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Perforated peptic ulcer disease: mid-term outcome among Iranian population

Perfore peptik ülser hastalığı: İran halkında orta vadeli sonuçlar

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Background/aims: *The aim of this study was to evaluate mid-term outcome of patients with perforated peptic ulcer disease and to determine the main predictors of mid-term mortality.* ***Methods:*** *Demographic and clinical characteristics of 56 patients with the diagnosis of perforated peptic ulcer who were hospitalized in Taleghani Hospital over a 10–year period (1996-2005) were retrospectively collected, and in-hospital mortality and morbidity were determined. Patients were also followed for one month, one year and five years after the operation.* ***Results:*** *Among these patients, 85.5% were treated with omental patch closure, 7.1% underwent vagotomy pyloroplasty, 5.3% underwent concurrent vagotomy and gastrojejunostomy, and 1.8% underwent antrectomy. In-hospital mortality and morbidity were 5.3% and 48.2%, respectively. Survival rates at one month, one year and five years after the operation were 92.9%, 89.3% and 78.6%, respectively. Advanced age (p=0.001), preoperative shock (p=0.003), history of malignancy before surgery (p=0.001), treatment delay (p=0.028), intensive care unit admission (p=0.032), and size of ulcer >5 cm (p=0.043) were the main predictors of five-year mortality in the followed patients.* ***Conclusions:*** *Mid-term mortality of treated perforated peptic ulcer disease among our population was notable, and the main predictors of mortality included advanced age, history of malignancy, treatment delay, intensive care unit admission, and ulcer size.*

Key words: Peptic ulcer disease, perforation, outcome, mortality, morbidity

Amaç: *Bu çalışmanın amacı, perfore peptik ülserli olgularda orta vadeli sonuçları değerlendirmek ve orta vadeli mortaliteye etki eden başlıca faktörleri bulmaktır.* ***Yöntem:*** *Taleghani Hastanesi'nde 10 yıllık sürede (1996 – 2005) perfore peptik ülser tanısıyla yatırılarak takip edilmiş 56 hastanın demografik ve klinik özellikleri retrospektif olarak değerlendirilerek, hastanede yatarken gerçekleşen mortalite ve morbidite oranları saptanmıştır. Ayrıca, hastaların ameliyattan sonraki 1. ay, 1. yıl ve 5. yılda takipleri yapılmıştır.* ***Bulgular:*** *Bu hastaların tedavisinde, %85,5'ine omental yamayla kapama uygulanmış, %7,1'ine vagotomi – piloroplasti yapılmış, %5,3'üne eş zamanlı vagotomi gastrojejunostomi operasyonu, %1,8'ine de antrektomi yapılmıştır. Hastanede yatış sırasındaki mortalite ve morbidite oranları sırasıyla %5,3 ve %48,2'dir. Ameliyattan 1 ay, 1 yıl ve 5 yıl sonraki sağ kalım oranları sırasıyla %92,9, %89,3 ve %78,6 olmuştur. Takip edilen hastalardaki 5 yıllık mortalitenin en önemli prediktörleri, ileri yaş (p=0,001), preoperatif şok (p=0,003), ameliyattan önce malignite öyküsü (p=0,001), tedavinin gecikmesi (p=0,028), yoğun bakımda yatış (p=0,032) ve ülser boyutunun 5 cm'den büyük olmasıdır.* ***Sonuç:*** *Halkımız arasında tedavi edilmiş perfore peptik ülser hastalığının orta vadeli mortalitesi kayda değer orandadır ve en önemli prediktörleri arasında ileri yaş, malignite öyküsü, gecikmiş tedavi, yoğun bakımda yatış ve ülser boyutu gelmektedir.*

Anahtar kelimeler: Peptik ülser hastalığı, perforasyon, sonuç, mortalite, morbidite

INTRODUCTION

It has been shown that the incidence of peptic ulcer disease has generally declined, and its prevalence has been estimated as 5-10% in the adult population in different countries (1). However, the number of patients affected by bleeding and perforation has not changed significantly (2) such that perforated ulceration affects up to 20% of peptic ulcer disease patients (3). The incidence of complicated ulcer disease, however, especially of duodenal ulcer, significantly decreased in some populations, such as in the Iranian population, in recent years (4). It seems that the main causes of these different incidences may be related to the treatment protocols and also to the different outcomes

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of these procedures. Some surgeons believe that many patients can be successfully managed medically with no operation and that better outcomes can be achieved. Moreover, several studies have indicated significant side effects, including diarrhea, dumping, vomiting, and weight loss due to ulcer operations (5, 6). Some others have suggested surgical management, especially simple closure (7). Therefore, selection of the best treatment protocol with minimized post-treatment complications and the best outcome in the treatment of perforated peptic ulcers is quite challenging. The aim of this study was to evaluate the mid-term outcome of patients suffering from perforated peptic ulcer disease and to determine the main predictors of mid-term mortality.

MATERIALS AND METHODS

In this study, the demographic and clinical characteristics of 56 patients with the final diagnosis of perforated peptic ulcer who were hospitalized in Taleghani Hospital over a 10–year period (1996-2005) were evaluated retrospectively from hospital records, and data were entered into a computerized database. Among these patients, 85.5% were treated with omental patch closure, 7.1% underwent vagotomy pyloroplasty, 5.3% underwent concurrent vagotomy and gastrojejunostomy, and 1.8% underwent antrectomy. The data included in the analysis were demographic characteristics, treatment delay (>24 hours), type of treatment, localization and size of ulcer, postoperative complications, drug history, in-hospital mortality, and length of hospital stay. In-hospital mortality was defined as death related to post-treatment complications occurring in the hospital before discharge, irrespective of whether the patients died earlier or later than 30 days after the operation (8).

Follow-Up

Mid-term outcomes were also determined from clinic records when available or from written correspondence with the patient's physician and direct patient contact via telephone interviews. Follow-up data included re-admission and re-hospitalization, mid-term survival, and the cause of mortality. We followed the patients for one month, one year and five years after the operation.

The study protocol was approved by research ethics committee of Shahid Beheshti University of Medical Sciences.

Statistical Analysis

Results were reported as mean ± standard deviation (SD) for quantitative variables and percentages for categorical variables. The groups were compared using the Student's t-test for continuous variables and the chi-square test or Fisher's exact test if required for categorical variables. Predictors exhibiting a statistically significant relationship with mid-term mortality in the univariate analysis (p value ≤0.15) were taken for a multivariate logistic regression analysis to investigate their independence. Odds ratios (OR) and 95% confidence intervals (CI) for OR were calculated. P values ≤0.05 were considered statistically significant. Further, p values ≤0.005 were considered significant in the univariate analysis. All statistical analyses were performed using SPSS version 13 (SPSS Inc., Chicago, IL, USA) and SAS version 9.1 for Windows (SAS Institute Inc., Cary, NC, USA).

RESULTS

Demographic characteristics and preoperative clinical data are illustrated in Table 1. The mean age of patients was 50.07±13.04 years (range: 23 to 75 years) and most were male. In more than two-thirds of the patients, defects were confirmed as duodenal ulcer, and the size of the ulcers was >5 cm in 78.6%. History of malignancies was positive in 7.1% of the studied patients and included colon cancer, urinary bladder cancer, acute lymphocytic leukemia, and chronic lymphocytic leukemia. The history of renal failure (serum creatinine concentration ≥2 mg/dl) was observed in 14.3% of patients.

Table 1. Demographic characteristics and clinical data (n=56)

Variables	Value
Male gender	87.5%
Age (years) (mean ± SD)	50.07±13.04
Corticosteroid administration	26.8%
Immunosuppressive treatment	17.9%
Preoperative shock	12.5%
History of malignancy	7.1%
Treatment delay (>24 hours)	17.9%
ICU admission	12.5%
Ulcer location:	
Gastric	30.4%
Duodenum	69.6%
Size of ulcer (>5 cm)	78.6%
Serum albumin concentration (mean ± SD)	2.96±0.27
Serum creatinine concentration (mg/dl) (mean ± SD)	1.27±0.49

Data are presented as mean ± SD or percentages

Table 2. Main etiologies of mid-term mortality (n=56)

Etiology	N (percent)
Cardiac events	30.7%
Malignancies	30.7%
Wound recurrent	7.6%
Accidents	7.6%
Others	23.4%

Among the patients, 85.5% were treated with omental patch closure, 7.1% underwent vagotomy pyloroplasty, 5.3% underwent concurrent vagotomy and gastrojejunostomy, and 1.8% underwent antrectomy.

Operative Mortality and Morbidity: In-hospital mortality and postoperative morbidity were 5.3% and 48.2%, respectively. There were 3 in-hospital deaths; 2 due to cardiac arrhythmia and 1 due to multiorgan failure and sepsis. The mean length of in-hospital stay was 12.05±5.31 days and 12.5% of patients were admitted to the Intensive Care Unit (ICU). Five patients required re-intubation during the ICU stay. Other common morbidities included wound infection (25.0%), pneumonia (16.1%) and pleural effusion (1.8%).

Survival rates at one month, one year and five years after the operation were 92.9%, 89.3% and 78.6%, respectively.

Causes of mid-term mortality are shown in Table 2. The most common causes of mortality were malignancies and cardiac events.

Multivariate logistic regression analysis showed that the factors of advanced age (p=0.001), preoperative shock (p=0.003), history of malignancy before surgery (p=0.001), treatment delay (p=0.028), ICU admission (p=0.032), and size of ulcer >5 cm (p=0.043) were the main predictors of five-year mortality in the followed patients (Table 3).

DISCUSSION

When selecting a patient for a definitive ulcer treatment, one must decide which procedure offers an acceptably low rate of recurrence while minimizing attendant side effects. In the present study, most of the patients were treated with omental patch closure, and only 14.2% underwent other invasive procedures. The approach to the best treatment has differed in the previous studies. In a study by Barczy*f*ski et al. (9), the main procedure was determined to be truncal vagotomy with pyloroplasty, performed in 95.6%, and simple ulcer suture in 4.4%, whereas in Bin-Taleb's study (10), simple perforation closure was used in 91.7% of the patients. Chernookov et al. (11) showed that palliative operations were performed in 22.0% of the patients. It seems that the selection of the best protocol for treatment should be based on the patient's condition and that his underlying factors may influence the outcome of the operation. Additionally, the surgeon's experience also plays a major role toward this aim. It is clear that many surgeons advocate performing definitive ulcer-curing surgery along with simple closure to prevent recurrence. However, due to the success of medical management and the subsequent decreasing role of elective surgical management in peptic ulcer disease, fewer surgeons are acquiring sufficient experience and expertise in performing definitive procedures such as highly selective vagotomy (5). We believe that combined medical therapy for *Helicobacter pylori* and simple closure of the perforation would be more desirable than undergoing a definitive operation, given at least a similar rate of ulcer recurrence.

In our study, early morbidity rate was 48.2%. Further, early postoperative mortality was estimated as 7.1% and was significantly increased to 21.4% at five years after the operation. Reported mortality and morbidity rates in the previous studies were also different. Avakimian et al. (12) noted an early morbidity rate of 51.6% in a follow-up of up to 12 years. Morbidity was reported as 24% in Kocer et al.'s study (13). In Bin-Taleb's (10) study, postoperative complication rate was 41% and overall postoperative mortality was 3.9%. According to the similar previous studies, early mortality rate varied widely, ranging between 3.9% and 30% (10,13-22). The mortality rate following surgery in elderly patients with perforated peptic ulcer is higher than in youn-

Table 3. Multivariate regression analysis for prediction of mid-term mortality (n=56)

Variable	Odds Ratio	95%	Confidence Intervals	P value
Age >50 years	17.471	2.065	147.774	0.001
Preoperative shock	15.000	2.419	93.007	0.003
History of malignancy	6.500	3.436	12.295	0.001
Treatment delay	5.571	1.271	24.421	0.028
ICU admission	6.833	1.276	36.581	0.032
Ulcer size	1.375	1.147	1.648	0.043

ger patients (37.7% vs. 1.4% in Kocer et al.'s study) (13), and it has been reported between 12% and 47% (13, 17). Age, delayed surgery, presence of shock, American Society of Anesthesiologists (ASA) risk, and definitive surgery have been reported as independent predictors for fatal outcomes in patients with emergency surgery for perforated peptic ulcer in various studies (13, 14, 19). These factors were also confirmed in our study. The duration of symptoms is the most important factor in the elderly that influences the prognosis after surgery and is responsible for the high mortality rate (13, 20).

In our study, age had a major role for prediction of mortality in these patients. In a study by Barczyƒski et al. (9), perioperative mortality in patients over 60 years old was 35.4%, and in patients over 70 years old this rate was 50%. Furthermore, Chernookov (11) indicated that according to the type of operation, the rate of postoperative complications ranged between 3.6-18.2%. As has been shown, mortality risk increased 16.5 times with definitive operation (13).

According to the results of our study, it seems that history of malignancies and admission to ICU also played a major role in the prediction of mid-term mortality in these patients, which should be investigated further in future studies.

In a recent study, in an effort to improve the outcome of patients, it was suggested that the concept of sepsis as a risk factor should be included in the existing knowledge and treatment of peptic ulcer perforation (23).

It can be concluded that perforated peptic ulcer disease carries considerable mid-term mortality that can be affected by age, treatment delay, size of ulcer, and admission to ICU. Furthermore, it is accompanied by a high frequency of postoperative complications that should be controlled by improving surgical skills, wound care, and administrative regulations.

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REFERENCES

1. Bernersen B, Johnsen R, Straume B, et al. Towards a true prevalence of peptic ulcer: the Sorreisa gastrointestinal disorder study. Gut 1990; 31: 989-92.
2. Jordan PH, Morrow C. Perforated peptic ulcer. Surg Clin North Am 1988; 68: 315–29.
3. Ashley SW, Evoy D, Daly JM. Stomach. In: Schwartz SI, Shires GT, Spencer FC, et al., eds. Principles of surgery. 7th ed, New York: McGraw-Hill, 1999; 1191–7.
4. Hosseini SV, Sabet B, Amini M. Surgical management of combined perforated and bleeding duodenal ulcer. IRCMJ 2008; 10: 30-3.
5. Barksdale AR, Schwartz RW. Current management of perforated peptic ulcer. Curr Surg 2000; 57: 594-9.
6. Svanes C, Salvesen H, Stangeland L, et al. Perforated peptic ulcer over 56 years. Time trends in patients and disease characteristics. Gut 1993; 34: 1666-71.
7. Jordan PH, Thornby J. Perforated pyloroduodenal ulcers. Long-term results with omental patch closure and parietal cell vagotomy. Ann Surg 1995; 221: 479-86.
8. Svanes C, Salvesen H, Espehaug B, et al. A multifactorial analysis of factors related to lethality after treatment of perforated gastroduodenal ulcer. 1935-1985. Ann Surg 1989; 209: 418-23.
9. Barczyƒski M, Reś F, Cichoń S, Barczyƒski M. Perioperative mortality for perforated duodenal and gastric ulcer--analysis of 226 patients. Przegl Lek 1999; 56: 192-7.
10. Bin-Taleb AK, Razzaq RA, Al-Kathiri ZO. Management of perforated peptic ulcer in patients at a teaching hospital. Saudi Med J 2008; 29: 245-50.
11. Chernookov AI, Naumov BA, Kotaev AIu, et al. Surgical treatment of patients with perforated peptic ulcers. Khirurgiia (Mosk) 2007; 6: 34-9.
12. Avakimian VA, Ashkhamaf MKh. Late results of surgical treatment of perforated pyloroduodenal ulcers. Klin Khir 1990; 8: 36-8.
13. Kocer B, Surmeli S, Solak C, et al. Factors affecting mortality and morbidity in patients with peptic ulcer perforation J Gastroenterol Hepatol 2007; 22: 565-70.
14. Testini M, Portincasa P, Piccini G, et al. Significant factors associated with fatal outcome in emergency open surgery for perforated peptic ulcer. World J Gastroenterol 2003; 9: 2338-40.
15. Paimela H, Oksala NKJ, Kivilaakso E. Surgery for peptic ulcer today. Dig Surg 2004; 21: 185-91.
16. Lee FY, Leung KL, Lai BS, et al. Predicting mortality and morbidity of patients operated on for perforated peptic ulcers. Arch Surg 2001; 139: 90-4.
17. Sillakivi T, Lang A, Tein A, et al. Evaluation of risk factors for mortality in surgically treated perforated peptic ulcer. Hepatogastroenterology 2000; 47: 1765-8.
18. Michelet I, Agresta F. Perforated peptic ulcer: laparoscopic approach. Eur J Surg 2000; 166: 405-8.
19. Nogueria C, Silva AS, Santos JN, et al. Perforated peptic ulcer. Main factors of morbidity and mortality. World J Surg 2003; 27: 782-7.
20. Uccheddu A, Floris G, Altana ML, et al. Surgery for perforated peptic ulcer in the elderly. Evaluation of factors influencing prognosis. Hepatogastroenterology 2003; 50: 1956-8.
21. Chiarugi M, Buccianti P, Goletti O, et al. Prognostic risk factors in patients operated on for perforated peptic ulcer. A retrospective analysis of critical factors of mortality and morbidity in a series of 40 patients who underwent simple closure surgery. Ann Ital Chir 1996; 67: 609-13.
22. Forsmo HM, Glomsaker T, Vandvik PO. Perforated peptic ulcer--a 12-year material. Tidsskr Nor Laegeforen 2005; 125: 1822-4.
23. Møller MH, Adamsen S, Wøjdemann M, et al. Perforated peptic ulcer: How to improve outcome? Scand J Gastroenterol 2009; 14: 15-22.