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ORIGINAL ARTICLE

A - 13 Years of Single-Center Experience in the Management and Outcome of Esophageal Perforation

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ABSTRACT

Objective: Esophageal perforation (EP) is a fatal status that continues to be challenging the management, with the incidence of mortality and morbidity has been reported to reach 40%. Its diagnosis may be tricky as it usually presents with a wide range of non-specific symptoms. Our study aims to report characteristics, relay our experience with EP management, and evaluate the various strategies used. **Methods:** This study retrospectively evaluated the management of 53 patients with EP over 13 years. The confirmed diagnosis was established by esophagogram with water-soluble contrast, contrast-enhanced computed tomography, and esophagus-gastro-duodenoscopy. Initial management was categorized as conservation, endoscopic stent, or surgery. Re-intervention and different outcomes were recorded and analyzed. **Results:** Thoracic EP is the most common location (71.7%). The most common cause of EP was iatrogenic (35.8%). About 58.5% of patients were diagnosed ≤ 24 hours. The mean Pittsburg severity score was 7.5. The initial management was conservation (35.8%), an endoscopic stent (17%), and surgical intervention (47.2%). ICU and organ support were needed in 35.8% and 20.8%, respectively. The mean hospital stay for all patients was 27.7 days. Morbidity and mortality were recorded at 30.2% and 18.9%, respectively. **Conclusion:** EP management should be flexible with a tailored strategy for every patient. Etiology, site, severity score, time to management, and patient reserve are significant factors in management and prognosis.

Keywords: Esophageal perforation, drainage, iatrogenic, spontaneous, conservation.

INTRODUCTION

Esophageal perforation (EP) is a life-threatening ailment that continues to provide therapeutic difficulties. A variety of factors can cause EP, although it is most commonly caused by an iatrogenic, traumatic foreign body, or spontaneous (as malignancy and Boerhaave syndrome) occurrences **[1]**. The incidence of mortality and morbidity of EP has been reported to reach 40% **[2].**

Numerous manifestations may contribute to diagnostic delay, particularly in asymptomatic patients. The time lag between EP and starting the management is considered a major factor determining the fate of EP. The esophagus does not have a serosal layer, so EP could disseminate infection and mediastinitis **[3]**. Over the last 3 decades, the prognosis has improved drastically, from an increased mortality incidence of approximately 30% to a little more tolerable incidence of 15%. **[4]**.

Broad-spectrum antibiotics, copious irrigation and drainage, septic eradication, and nothing per os (NPO) are the basic management principles **[2,5]**. There is still debate over the best way to treat EP to achieve the core principles of EP management. Many surgeons preferred aggressive surgical therapy, including basic primary surgical repair or esophagectomy **[6]**. However, current researches suggest that conservative treatment may be appropriate in some circumstances **[2,4,7]**. Metallic stents have been used to fix primary EP since about the nineties **[8]**.

Our study aims to report characteristics, relay our experience with EP management, and evaluate the various strategies used.

METHODS

Over thirteen years, from 8/2007 to 7/2020, EP cases at Zagazig university hospitals were

retrospectively identified, and clinical notes were extracted All participants provided written informed consent, and the study was approved by the Faculty of Medicine, Zagazig University's ethical research committee. The study was conducted by the World Medical Association's Code of Ethics (Declaration of Helsinki) for human studies. We identified the time of management (TOM) as follows; early TOM if it was done ≤ 24 hours from manifestations onset and late TOM if it > 24 hours. Other demographic and clinical data were recorded. Perforation size analysis couldn't be conducted as the size record was usually lacking or without specific measurements.

The confirmed diagnosis was established by one or more of the following tools; esophagogram with water-soluble contrast, contrast-enhanced computed tomography (CT), and esophago-gastro-duodenoscopy (EGD). Initial management was categorized as conservation, endoscopic stent, or surgery (including drainage and debridement and/or repair of perforation). Esohagogram or CT with water-soluble substance was done 8 to 10 days later, and oral intake was initiated if there was no dye leakage. The need for secondary intervention due to leakage for more than 8-10 days was documented by recording dye extravasation in contrast imaging. Intensive care unit (ICU), organ support, morbidity, mortality, and hospital stay duration were viewed and analyzed for all patients.

Pittsburg severity score (PSS) was calculated for all patients, as per Abbas et al.'s criteria described in 2009 [9]. PSS is between 0 and 18, based upon 10 clinical variables responsible for injury severity and outcome. The rating of patients was as follows; one point for age >75, tachycardia (>100 bpm), leukocytosis (>10,000 WBC/ml), pleural effusion; two points for fever (>38.5°C), non-contained leak, respiratory compromise (respiratory rate >30, increasing oxygen requirement, or need for mechanical ventilation), time to diagnosis >24 hours; and three points for the presence of cancer, or hypotension.

Statistical analysis:

Data were analyzed using SPSS software version 22 (USA). The data were expressed as mean ± SD & median (Min-Max). One-way ANOVA test was used for parametric data, while the Kruskal Wallis test was for non-parametric data. Categorical data was done using the Chi-square test.

RESULTS

The clinical and demographic characteristics of 53 patients are listed in the table (1). The mean age was 37.4 years, 64.2% of patients were men, and 58.5% were early TOM. Thoracic EP is the most common location (71.7%). The most common cause of EP was iatrogenic (19, 35.8%): eleven occurred during EGD (3 with esophageal cancer (ECa) biopsy/stenting, 4 with FB extraction, 1 with varices therapy, 3 with stricture dilatation), and eight occurred with different interventions (1 bronchoscopic biopsy, 1 trans-esophageal echocardiography, 3 tracheostomies, 1 endotracheal tube insertion, 2 spinal cord surgery). FB perforation was the 2nd cause (16, 30.2%). The 3rd cause of EP was spontaneous (15, 28.3%): nine patients had Esophageal tumors, one patient had Boerhaave syndrome, and five patients had esophageal diverticulum. The last cause of EP was external trauma (3, 5.7%); two occurred by stab wounds, and one occurred by missile injury.

The mean and median PSS were 7.5 and 6, respectively. The initial management was conservation (35.8%), an endoscopic stent (17%), and surgical intervention (47.2%). The varieties of surgery were drainage, primary repair (PR), exclusion and diversion, and esophagectomy. 35.8% of patients were admitted to the ICU, and 20.8% needed organ support. Re-leakage was recorded in 30.2% of patients, and all of them required surgical re-intervention.

The mean hospital stay was 27.7 days. The morbidity rate was 30.2% in the form of sepsis, esophageal fistula, empyema, acute renal failure, mediastinitis, multiorgan failure, and septic shock. The incidence of mortality was 18.9%.

We evaluated if TOM was correlated with different outcomes, the results are shown in table (2). Early TOM was significantly linked to a 63% reduction in ICU admissions (P<0.001), a 34.4% reduction in organ support (P=0.04), a 49.4% reduction in re-intervention (P<0.001), and a 53.7% reduction in the mean hospital stay (P<0.001). A significant association between late TOM and morbidity was recorded (P<0.001). No significant difference was found regarding mortality between early and late TOM (9.7% vs. 31.8%, P=0.07).

A comparison between presentations and different outcomes of the recruited patients based on management is listed in the table (3). There were significant statistical differences regarding the etiology of perforation (P=0.027), ICU (P<0.001), support (P=0.004), and re-intervention (P=0.001). The mean PSS was significantly higher with surgery (10.6) when compared with endoscopy (5.73) or with conservation (4.06), P<0.001.

The hospital stay was significantly prolonged with surgery (36.8 days) than with endoscopy (21.1 days) or with conservation (18.4 days). Morbidity was significantly higher with surgical management (52%) than with endoscopic management (11.1%) and conservative management (10.5%), P<005. We recorded no significant differences in mortality with 3 management options.

The correlation between re-intervention with presentation and primary outcomes is listed in the table (4). We found a substantial relationship between re-intervention with mean PSS (P<0.001). A significant association was recorded between re-intervention with morbidity and mortality (P<0.001).

Table (5) shows the relationship between primary outcomes and clinical presentation. There was a significant association between perforation site and morbidity (P=0.042), but not with mortality (P=0.088). The mean PSS and mean hospital stay significantly impacted primary outcomes (P<0.001).

Table (1): Clinical and demographic data of the recruited patients

Variables	Patients (n=53)
Age Mean ± SD Median (Min-Max)	 37.4 ± 22.8 38 (3-77)
Sex, n (%) Male Female	 34 (64.2%) 19 (35.8%)
Time to management, n (%) Early Late	 31 (58.5%) 22 (41.5%)
Perforation site, n (%) Cervical Thoracic Abdominal	 11 (20.8%) 38 (71.7%) 4 (7.5%)
Etiology, n (%) Iatrogenic FB Spontaneous Traumatic	 19 (35.8%) 16 (30.2%) 15 (28.3%) 3 (5.7%)
PSS Mean ± SD Median (Min-Max)	 7.5 ± 4.9 6 (0-18)
Management, n (%) Conservation Endoscope Surgery	 19 (35.8%) 9 (17%) 25 (47.2%)
ICU, n (%)	19 (35.8)
Organ support, n (%)	11 (20.8)
Re-intervention n, (%)	16 (30.2%)
Duration of hospital stay Mean ± SD Median (Min-Max)	 27.7 ± 15.4 25 (8-57)
Morbidity, n (%)	16 (30.2%)
Mortality, n (%)	10 (18.9%)

PSS Pittsburg severity score, ICU intensive care unit

Table (2): Correlation between the TOM with overall outcomes

Variables	Early (n = 31)	Late (n = 22)	P value
ICU, n (%)	3 (9.7%)	16 (72.7%)	<0.0001*
Organ support, n (%)	2 (6.5%)	9 (40.9%)	0.04*
Re-intervention	3 (9.7%)	13 (59.1%)	<0.0001*
Hospital stay Mean ± SD Median (Min-Max)	 18.7 ± 11.5 14 (8 – 53)	 40.4 ± 10.7 40 (13- 57)	<0.0001*
Morbidity, n (%)	3 (9.7%)	13 (59.1%)	<0.0001*
Mortality, n (%)	3 (9.7%)	7 (31.8%)	0.073

* Significant, TOM time of management, ICU intensive care unit

Table (3): Comparison between clinical data of the recruited patients based on management

Variables	Conservation group (n=19)	Endoscopy group (n=9)	Surgery group (n=25)	P value
Age Mean ± SD Median (Min-Max)	 28.4 ± 21.8 23 (6-61)	 40.1 ± 17.7 44(10-65)	 42.2 ± 24.4 45 (3-77)	P=0.14
Sex, n (%) Male Female	 11 (64.7%) 6 (35.3%)	 6 (66.7%) 3 (33.3%)	 15 (60%) 10 (40%)	P=0.83
Etiology, n (%) FB Spontaneous Iatrogenic Traumatic	 9 (47.4%) 0 (0%) 9 (47.4%) 1 (5.3%)	 1(11.1%) 4 (44.4%) 4 (44.44%) 0 (0%)	 6 (24%) 11 (44%) 6 (24%) 2 (8%)	P=0.027*
Perforation site, n (%) Cervical Thoracic Abdominal	 7 (36.8%) 12 (63.2%) 0 (0%)	 0 (0%) 8 (88.9%) 1(11.1%)	 4 (16%) 18 (72%) 3 (12%)	P=0.12
ICU, n (%)	0 (0%)	2 (22.2%)	17 (68%)	P<0.001*
Organ support, n (%)	0 (0%)	1(11.1%)	10 (40%)	P=0.004*
PSS Mean ± SD Median (Min-Max)	 4.06 ± 2.01 4 (1-7)	 5.73 ± 3.2 4 (0-12)	 10.6 ± 5.1 [ab] 11(2-18)	P<0.001*
Re-intervention, n (%)	1 (5.3%)	1 (11.1%)	14 (56%)	P=0.001*
Duration of hospital stay Mean ± SD Median (Min-Max)	 18.4 ± 9.02 13 (9-39)	 21.1 ± 11.2 19 (8-44)	 36.8 ± 15.6 [ab] 41 (8-57)	P<0.001*
Morbidity, n (%)	2 (10.5%)	1 (11.1%)	13 (52%)	P=0.005*
Mortality, n (%)	1 (5.3%)	1 (11.1%)	8 (32%)	P=0.07

* Significant, FB foreign body, ICU intensive care unit, PSS Pittsburg severity score

Table (4): Correlation between re-intervention with clinical presentation and primary outcomes

Variables	Re-intervention (n = 16)	P value
Etiology n, (%) FB Spontaneous Iatrogenic Traumatic	 3 (18.8%) 7 (43.8%) 5 (31.3%) 1 (6.3%)	0.38

Variables	Re-intervention (n = 16)	P value
Site n, (%) Cervical Thoracic Abdominal	 0 (0%) 14 (87.5%) 2 (12.5%)	0.43*
PSS Mean ± SD Median (Min-Max)	 13.38±2.96 14 (6 – 18)	<0.0001*
Morbidity n, (%)	14 (87.5%)	<0.0001*
Mortality n, (%)	8 (50%)	<0.0001*

* Significant, FB foreign body, PSS Pittsburg severity score

Table (5): Correlation between primary outcomes with clinical presentation

Variables	Morbidity (n = 16)	P value	Mortality (n = 10)	P value
Etiology, n (%) FB Spontaneous Iatrogenic Traumatic	 3 (18.8%) 6 (37.5%) 6 (37.5%) 1 (6.2%)	0.635	 1 (10%) 4 (40%) 5 (50%) 0 (0%)	0.302
The site, n (%) Cervical Thoracic Abdominal	 0 (0%) 15 (93.7%) 1 (6.3%)	0.042*	 0 (0%) 10 (100%) 0 (0%)	0..088
PSS Mean ± SD Median (Min-Max)	 14.06±2.4 14 (10 – 18)	<0.0001*	 15.2±1.9 14.5 (12 – 18)	<0.0001*
Hospital stay Mean ± SD Median (Min-Max)	 45.3±8.6 48 (29-57)	<0.0001*	 47.8±7.3 49 (29-55)	<0.0001*

* Significant, FB foreign body, PSS Pittsburg severity score

DISCUSSION

EP is an uncommon problem that affects 3.1 out of every 1,000,000 people each year with poor outcomes due to complex complications, late TOM, and difficult decision-making **[10]**. Its diagnosis by CT with oral dye should be performed when the suspicion index is jumping because it reveals the location of collections and other pathologies. EGD is a useful tool for determining the location and size of thoracic EP, with a sensitivity and specificity of 100% and 83%, respectively **[11]**.

In our study, iatrogenic EP was the most common cause (35.8%). Our result goes with Sari and associates' results, who reported the iatrogenic EP as the most common etiology (53.8%) **[2]**. Many series also documented that iatrogenic EP is the most common etiology **[4,6,7,10]**. On the contrary, Law and associates reported that spontaneous EP (45.5%) is the most common cause **[11]**. Another study by Deng and associates recorded the traumatic FB (73%) as the most common cause of EP **[5]**. The last two studies did a limited survey of their department and did not collect other EP patients in other departments, and this was the cause of etiology differences.

Even if EP was detected by endoscopy, CT-chest has to be done to evaluate the incidence of mediastinitis, emphysema, and collection early **[12,14]**. Our study depends on a contrast esophagogram as the basic method for diagnosis, and CT is indicated with a negative esophagogram, unusual manifestations, or undetected perforation site. EGD is applied when a stent is indicated for EP

management to visualize EP, measure perforation size, and evaluate epithelial viability. Vermeulen and his co-worker showed compatible diagnostic basics to our study **[3]**. Finally, the primary diagnostic tool should be tailored to the cause of EP.

TOM is the most crucial factor that influences the outcome of EP **[15,16]**. In our study, patients with late TOM had significantly higher rates of ICU admission, organ support need, re-intervention, mean hospital stay, and morbidity. The incidence of mortality was higher in the late group, but it was non-significant (P=0.073). Vermeulen and his co-worker, who conducted an individual patient data meta-analysis on 960 patients, reported identical results to us **[3]**. Many studies reported no mortality in the early group **[6,7,17]**. Other studies documented that early TOM of EP significantly decreases primary and secondary outcomes **[4,15,17]**.

Due to incidents' low frequency and unpredictability, no single organization can amass a substantial considerable experience [(18)]. The basic principles in EP therapy are eradication of septic focus and drainage of collection to abort failure of many organs. Currently, no 'fundamental basis' can fix these objectives **[1]**. Many surgeons advocated vigorous surgical techniques to ensure a reduced incidence of mortality **[17,19,20]**. Other doctors recommended conservative management for EP with a comparable incidence of mortality **[6,7,21,22]**.

Abbas and associates revealed a superior outcome with the conservation of sepsis and fixing EP leakage **[9]**. We recorded in our study that; conservative therapy was more often used for iatrogenic and FB than spontaneous perforations, which were more candidates for surgical intervention. That is because iatrogenic EP are commonly discovered early and are well-contained with little mediastinal soiling, so conservative therapy looks to be a successful therapeutic method. Unlike spontaneous perforations are commonly accompanied by gross contamination and devitalized edges which necessitates surgical management. Many series reported a competent result to our result **[2,4,6]**.

The Association of Western Trauma published some guidelines in 2015; they advocated endoscopic management for small thoracic EP with a stable general condition **[18]**. Marker and associates did a large retrospective study centered on spontaneous EP and recorded low surgical need with the exemplary implementation of endoscopic **[23]**. Our study recorded significant improvement in patients who underwent stent application than those with operative intervention regarding ICU, organ support, re-intervention, hospital stay, and morbidity. We recorded a non-significant lower mortality rate of stent application. Sari and co-workers reported comparable data to us **[2]**. Brinkmann and associates showed significantly better outcomes with stents **[24]**.

On the contrary, Ali and co-workers reported patients with stent therapy were no different from those who underwent surgery regarding outcomes [(18)]. The significant improvement in our patients who underwent stent application may be attributed to the significantly higher PSS in patients who underwent surgical management. Kovács and associates reported that; the Stent application didn't result in beneficial outcomes outside the range of ICU needs. They ensured that; stent deployment in cervical and abdominal locations is contraindicated because of the high incidence of stent migration. Specialized stents were introduced recently for these sections **[4]**.

We recorded a substantial correlation between re-intervention and high PSS. Many series showed consistent results regarding re-intervention **[2,9,18,25,26]**. We recorded a morbidity incidence of 30.2% and a mortality incidence of 18.9%. Our morbidity incidence is substantially lower than in recently published articles, and mortality incidence in our study is lower than mid-way of the recently published range **[24,27,28]**. Recent reports from different studies and meta-analyses showed a range of mortality rates between 12% to 28% **[4,11,24,27]**.

Our mortality incidence correlated significantly with prolonged hospital stay and high PSS, but we found no significant association between it and the perforation site. A recent study by Petousis and associates reported a high mortality incidence of 38.4%, 2-fold of our mortality incidence **[29]**; this may be attributed to a higher PSS and more late TOM. The morbidity incidence in our study correlated significantly with perforation sites, prolonged hospital stay, and high PSS. Our primary outcomes correlations go with many recently published articles **[2,4,9,24,29]**.

In conclusion, as EP is an emergent, potentially fatal condition without well-established guidelines for management, there should be flexibility in the protocol of EP management with a

tailored strategy for every patient. Surgical intervention should have supremacy if EP is associated with late diagnosis, septic manifestations, high PSS, or probable system failure. Nevertheless, suppose a stable general status with low PSS is detected, and the patient was diagnosed in an early period; in that case, we should determine which management (conservation, endoscopy, or surgery) could benefit septic elimination and control leak. In this way, cause, site, severity score, time to management, and patient reserve are considered significant factors in management and prognosis.

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