidazole) which was continued postoperatively if severe peritonitis was found. Medical treatment with proton-pump inhibitors was begun (omeprazole 80 mg per day) preoperatively in every patient and continued for a minimum of 14 days (in combination with oral eradication therapy in *H. pylori* positive patients). Antifungal therapy (fluconazole) was only administered if patients with severe sepsis had positive both microbiological and histological samples, or positive blood cultures.

Surgical procedures included nonresectional procedures in perforated ulcers type A and B (laparoscopic suturing with omentoplasty, open excision) and gastric resection in type C (Billroth I, Billroth II, or atypical resection). Excision of type B ulcer was primarily performed due to technical reasons (large defect, safe closure, histopathology including *H. pylori* status). In our policy, programmed relaparotomy was performed within 24 h if severe four-quadrant peritonitis was found in emergency procedure to reduce toxic potential [5]. All tissue excised or resected was examined histopathologically to exclude malignancy, or to possibly show *H. pylori* infection. Patients who underwent laparoscopic closure by suture had endoscopy with biopsy to identify treatable *H. pylori* infection postoperatively according to [2].

Statistical analysis

Univariate analysis was performed to determine risk factors for mortality after emergency surgery for perforated ulcer by χ^2 test and Student's *t* test using SPSS software (SPSS, Chicago, Ill., USA). Statistically significant variables assessed by univariate analysis were entered into a multivariate logistic regression analysis to determine independent factors predictive of mortality using NCSS software (NCSS, Kaysville, Utah, USA). For logistic regression analysis data were coded as dichotomous variables in terms of time of surgery (<24 h after onset of symptoms or >24 h after onset of symptoms). Statistical significance was accepted at the probability of randomness level of $P<0.05$.

Results

Results of surgery

Simple closure with omentoplasty was carried out laparoscopically in all patients with type A ulcer. In those with type B ulcer open excision with primary closure of the abdomen was performed in 75%, whereas programmed re-laparotomy (relavage) due to four-quadrant peritonitis was carried out in 25%. One-third of patients with type C ulcer had programmed relavage related to peritonitis. Sixty percent of penetrations occurred into the pancreas, followed by penetration into biliary tract or liver. Most common type of gastric resection was Billroth II resection in 75%, followed by Billroth I resection in 15%, and atypical (limited) gastric resection in 10% of patients.

Morbidity and mortality

As demonstrated in Table 2, morbidity rates were lower in type A ulcer perforation than in type B and type C

Table 2 Deaths

Reason for morbidity	Type A	Type B	Type C
Leakage	1	1	1
Intra-abdominal abscess	0	2	0
Pancreatitis	0	0	2
Pulmonary embolism	0	0	2
Pneumonia	0	3	2
Myocardial infarction	1	3	3
Others	0	2	0
Total*	2 (9%)	11 (22%)	10 (34%)

* $P<0.05$ type A vs. types B and C (χ^2)

($P<0.05$), while morbidity rates did not differ significantly between type B and C ulcers. Insufficiency of laparoscopic suture, excision, or resection (Billroth I resection) occurred only once observed per group. Only three patients (two type B, one type C) died due to septic multiorgan failure. Most common causes of death were cardiopulmonary conditions (pneumonia, heart failure) without intra-abdominal sepsis postoperatively. Mortality rates were significantly lower in type A (mortality 4%, one from heart failure following myorcardial infarction) than in type B (mortality 20%, three from pulmonary decompensation following pneumonia, three from heart failure, two from septic multiorgan failure) or C (mortality 17%, two from pulmonary decompensation following pneumonia, two from heart failure, one from intra-abdominal sepsis with multiorgan failure).

Univariate analysis demonstrated that age, ASA status, time of surgery, severity of peritonitis, immunosuppression, and concomitant malignant disease were related to mortality ($P<0.05$). However, multivariate analysis identified age, ASA status and time of surgery as significantly predictive of mortality – with a significant worse prognosis in patients over 65 years of age, with ASA status III or IV, and with a delay of surgery 24 h after onset of symptoms. According to regression analysis, combined probability of mortality is 60.5% in the presence of all four risk factors together.

Discussion

Emergency surgery for perforated ulcer presently carries a mortality risk of up to 30% [2, 4]. Within the past decade several retrospective and prospective studies have identified risk factors predictive of mortality including age, delay to surgery, shock on admission, low albumin concentration, concurrent medical illness, ulcer location, renal failure, liver cirrhosis, and immunosuppression [2, 4, 6, 7, 8, 9, 10, 11, 12, 13]. Concomitant medical comorbidity, particularly cardiovascular, pulmonary, and metabolic (diabetes mellitus) which is present in 40–60% of patients with ulcer perforation has been shown to increase postoperative mortality to 50% or more [7, 8, 11, 14]. Moreover, studies have confirmed that if preoperative shock, perforation for more than 24 h, age over 70 years, and concomitant medical illness are simultaneously present, mortality reaches 100% [15, 16]. Additionally there is considerable postoperative morbidity which affects up to two-thirds of the patients and includes pneumonia, wound infection, and intra-abdominal abscess. As surgery for perforated ulcers is performed frequently in the elderly, the postoperative course is usually complicated by morbidity directly associated with cardiovascular or metabolic illness [2, 4, 14, 16].

Many scoring systems have been introduced to assess prognosis objectively after emergency surgery that attempt to identify patients with a higher risk of morbidity and mortality. In 1987 Boey and colleagues [15] introduced a risk stratification system, the so-called Boey score, to identify patients with a higher risk of mortality after open surgery for perforated ulcers. They prospectively stratified their patients related to three prognostic factors: preoperative shock, perforation for more than 24 h, and associated medical illness. Patients with no, one, two, and three risk factors were documented to show mortality rates of 0%, 10%, 45.5%, and 100%, respectively [15]. Lee and colleagues [17] analyzed 436 patients with perforated peptic ulcers and identified the Acute Physiology and Chronic Health Evaluation II (APACHE II) score, which is commonly used in surgical intensive care, as an independent predictor of mortality and morbidity. They suggested dividing APACHE II score at the median to distinguish between a "low-risk" (<5 points) and a "high-risk" group (>5 points). However, they claimed that different surgical procedures entail similar morbidity and mortality rates, and the cutoff point (score 5) which they used is controversial as previous studies have shown that APACHE II scores of 11 or less are negligible [18, 19].

In the discussion of surgery for perforated ulcer, surgeons know that young, healthy patients who present early with perforation have an excellent prognosis, while older patients with comorbid conditions with neglected perforation have a poor prognosis. Therefore the aim of this study was to assess both surgical concept and prognosis of perforated gastroduodenal ulcer classified into three types according to ulcer location and surgical procedure.

The current results indicate that emergency surgery for type A ulcers can be performed safely by laparoscopy with acceptable morbidity and mortality rates. In type B and C ulcers morbidity and mortality were affected primarily by age, ASA status, and delayed treatment. This has been verified by multivariate analysis and has been demonstrated by other series as well [9, 12, 13, 17].

There is an ongoing debate over whether simple closure (with or without omentoplasty) is safe and sufficient

to treat perforated ulcer, or whether resectional surgery ("definitive surgery") which has been commonly performed in recent decades and is still commonly used in Japan, Asian countries, and Eastern Europe, should be the preferred surgical option [2, 20, 21, 22]. In Japan high rates of gastric resection are reported (up to 80%), while simple closure or fibrin glue is performed in less than 5% of cases [10, 20]. Previously published data of the Copernicus Study Group and Acute Abdominal Pain Study Group have shown that the proportion of resections is significantly higher in Eastern Europe (41.1%) than in Germany (16.1%) [23]. Additionally, since its introduction in 1990 laparoscopic surgery for perforated ulcer has been performed safely in many centers [24, 25, 26, 27], although a prospective randomized study published by Lau and colleagues [28] in 1996 showed no significant benefits of the laparoscopic approach in comparison to open surgery.

Concerning surgical technique, our results demonstrate that type A ulcers can be managed by simple closure with omentoplasty by the laparoscopic technique. No conversion was required, and insufficiency requiring relaparoscopy occurred in only one case. However, postoperative endoscopy with biopsy to identify treatable *H. pylori* infection and to exclude malignancy is mandatory. In type B ulcers, excision with closure is carried out primarily for technical reasons, such as when the defect is too large only to be sutured laparoscopically. As type C ulcer perforation always presents with a substantial destruction of the proximal duodenum, and penetration into adjacent organs, mainly pancreas, is not uncommon, it is our policy to perform a resection (Billroth I or II), whereas Billroth II resection frequently had to be performed in type C ulcers with significant destruction of the duodenum. Reconstruction was performed by Roux-en-Y drainage, alternatively by an omega sling. Our results also indicate that in comparison to type B ulcers the resection does not increase morbidity or mortality significantly. However, the term "definitive" surgery for these types of perforated ulcers is no longer justified, as simple closure in type A, or excision and closure in type B, is also safe, and "definitive" surgery implicates that nonresectional surgery is disadvantageous or associated with high recurrence rates.

Finally, controversy surrounds whether conservative treatment of perforated gastroduodenal ulcer is justified in selected patients [8, 29, 30]. According to the review of Zittel and colleagues [2], conservative treatment is possible in 60% of cases, while 30% of patients need emergency surgery. However, in clinical practice, nonoperative management is controversial, and commonly accepted guidelines do not exist. Conversely, reflecting our results, a majority of patients with type B and type C ulcer perforation were admitted to clinic too late, and diagnosis was neglected in many patients of advanced age with high coincidence of comorbid conditions, so that surgery was performed with considerable delay. This potentially explains the high morbidity and mortality rates after surgery for type B and type C ulcer perforation in the current series, reflecting a prejudicially stratified series of patients. Therefore our policy, in accordance with that of Marshall and colleagues [30], is that particularly these patients need an early decision for surgery.

Conclusion

Prognosis of perforated ulcer disease is highly correlated with age, comorbid conditions (ASA status), and time of surgery. The proposed classification system helps to identify patients at risk of mortality and shows that type A ulcer perforation entails no mortality if laparoscopic repair is performed without delay, whereas mortality is extraordinarily high if type B or type C are simultaneously related to delayed surgical treatment in ASA III or IV patients with advanced age and with concomitant immunosuppression due to malignant disease of other origin. Therefore surgical treatment should not be delayed, and prognosis is affected primarily by comorbid conditions in the elderly.

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