

Results of conservative treatment for perforated gastroduodenal ulcer in patients not eligible for surgical repair

Pascal Bucher, Wassila Oulbaci, Philippe Morel, Frederic Ris, Olivier Huber

Clinic of Visceral Surgery, Department of Surgery, Geneva University Hospital

Summary

Background: Conservative treatment of perforated gastroduodenal ulcer has been shown to be associated with good results in patients whose general condition is good. However, its use in patients not eligible for surgical repair has not been supported. The aim of this study is to evaluate the results of conservative treatment in these patients in the era of proton pump inhibitor.

Material and methods: In the period 1978–2004, 533 patients were admitted for perforated gastroduodenal ulcer. 503 patients underwent surgery, while 30 (median age 79 [42–98] years) were allocated to conservative treatment due to poor general condition. Conservative treatment consisted of nasogastric aspiration, antibiotics and antisecretory therapy (H₂-blockers from 1978–1995, 11 patients, and proton pump inhibitors (PPI) from 1996, 19 patients). Endpoints were: hospital morbidity and mortality and hospital stay.

Results: Overall morbidity and mortality were 33% and 30%. Median hospital stay was 11 days (range 0–32). General complications developed in 73% versus 16% of patients ($p = 0.023$) and mortality was 64% versus 11% ($p = 0.008$) for the H₂-blocker and PPI groups respectively. On multivariate analysis mortality correlated with presence of shock at admission and type of antisecretory therapy.

Conclusion: In the era of PPI conservative treatment for perforated ulcer is possible with acceptable morbidity and mortality in patients not eligible for surgical repair. However, presence of shock at admission was associated with high mortality and, even in these patients, militates in favour of a surgical approach.

Key words: *gastroduodenal ulcer; perforation; surgery; conservative treatment; proton pump inhibitor (PPI); Boey's criteria*

Introduction

Despite dramatic improvements in peptic ulcer management in the last two decades (new potent anti-secretory drugs as well as *Helicobacter pylori* eradication) [1], the frequency of emergency surgery for perforated gastroduodenal ulcer has remained stable or even increased [2]. This may be due to an increase in prescription of aspirin and/or non-steroidal anti-inflammatory drugs, especially in older subjects [3, 4].

Prompt surgical repair is the standard of care for perforated peptic gastroduodenal ulcer [5–7]. While the results of surgery are excellent in subjects in good general condition [5, 8], these procedures are still associated with high mortality in elderly patients, with reported rates between 8% and 41% [9–11].

While the first conservative treatment series for perforated peptic ulcer was described by Taylor in 1946, it has not yet gained widespread acceptance [12]. This treatment was first proposed in

1935 by Wangensteen [13], who reported the case of a patient unfit for surgery who was treated successfully by conservative means. The merit of Taylor was to codify this method, limiting its indication to patients in good general condition [14–16]. These good results were confirmed by some other series where its use was similarly restricted to relatively healthy patients [17–19]. On the other hand, conservative treatment in patients not eligible for surgical repair because of severe comorbidities has not yet been validated. Avoiding surgery in this population could be particularly valuable as they are at high risk of complications after surgical repair [20].

The aim of this retrospective study was to evaluate the results of conservative treatment of perforated gastroduodenal ulcer in patients not eligible for surgical repair in the era of proton pump inhibitor.

Materials and methods

We retrospectively identified 30 patients treated conservatively for perforated gastroduodenal ulcer in the period 1978–2004. During the study period, 503 other patients were admitted and underwent emergency surgery for perforated gastroduodenal ulcer. The results of surgical treatment will serve as standard for the results of the conservative approach. Diagnosis was based on the presence of free peritoneal air and/or clinical signs of digestive perforation, after ruling out bowel perforation by computed tomography scan. Indications for conservative treatment were severe comorbidities contraindicating surgery. Conservative treatment consisted of fasting, nasogastric tube aspiration, intravenous broad-spectrum antibiotics and antisecretory drugs: H₂-blockers from 1978–1995 (ranitidine 150 mg bid), 11 patients, and proton pump inhibitors (PPI) from 1996 (omeprazole, 40 mg/d), 19 patients. Eleven patients included in this series (those from the pre-PPI era – 1978–95) were previously reported on by our team in 1997 [21] and will be treated

as a historical control group. *Helicobacter pylori* eradication was systematically administered from 1996. Patients' data were collected by reviewing in-hospital files and radiological reports. Boey's classification [22, 23] was used to stratify patients' medical condition and risk at admission. Complications of treatment were classified according to Clavien et al. [24].

Statistical analysis was performed on a personal computer using GraphPad InStat (GraphPad Software, San Diego, CA, USA) and GB-STAT (Dynamic Microsystems Inc, Silver Spring, MD, USA). Variables were analysed using two-sided chi-squared or Mann Whitney tests, when appropriate. Univariate and multivariate analyses were performed using logistic regression models. For multivariate analysis the only independent factors found to have a significant correlation ($p < 0.05$) with a dependent variable on univariate analysis were included. For all tests, a p value of < 0.05 was considered statistically significant.

Results

Study population

During the study period (1978–2004) 30 patients were allocated to conservative treatment due to ineligibility for surgery. The median age of patients on conservative treatment was 79 (range 42–98) years. Among the comorbidities encountered in these patients 53% had severe heart failure, 43% were diabetic with severe complications, 33% had severe pulmonary disease, 23% had

chronic renal insufficiency, 20% had liver cirrhosis, 47% had severe hypertension, and 23% had an endocrine disorder (median more than 2 comorbidities/patient). All patients presented at least one criterion of gravity according to Boey's classification.

Patient outcomes

Overall morbidity was 33% and hospital mortality was 30%. This should be compared with 13% mortality observed in the 503 surgical patients during the same period. Among the 30 patients allocated to conservative treatment, 11 received H₂-blockers and 19 PPI (Table 1). Morbidity was 73% versus 16% ($p = 0.023$) for H₂-blocker and PPI groups respectively. Of the patients presenting general complications in the H₂-blocker group, all were classified grade IV according to Clavien et al. [24], while in the PPI group one was grade II and two were grade IV. Hospital mortality rates were 64% vs 11% ($p = 0.008$) for the H₂-blocker and PPI groups.

Table 1
Patients' clinical features according to type of antisecretory therapy.

	H ₂ -blockers PPIs		P
	[N = 11]	[N = 19]	
Median age (range)	85 (67–93)	71 (42–98)	0.054
Median delay (range)	11 (4–24)	24 (6–96)	0.031
Comorbidity	11	19	0.80
Shock index ≥ 1 at admission	5	2	0.068
ASA			0.51
General complications	7	3	0.023
Mortality	7	2	0.008
Median hospital stay (range)	8.8 (0–32)	14 (2–30)	0.17

Table 2
Relation between mortality and clinical variables among all patients.

	Mortality		p	
	No (n = 21)	Yes (n = 9)	Univariate analysis	multivariate analysis
Median age (range)	74 (42–98)	86 (67–92)	0.005	0.17
Median delay (range)	36 (4–96)	24 (12–48)	0.58	
Comorbidity	21	9	0.99	
Shock index ≥ 1 at admission ^a	0	7	<0.001	<0.001
ASA			0.078	
Anti-secretory therapy			0.001	0.019
H ₂ -blockers	4	7		
PPIs	17	2		

^a Shock index calculated as pulse/systolic BP.

Table 3

Relation between mortality and clinical variables among patients treated with PPI.

	Mortality		p	
	No (n = 17)	Yes (n = 2)	Univariate analysis	multivariate analysis
Median age (range)	66 (32-98)	89 (88-90)	0.22	
Median delay (range)	36 (6-96)	30 (12-48)	0.82	
Comorbidity	17	2	0.54	
Cirrhosis	4	0	0.47	
Shock index ≥ 1 at admission ^a	0	2	<0.0001	<0.0001
ASA			0.39	

^a Shock index calculated as pulse/systolic BP

Prognostic factors

Univariate analysis results are reported in Tables 2 and 3. On multivariate analysis, risk factors for patient death among all patients were presence of shock at admission (odds ratio 0.007; 95% CI: 0.0003 to 0.181), type of antisecretory therapy (odds ratio 0.07; 95% CI: 0.0099 to 0.455) (Table

2). Among the 19 patients treated with PPI the only risk factor at admission for patient death was the presence of shock, odds ratio 0.006 (95% CI 9.109E-05 to 0.359) (Table 3).

A strong correlation between Boey's classification score and patient survival was found in the PPI groups ($p = 0.008$).

Discussion

In this study we analysed the safety of conservative treatment (known as the Taylor method) of perforated gastroduodenal peptic ulcer in patients not eligible for emergency surgical repair. Our results show that in the era of PPI this approach can be applied to these patients with acceptable morbidity and mortality.

Study of the natural history of gastroduodenal ulcer perforation during the first half of the 20th century [16, 20], has shown that, after perforation occurs, it is promptly sealed by adjacent organs. A fibrin clot appears quickly on and around the perforation. This is the start of a definitive closure which associates adhesion between perforated and adjacent organs and healing of the digestive tract wall. According to Donovan, this phenomenon of self-healing is efficient in at least 50% of patients [25]. Indeed, it is a common experience for surgeons who operate for perforated ulcer to observe that they first have to mobilize the perforation from adjacent organs before being able to suture it. Moreover, in the event of gastroduodenal perforation the peritoneal cavity usually remains sterile for 12 hours, the bacterial load being low in the upper gastrointestinal tract. However, some patients experience peritonitis as well as septic complications. This can be due to continuous fluid extravasation, stronger bacterial load of the proximal digestive tract and/or poor healing ability impairing spontaneous sealing of the perforation. These observations were the basis for the development of conservative treatment [16], which associates fasting, nasogastric tube aspiration, systemic antibiotics and antisecretory therapy.

Conservative treatment has not gained widespread acceptance as an alternative approach to surgery for perforated gastroduodenal ulcer. It was developed at a time when surgical closure was as-

sociated with high mortality [16, 26]. As surgical and anaesthetic patient care have improved, the morbidity and mortality of emergency surgical ulcer closure have markedly decreased, so that mortality figures are currently in the range of 3-9% [5-7]. During the same period, the results of the sparse series of conservative treatment for "fit" patients have remained stable: while mortality associated with the Taylor method was 5.2% in Taylor's initial series in 1957, rates between 0% and 8% have been reported in more recent publications [17-19, 27-31]. On the other hand, the failure rate of conservative treatment is not inconsiderable (13-46%) [17-19, 28, 29]. Failure of conservative treatment is generally defined as development of septic shock, multiple organ failure or intra-abdominal abscess [17-19, 28, 29]. Conservative treatment failure exposes patients to the risk of delayed surgical closure with mortality rates between 3 and 50% [17, 32], depending on the criteria used to define conservative treatment failure and the timing of secondary surgery [26]. Nevertheless, none of these studies on conservative treatment was performed exclusively in patients treated with PPI and/or benefiting from *Helicobacter pylori* (HP) eradication. As better control of gastric acidity is achieved by PPI than by H₂-blockers [33], and as HP infection has been shown to play a role in some cases of gastroduodenal ulcer perforation [4, 34], it may be anticipated that these therapeutic improvements could further better the success rate of conservative treatment which our study seems to confirm.

While conservative treatment was first proposed to patients not eligible for surgery [13], only a few series have investigated this approach in these patients [13, 20, 21]. In fact these studies have reported high mortality (up to 63%) compared to the

results achieved by surgical repair in elderly or medically frail patients [9–11]. The systematic introduction of PPI use and HP eradication seems to have favourably influenced the results of conservative therapy in this series, which showed mortality of 11% only for the PPI group. However, we could not rule out that improvement in resuscitative care may have at least partly influenced these results.

Definition of prognostic factors for conservative treatment has been a concern for all investigators who have published their results [26]. The present series appears to show that the presence of shock at admission is a major criterion for conservative treatment failure, which corroborates previous reports [17, 28] and Taylor's guideline [16]. This implies that, even in a moribund patient, the presence of haemodynamic instability militates in favour of prompt surgery. The presence of shock being one of the Boey criteria, we attempted to apply, for the first time, the Boey classification in the setting of conservative treatment. We found a strong correlation between Boey's criteria and mortality. Boey's classification could be used in future reports on conservative treatment to facilitate comparison of results with the surgical approach,

for which it is a well established prognostic classification. Some authors have set an age limit, of 70 [18] or even 59 years [17], for success of the conservative approach. However, we found no correlation between patient age and treatment failure, a negative finding possibly related to the high proportion (70%) of patients aged over 70 in this series.

In conclusion, conservative treatment of perforated ulcer is, in the PPI era, a valid therapeutic option in patients not eligible for surgical repair due to poor medical condition. However, the presence of shock at admission is still associated with extremely high mortality and should encourage a surgical approach even in these frail patients.

Correspondence:

Pascal Bucher

Department of Surgery

Geneva University Hospital

24, Rue Micheli-du-Crest

CH-1211 Geneva 14

Switzerland

E-Mail: Pascal.Bucher@hcuge.ch

References

- Paimela H, Paimela L, Myllykangas-luosjarvi R, et al. Current features of peptic ulcer disease in Finland: incidence of surgery, hospital admissions and mortality for the disease during the past twenty-five years. *Scand J Gastroenterol.* 2002;37:399–403.
- Paimela H, Oksala N, Kivilaakso E. Surgery for peptic ulcer today. A study on the incidence, methods and mortality in surgery for peptic ulcer in Finland between 1987 and 1999. *Dig Surg.* 2004;21:185–91.
- Higham J, Kang J, Majeed A. Recent trends in admissions and mortality due to peptic ulcer in England: increasing frequency of haemorrhage among older subjects. *Gut.* 2002;50:460–4.
- Gisbert J, Legido J, Garcia-Sanz I, et al. Helicobacter pylori and perforated peptic ulcer: prevalence of the infection and role of non-steroidal anti-inflammatory drugs. *Dig Liver Dis.* 2004;36:116–20.
- Lau H. Laparoscopic repair of perforated peptic ulcer: a meta-analysis. *Surg Endosc.* 2004;18:1013–21.
- Siu W, Chau C, Law B, et al. Routine use of laparoscopic repair for perforated peptic ulcer. *Br J Surg.* 2004;91:481–4.
- Siu W, Leong H, Law B, et al. Laparoscopic repair for perforated peptic ulcer: a randomized controlled trial. *Ann Surg.* 2002;235:313–9.
- Tsumura H, Ichikawa T, Hiyama E, et al. Laparoscopic and open approach in perforated peptic ulcer. *Hepatogastroenterology.* 2004;51:1536–9.
- Rabinovici R, Manny J. Perforated duodenal ulcer in the elderly. *Eur J Surg.* 1991;157:121–5.
- Uccheddu A, Floris G, Altana M, et al. Surgery for perforated peptic ulcer in the elderly. Evaluation of factors influencing prognosis. *Hepatogastroenterology.* 2003;50:1956–8.
- Tsugawa K, Koyanagi N, Hashizume M, et al. The therapeutic strategies in performing emergency surgery for gastroduodenal ulcer perforation in 130 patients over 70 years of age. *Hepatogastroenterology.* 2001;48:156–62.
- Taylor H. Perforated peptic ulcer treated without operation. *Lancet.* 1946;2:441–4.
- Wangensteen O. Non-operative treatment of localized perforations of the duodenum. *Minn Med.* 1935;18:477.
- Chamberlain D, Taylor H, Bentley J, et al. Discussion on the operative and conservative treatment of perforated peptic ulceration. *Proc R Soc Med.* 1951;44:273–82.
- Taylor H. Perforated acute and chronic peptic ulcer; conservative treatment. *Lancet.* 1956;270:397–9.
- Taylor H. The non-surgical treatment of perforated peptic ulcer. *Gastroenterology.* 1957;33:353–68.
- Songne B, Jean F, Foulatier O, et al. Traitement non opératoire des perforations d'ulcère gastroduodénal. Résultats d'une étude prospective. *Ann Chir.* 2004;129:578–82.
- Crofts T, Park K, Steele R, et al. A randomized trial of nonoperative treatment for perforated peptic ulcer. *N Engl J Med.* 1989;320:970–3.
- Giacchi R, Fattori A, De Poda D, et al. A conservative Taylor's method in the treatment of peptic perforation. *G Chir.* 1990;11:640–2.
- Staed J. Conservative treatment of perforated peptic ulcer. *Lancet.* 1951;1:12–7.
- Alizadeh N, Buhler L, Huber O, et al. Traitement conservateur des perforations peptiques gastroduodénales: indications et résultats. *Schweiz Med Wochenschr.* 1997;127(Suppl 89):17S–19S.
- Boey J, Choi S, Ong G. A prospective study of operative risk factors in perforated duodenal ulcers. *Ann Surg.* 1982;195:265–9.
- Boey J, Choi S, Poon A, et al. Risk stratification in perforated duodenal ulcers. A prospective validation of predictive factors. *Ann Surg.* 1987;205:22–6.
- Dindo D, Demartines N, Clavien P. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg.* 2004;240:205–13.
- Donovan A, Berne T, Donovan J. Perforated duodenal ulcer: an alternative therapeutic plan. *Arch Surg.* 1998;133:1166–71.
- Menegaux F. Taylor method: antiquity or reality. *Ann Chir.* 2004;129:561–2.
- Steeley S, Campbell D. Nonoperative treatment of perforated duodenal ulcer: a further report. *Surg Gynecol Obstet.* 1956;102:435–46.
- Leconte D, Hiebel G. La méthode de Taylor dans le traitement des ulcères gastro-duodénaux perforés: est-elle vraiment désuète? *Ann Gastroenterol Hepatol.* 1986;22:261–6.
- Bugnon P, Rivoalan F, Gautier-Benoit C. Present status of the Taylor method in perforated ulcer of the duodenal bulb. *J Chir.* 1986;123:463–6.
- Keane T, Dillon B, Afdhal N, et al. Conservative management of perforated duodenal ulcer. *Br J Surg.* 1988;75:583–4.
- Berne T, Donovan A. Nonoperative treatment of perforated duodenal ulcer. *Arch Surg.* 1989;124:830–2.
- Marshall C, Ramaswamy P, Bergin F, et al. Evaluation of a protocol for the non-operative management of perforated peptic ulcer. *Br J Surg.* 1999;86:131–4.
- Huang J, Hunt R. Pharmacological and pharmacodynamic essentials of H2 receptor antagonists and proton pump inhibitor for the practising physician. *Best Pract Res Clin Gastroenterol.* 2001;15:355–70.
- Metzger J, Styger S, Sieber C, et al. Prevalence of Helicobacter pylori infection in peptic ulcer perforations. *Swiss Med Wkly.* 2001;131:99–103.

Official journal of the Swiss Society of Infectious diseases, the Swiss Society of Internal Medicine and the Swiss Respiratory Society

The many reasons why you should choose SMW to publish your research

What Swiss Medical Weekly has to offer:

- SMW's impact factor has been steadily rising. The 2005 impact factor is 1.226.
- Open access to the publication via the Internet, therefore wide audience and impact
- Rapid listing in Medline
- LinkOut-button from PubMed with link to the full text website <http://www.smw.ch> (direct link from each SMW record in PubMed)
- No-nonsense submission – you submit a single copy of your manuscript by e-mail attachment
- Peer review based on a broad spectrum of international academic referees
- Assistance of our professional statistician for every article with statistical analyses
- Fast peer review, by e-mail exchange with the referees
- Prompt decisions based on weekly conferences of the Editorial Board
- Prompt notification on the status of your manuscript by e-mail
- Professional English copy editing
- No page charges and attractive colour offprints at no extra cost

Editorial Board

Prof. Jean-Michel Dayer, Geneva
Prof. Peter Gehr, Berne
Prof. André P. Perruchoud, Basel
Prof. Andreas Schaffner, Zurich
(Editor in chief)
Prof. Werner Straub, Berne
Prof. Ludwig von Segesser, Lausanne

International Advisory Committee

Prof. K. E. Juhani Airaksinen, Turku, Finland
Prof. Anthony Bayes de Luna, Barcelona, Spain
Prof. Hubert E. Blum, Freiburg, Germany
Prof. Walter E. Haefeli, Heidelberg, Germany
Prof. Nino Kuenzli, Los Angeles, USA
Prof. René Lutter, Amsterdam, The Netherlands
Prof. Claude Martin, Marseille, France
Prof. Josef Patsch, Innsbruck, Austria
Prof. Luigi Tavazzi, Pavia, Italy

We evaluate manuscripts of broad clinical interest from all specialities, including experimental medicine and clinical investigation.

We look forward to receiving your paper!

Guidelines for authors:

http://www.smw.ch/set_authors.html



All manuscripts should be sent in electronic form, to:

EMH Swiss Medical Publishers Ltd.
SMW Editorial Secretariat
Farnsburgerstrasse 8
CH-4132 MuttENZ

Manuscripts: submission@smw.ch
Letters to the editor: letters@smw.ch
Editorial Board: red@smw.ch
Internet: <http://www.smw.ch>
