

## High mortality rate of oesophageal perforation is associated with delayed hospital admission : a prospective observational case series study

S. Petousis<sup>2</sup>, C. Margioulas-Siarkou<sup>2</sup>, B. Lorenzi<sup>1</sup>, A. Charalabopoulos<sup>1</sup>, E. K. Sdralis<sup>1,2</sup>

(1) Regional Oesophagogastric Centre, Department of Upper Gastrointestinal Surgery, Broomfield Hospital, Mid Essex Hospital Services NHS Trust, Chelmsford, Essex, UK ; (2) Unit of Bariatric Surgery and Metabolic Disorders, Interbalkan Medical Center, Thessaloniki, Greece.

### Abstract

**Background :** To assess mortality rate of oesophageal perforation cases and study their etiology, diagnosis and management in a single specialized UK centre.

**Patients and methods :** A prospective observational study was performed between January 2012 and January 2015. All consecutive patients admitted with acute iatrogenic or spontaneous esophageal perforation were included. Anastomotic leak patients were excluded. Patients were managed conservatively, endoscopically, surgically or with a combination of the above. Primary outcome was mortality rate and its association with time to hospital admission. Secondary outcomes were nature of perforation, anatomic location, type of management as well as length of hospital stay and surgical complication rate.

**Results :** There were 13 cases included. Mean patients' age was 58.3 years. Overall 90-day mortality rate was 38.4% (n=5), while 30-day mortality rate 30.8% (n=4). Admission within 24 hours of perforation was recorded in 69.2% of patients (n=9). The main anatomic location of perforation was the lower third of the esophagus in 53.8% (n=7). Operative management was adopted in 53.8% of cases (n=7). Mean hospital stay was 58.3 days. Mean follow-up was 3.1 years, while no patient developed any complication from the perforation or surgery.

**Conclusions :** Mortality following esophageal perforation is at approximately 40%, while there is a significant impact of time of presentation on prognosis. (*Acta gastroenterol. belg.*, 2020, 83, 11-14).

**Key words :** esophageal, esophageal perforation, Boerhaave's syndrome, mortality.

### Introduction

Oesophageal perforation is a potentially life-threatening condition, with diverse aetiology, for which no consensus exists regarding diagnosis and management. Review of published studies indicates great controversies regarding commonly defined and recorded parameters such as mortality rates (1-3). Specifically, mortality rate is reported to range between 4-80% according to Bayram et al (4), while the systematic approach of evidence yields absence of randomized controlled trials (RCT) or prospective cohorts, therefore implying the need for research.

This great range of mortality rate may represent differences in the level of expertise. As oesophageal perforation is associated with high mortality, it is reasonable to expect higher mortality rates in centres receiving complicated cases. Furthermore, it is of great interest to investigate the association between mortality and admission time as delay over 24 hours has been correlated with significant increase in mortality rate

(4,5). Furthermore, an issue of great importance to take into consideration when analyzing mortality of esophageal perforations is their aetiology. Spontaneous and iatrogenic perforation, which represent the two main causes are totally different clinical entities as their diagnosis, management and therefore prognosis differs significantly.

Prospectively collected records of oesophageal perforation mortality rate in high-level tertiary centers and correlation with admission time remain of paramount importance in an effort to understand the pathophysiology of the condition and achieve a better outcome for these patients.

Main objective of the present case series was to assess prospectively the mortality rate of oesophageal perforations treated in our tertiary oesophagogastric centre in regards with admission time. Furthermore, we aimed to record all relative parameters regarding aetiology, diagnosis and management of the condition, together with short-term outcomes over a 3-year period.

### Materials and Methods

#### Type of study

A prospective observational study was performed in the Department of Upper Gastrointestinal Surgery, at Broomfield Hospital. Our Department is a regional oesophagogastric tertiary center accepting referrals of complex upper gastrointestinal cases including cancer with a catchment population of about 1.9 million. The study was conducted over a 3-year period, between January 2012 and January 2015 and data were prospectively collected. Institutional Review Board approved this study and individual consent was obtained for study purpose.

#### Type of patients

All consecutive patients regardless of age, gender or race admitted with acute iatrogenic or spontaneous

Correspondence to : Stamatios Petousis, Falireos 16, Evosmos, Thessaloniki, Greece.

Email: petousisstamatios@gmail.com

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oesophageal perforation were included in the study. Oesophageal anastomotic leaks were excluded from the study.

#### *Type of intervention*

Patients were managed conservatively, endoscopically, surgically or with a combination of the above. Decision of management depended both on aetiology and size of the perforation. Tissue debridement and wash out was the main stay of the surgical approach. Depending predominantly on the patient's physiologic response and reserve and not particularly on the time of presentation, simple drainage with chest drains, endoscopic stent insertion, thoracotomy with primary oesophageal repair (with or without a T-Tube or a patch of nearby tissue) as well as oesophageal resection with primary or delayed reconstruction were the options used. Establishing a way of enteral nutrition by either a naso-jejunal tube or a surgical feeding jejunostomy tube was of paramount importance in all cases.

#### *Outcome measures*

Primary outcome was the association of mortality rate with hospital admission time and predominantly before or after the first 24 hours of symptom onset. Secondary outcomes were the nature of perforation, the anatomic location, the type of management (conservative or surgical), length of hospital stay, surgical complication rate and 30- and 90-day mortality rate.

#### *Statistical analysis*

Numeric data were expressed as mean  $\pm$  SD, while categorical data as n (%). Chi-square analysis was used to compare categorical data, while Mann-Whitney test for numeric data. Level of statistical significance was defined at  $P < 0.05$ . SPSS 17.0 (Chicago, Illinois) was used to perform the statistical analysis.

## **Results**

There were 13 cases of oesophageal perforation admitted to our department between January 2012 and January 2015. 61.5% were male and 39.5% were female. Mean age of patients was 58.3 years (IQR, 36.4-80.2 years), with no significant difference between male and female patients ( $54.5 \pm 21.9$  vs.  $64.4 \pm 22.9$ ,  $P = .35$ ).

#### *Primary outcomes*

Overall 90-day mortality rate was 38.4% ( $n = 5$ ), while 30-day mortality rate 30.8% ( $n = 4$ ). Admission within 24 hours of perforation was recorded in 69.2% of patients ( $n = 9$ ), while admission after 24 hours in 31.8% of patients ( $n = 4$ ). 90-day mortality rate was 11.1% (1 out of 9) for early admission vs. 100.0% (4 out of 4) for late

admission ( $P < 0.001$ ), while 30-day mortality rate 11.1% (1 out of 9) for early admission vs. 75.0% (3 out of 4) for late admission ( $P < 0.001$ ). Admission within 24 hours was a significant predictor for mortality, independently from the severity and aetiology of lesion according to regression analysis.

#### *Secondary outcomes*

The main anatomic position of perforation was the lower third of the esophagus in 53.8% ( $n = 7$ ), the mild esophagus in 23.1% ( $n = 3$ ) and the upper third in 23.1% ( $n = 3$ ). Aetiology was iatrogenic in 3 cases and spontaneous in other 10 cases (23.1% and 76.9% respectively).

Mean hospital stay was 58.3 days (range 20-84), while when excluding cases with in-hospital mortality, the mean length of stay was 21.5 days.

Finally, the management of cases was operative in 7 cases (53.8%) and non-operative in six (46.2%). All cases treated operatively were considered as large perforations, while size of perforation was more limited in the conservatively treated cases. Out of surgically treated cases, oesophagectomy was performed in 4 cases (30.8%), of which 3 cases having immediate reconstruction with stomach and 1 having oesophagostomy and delayed reconstruction with stomach as a conduit. Primary closure over T-tube was performed in 1 case. Thoracotomy with debridement and washout, combined with laparoscopy and placement of venting gastrostomy and feeding jejunostomy was performed in 1 case, whereas thoracotomy only with debridement and wash out with a combination of an endoscopically placed self-expandable, partially-covered stent, was performed in another one. Of the 6 cases treated non-operatively, management consisted of insertion of intercostal chest drains and triple lumen nasojejunal (NJ) tube (Freka® Trelumina, Fresenius Kabi, UK) for gastric decompression and jejunal feeding in 2 cases, radiologically inserted nasogastric tube and parenteral nutrition in 2 cases, endoscopically placed triple lumen NJ tube without chest drain insertion in 1 case and endoscopic stent placement in 1 case.

Mean follow-up was 3.1 years (IQR, 2.1-5years), with all patients discharged from hospital, not having developed any post-operative complications. There was 1 unrelated death, while the rest of patients are alive for a mean of 2.6 years (IQR, 2-4years.)

Epidemiological, clinical characteristics and outcome of cases included in the present study are presented in Table 1.

## **Discussion**

The present prospective observational study highlighted two major points. Firstly, the overall mortality rate was observed to be around 40%, which is rather in the middle of the range reported by relative publications.

Table 1. — Epidemiological, clinical characteristics and outcome of cases included in the present study

No	Sex	Age	Site of perforation	Admission from symptom onset	Cause	Management	Length of stay (days)	Outcome
1	Male	84	Lower	Early (<24 hours)	Spontaneous	oesophagectomy with primary reconstruction	24	Mortality
2	Male	20	Upper	Early (<24 hours)	Spontaneous	conservative-with radiological NG tube	1	Survival
3	Female	80	Upper	Early (<24 hours)	Iatrogenic	conservative with radiological NG tube	7	Survival
4	Male	60	Lower	Early (<24 hours)	Spontaneous	oesophagostomy with delayed reconstruction	7	Survival
5	Male	49	Middle	Early (<24 hours)	Spontaneous	oesophagectomy with primary reconstruction	21	Survival
6	Male	77	Middle	Late (>24 hours)	Spontaneous	chest drain & radiologically placed NJ feeding tube	37	Mortality
7	Male	69	Lower	Late (>24 hours)	Spontaneous	endoscopic stent placement	9	Mortality
8	Female	24	Upper	Early (<24 hours)	Spontaneous	endoscopic placement of NJ triple lumen feeding tube	11	Survival
9	Female	77	Middle	Late (>24 hours)	Spontaneous	chest drain & radiologically placed NJ feeding tube	7	Mortality
10	Male	40	Lower	Early (<24 hours)	Spontaneous	thoracotomy for debridement and wash out + laparoscopic venting gastrostomy & feeding jejunostomy	60	Survival
11	Female	71	Lower	Early (<24 hours)	Spontaneous	oesophagectomy with primary reconstruction	28	Survival
12	Female	70	Lower	Early (<24 hours)	Iatrogenic	primary closure over T tube	23	Survival
13	Male	37	Lower	Late (>24 hours)	Iatrogenic	thoracotomy and endoscopic stent	6	Mortality

Secondly, the fact that the majority of oesophageal perforations were admitted to hospital after the critical interval of the first 24 hours.

The observed mortality rate of 38.4% falls within the reported range according to published literature (4). However, there is approximately a 3-fold increase compared to mortality rate of 13.3% that was recently shown in a meta-analysis by our team (6). A study reporting similar mortality rate with our study, was that of Bayram et al, in which an overall mortality rate of 30% was demonstrated (5). It is important to consider that no prospective cohort study with large sample size has been published in the English literature; our study is one amongst few with a prospective character reporting a mortality rate in the area of 40%. The low quality of studies regarding oesophageal perforation may explain the heterogeneity of reported numbers. Consequently, further prospective studies with larger number of patients should be performed.

A major explanation about the higher mortality rate observed in our series may lie in the kind of cases enrolled. As our Department serves as a large tertiary center, there are received cases of higher severity and mainly of spontaneous aetiology, which are rather associated with detrimental prognosis. It is also potential that many iatrogenic perforations are not admitted to our hospital, which also explains the relatively low rate of cases with iatrogenic aetiology. Therefore, it is crucial to mention that potentially the nature of our Department may create a bias in the estimation of overall mortality,

both because of severity and different aetiology of cases admitted to our Department.

The second principal remark of our study is that the majority of cases that resulted in mortality were admitted late to hospital. It has been reported that early admission to specialized units is the basic confounder of survival after esophageal perforation (7-12). Indeed, Keeling et al, in a study including 147 patients, have indicated that mortality is lower than 10% for cases admitted within 24 hours (2), while Amudhan et al, in a retrospective study enrolling 47 patients, demonstrated that late diagnosis is associated with increased mortality and prolonged hospital stay (7). Furthermore, the recent systematic review by Sdralis et al that included 52 studies, indicated that presentation to hospital within 24 hours of symptom initiation, is slightly over 50%, which means that only 1 in 2 cases of oesophageal perforation is admitted early enough to reassure successful management and favorable outcome (6). This is probably multifactorial but may be also attributed to the inconsistency in the severity of the disease presentation as well as the nature of the perforation. Another reason could be delay in establishing the diagnosis with time-consuming investigations and subsequent delay in patient transfer to a tertiary upper gastrointestinal centre, with availability of intensive care unit bed, which is nowadays standard practice. This delay in treatment may essentially be accountable for the increased morbidity and mortality that accompanies delayed presentations.

The present study has certain limitations. It included a rather restricted sample size of 13 patients. However, it is one among few prospective studies derived by a tertiary referral institution with specialized clinicians, indicating a relatively high mortality rate, worse for cases with delayed presentation of over 24 hours.

## Conclusion

In conclusion, the present study highlighted the high mortality following oesophageal perforation and the significant impact of time of presentation on prognosis. Further large multi-center prospective observational or RCT studies are needed in order to advance diagnostic and therapeutic approaches and reach safer conclusions in the management of such a challenging condition.

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## Disclosure

Authors report no conflict of interest. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions. Informed consent or substitute for it was obtained from all patients for being included in the study.

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## References

- BRINSTER CJ, SINGHAL S, LEE L, MARSHALL MB, KAISER LR, KUCHARCZUK JC. Evolving options in the management of esophageal perforation. *Ann Thorac Surg.*, 2004, **77** : 1475-83.
- KEELING WB, MILLER DL, LAM GT, KILGO P, MILLER JI, MANSOUR KA et al. Low mortality after treatment for esophageal perforation: a single-center experience. *Ann Thorac Surg.*, 2010, **90** : 1669-73.
- VOGEL SB, ROUTWR, MARTIND, ABBITT PL. Esophageal perforation in adults: aggressive, conservative treatment lowers morbidity and mortality. *Ann Surg.*, 2005, **241** : 1016-21.
- BAYRAM AS, EROL MM, MELEK H, COLAK MA, KERMENLI T, GEBITEKIN C. The success of surgery in the first 24 hours in patients with esophageal perforation. *Eurasian J Med.*, 2015, **47** : 41-7.
- DIMOU F, VELANOVICH V. Perforations of the esophagus and stomach: what should I do? *J Gastrointest Surg.*, 2015, **19** : 400-6.
- SDRALIS E., PETOUSIS S., RASHID F., LORENZI F., CHARALABOPOULOS A. Epidemiology, diagnosis and management of oesophageal perforations: systematic review. *Diseases of Esophagus*, 2017, **30** : 1-6.
- AMUDHAN A, RAJENDRAN S, RAJ VV, RAJARATHINAM G, JYOTIBASU D, RAVICHANDRAN P et al. Management of esophageal perforation: experience from a tertiary center in India. *Dig Surg.*, 2009, **26** : 322-8.
- CHAO YK, LIU YH, KO PJ, WU YC, HSIEH MJ, LIU HP et al. Treatment of esophageal perforation in a referral center in Taiwan. *Surg Today.*, 2005, **35** : 828-32.
- RICHARDSON JD. Management of esophageal perforations: the value of aggressive surgical treatment. *Am J Surg.*, 2005, **190** : 161-5.
- NAVANEETHAN U, LOURDUSAMY V, DUVURU S, LOURDUSAMY D, MEHTA D, RAJA S. Timing of esophageal stent placement and outcomes in patients with esophageal perforation: a single-center experience. *Surg Endosc.*, 2015, **29** : 700-7.
- KROEPIL F, SCHAUER M, RAFFEL AM, KRÖPIL P, EISENBERGER CF, KNOEFEL WT. Treatment of early and delayed esophageal perforation. *Indian J Surg.*, 2013, **75** : 469-72.
- HERMANSSON M, JOHANSSON J, GUDBJARTSSON T, HAMBREUS G, JÖNSSON P, LILLO-GIL R et al. Esophageal perforation in South of Sweden: results of surgical treatment in 125 consecutive patients. *BMC Surg.*, 2010, **10** : 31