Current Concepts in the Management of Esophageal Perforations: A Twenty-Seven Year Canadian Experience

Pankaj Bhatia, MD, Dalilah Fortin, MD, Richard I. Inculet, MD, and Richard A. Malthaner, MD

Division of Thoracic Surgery, The University of Western Ontario, London, Ontario, Canada

GENERAL THORACIC

Background. Perforation of the esophagus remains a challenging clinical problem.

Methods. A retrospective review was performed of patients diagnosed with an esophageal perforation admitted to the London Health Sciences Centre from 1981 to 2007. Univariate and multivariate logistic regression was used to determine which factors had a statistically significant effect on mortality.

Results. There were 119 patients; 15 with cervical, 95 with thoracic, and 9 with abdominal perforations. Fifty-one percent of all the perforations were iatrogenic and 33% were spontaneous. Multivariate logistic regression analysis revealed that patients with preoperative respiratory failure requiring mechanical ventilation had a mortality odds ratio of 32.4 (95% confidence interval [CI] 3.1 to 272.0), followed by malignant perforations with 20.2 (95% CI 5.4 to 115.6), a Charlson comorbidity index of 7.1 or greater with 19.6 (95% CI 4.8 to 84.9), the presence of a pulmonary comorbidity with 13.9 (95% CI 2.9 to 97.4), and sepsis with 3.1 (95% CI 1.0 to 10.1). A wait time of greater than 24 hours was not associated with an increased risk of mortality ($p = 0.52$).

Conclusions. Malignant perforations, sepsis, mechanical ventilation at presentation, a higher overall burden of comorbidity, and a pulmonary comorbidity have a significant impact on the overall survival. Time to treatment is not as important. Restoration of intestinal continuity, either by primary repair or by excision and reanastomosis can be attempted even in patients with a greater time from perforation to treatment with respectable morbidity and mortality rates.

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Perforation of the esophagus remains a challenging clinical problem in the world of thoracic surgery. The management options for esophageal perforations vary depending on the location of the perforation, its etiology, the time from its occurrence to the intervention, and the overall condition of the patient [1–6]. Delay in the diagnosis and treatment can significantly influence the overall outcomes of patients sustaining perforations, as can the location of the perforation and the presence of underlying esophageal pathology such as a malignancy. This multivariate influence on the natural history and outcome of esophageal perforations is reflected in the wide range of mortality rates reported in various studies examining the outcomes of patients sustaining a disruption [2, 5, 7–10]. The evolution of management of esophageal perforations has taken us from routine diversion to esophageal resection to primary repair and stenting of perforations, yet controversy continues to exist with respect to the best way to treat the aforementioned subtypes of esophageal rupture. It is also accepted that despite the surgical procedure used, 30% of patients will continue to have esophageal leaks postoperatively that can often be managed nonoperatively [1]. Obviously, this adds to the debate as to the optimal management of esophageal perforations.

In the contemporary era, primary repair of esophageal perforations is becoming widely accepted as the treatment of choice, and several studies [2, 11–14] have demonstrated respectable mortality and morbidity rates with benign perforations, even with delayed presentation. Obviously, if the esophagus is devitalized or contains malignant disease, alternative methods of treatment other than primary repair should be undertaken. These patients have been shown to have a worse outcome [3, 11] in a number of retrospective reviews, including a review in 2004 [2]. This has led us to postulate that time to treatment is perhaps not as critical a factor in patient mortality as many textbooks suggest. The overall presentation of the patient, be it hemodynamically stable to sepsis to florid shock, is far more predictive of outcome.

The fact that several options exist for managing the various types of esophageal perforations has prompted several authors to review their experience with this challenging and potentially deadly entity. We present here our contemporary experience in the hopes of answering some of the questions surrounding the management of this important surgical problem. Our hypotheses

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Address correspondence to Dr Malthaner, Divisions of Thoracic Surgery and Surgical Oncology, London Health Sciences Centre, 800 Commissioners Rd E, Ste E2-124, London, Ontario, Canada N6A 5W9; e-mail: richard.malthaner@lhsc.on.ca.

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are that time to treatment of an esophageal perforation is not as critical a predictor of mortality and morbidity as previously thought, that malignant perforations of the esophagus carry with them a higher mortality and morbidity than benign perforations, and that the nature of the patient's presentation is a more critical predictor of mortality than time to treatment.

Patients and Methods

Approval for our study was obtained from the ERB (Ethics Review Board) of London Health Sciences Centre and the University of Western Ontario. Individual patient consents were waived by the ERB because individual patients were not identified in the manuscript.

We conducted a retrospective review of our prospective thoracic database of patients diagnosed with an esophageal perforation admitted to the London Health Sciences Centre from 1981 to 2007. We excluded esophageal perforations discovered intraoperatively during other thoracic surgery procedures such as lobectomies and repaired by the surgeon at the time of this first. The included patients were subsequently tabulated according to the location of the perforation (cervical, thoracic, abdominal), and the etiology of the perforation (iatrogenic, malignant, spontaneous, foreign body). The time from onset of symptoms to treatment, as well as the method of treatment (primary repair, diversion, surgical drainage, conservative) were analyzed for each patient. Mortality, defined as death within 30 days of admission to hospital or during the same admission for an esophageal perforation, length of stay, and reoperation were examined for each location and treatment group. The initial presentation of patients and their underlying comorbid medical issues were also examined. An empiric comorbidity score was given for each patient, with patients receiving one point if a comorbidity was present in each of 9 domains (cardiac, pulmonary, hepatic, renal, smoking, diabetic, alcohol abuse, malnutrition, steroid use) for a total score out of a possible nine points. In addition, we also calculated the Charlson comorbidity index for each patient as outlined by Charlson and colleagues in 1987 [15].

With respect to outcome measures, we defined mortality as any death occurring within 30 days of the primary treatment or at any point during the index hospital admission. Esophageal leak was defined as any secondary violation of the remnant esophageal conduit at any point during the hospital admission after resolution of the initial perforation by the primary treatment.

Follow-up was available for all patients and consisted of a single postoperative visit approximately 4 weeks after discharge from hospital. Further visits were scheduled based on patient need (underlying esophageal pathology, management of postoperative complications).

In an attempt to ascertain the determinants of mortality for our patient population, a number of predictor variables, listed in Table 1, were then analyzed using univariate and multivariate logistic regression to determine which factors had a statistically significant effect on mortality. Categoric variables were analyzed using the Fisher exact test and continuous variables were analyzed using the Wilcoxon two-sample rank test. Statistically significant variables (variables with p values less than or equal to 0.1) in the univariate analysis were then included in a multivariate logistic-regression analysis to determine the magnitude of their influence on mortality in the form of odds ratios and the associated 95% confidence interval (CI).

Results

One hundred nineteen patients were treated for esophageal perforations between 1981 and 2007. Of these 119 patients, 15 suffered cervical perforations, 95 patients sustained thoracic perforations, and 9 sustained abdominal perforations (Fig 1).

In our series, 51% (n = 61) of all the perforations were iatrogenic in nature. Spontaneous perforations accounted for 33% (n = 39), whereas malignant perforations accounted for 15% (n = 18) of the total. There was a single perforation because of an ingestion of a caustic substance. Perforations because of an ingested foreign body resulting in attempted instrumentation to remove it constituted 4% (n = 5) of all perforations and are included in the iatrogenic group, as the endoscopic procedure resulted in the perforation in all cases.

Patients with abdominal perforations tended to be considerably younger, with an average age of 50.5 years (median, 42 years; range, 22 to 84 years), as compared with thoracic (mean age = 65.5 years; median, 64 years; range, 8 to 92 years) and cervical (mean age of 67.1 years; median, 69 years; range, 39 to 85 years) (Table 2). There was a predominance of males (74%) in the thoracic perforation category. Patients with malignant thoracic perforations had the highest comorbidity score (mean 2.5), American Society of Anesthesiologists (ASA) score (3.7), and Charlson comorbidity index (6.3) among all the groups.

The average time of perforation to treatment was 37 hours (median, 11 hours; range, 0.8 to 240 hours) in the cervical group, 19 hours (median, 8 hours; range, 0.5 to 72 hours) in the abdominal group, 129 hours (median, 24 hours; range, 0.5 to 480 hours) in the malignant thoracic group, and 65 hours (median, 27 hours; range, 0 to 480 hours) in the benign thoracic group (Table 3). Of note, the vast majority of benign thoracic perforations (72%), abdominal (67%), and cervical (67%) were repaired primarily (Table 3). Conservative treatment, classified as treatment of an esophageal perforation with a closed-chest tube thoracostomy, expandable stent, or compassionate care accounted for 27% of cervical perforations, 0% of all abdominal perforations, 31% of all malignant thoracic perforations, and 19% of all benign thoracic perforations. Diversion was only performed twice in the abdominal perforation group (one of these was due to a severe caustic injury), twice in the malignant thoracic group, and 7 times in the benign thoracic group. No diversions were performed in the cervical perforation group.

With respect to perioperative mortality, there were

Table 1. Univariate Analysis

Factor	No Mortality (n = 97)	Mortality (n = 22)	*p* Value
Mean age	60.8	65.7	$p = 0.99$
Median age (range)	60 (8–92)	63.5 (46–85)	$p = 0.99$
Female gender	28 (28.9%)	7 (31.8%)	$p = 0.80$
Perforation type			
Malignant	7 (7.2%)	10 (45.5%)	$p = 0.0008$[a]
Iatrogenic	35 (36.1%)	4 (18.2%)	$p = 0.32$
Spontaneous	46 (47.4%)	8 (36.4%)	$p = 0.66$
Postoperative	9 (9.2%)	0 (0%)	$p = 1$
Preop morbidity			
Cardiac	18 (18.6%)	4 (18.1%)	$p = 1$
Pulmonary	14 (14.4%)	10 (45.5%)	$p = 0.02$[a]
Smoker	46 (47.4%)	16 (72.3%)	$p = 0.26$
Renal failure	2 (2.1%)	1 (4.5%)	$p = 0.47$
Diabetes	7 (7.2%)	2 (9.1%)	$p = 0.68$
Hepatic disease	3 (3.1%)	3 (13.6%)	$p = 0.11$
Alcohol abuse	23 (23.7%)	5 (22.7%)	$p = 1$
Malnutrition	12 (12.3%)	13 (59.1%)	$p = 0.001$[a]
Steroid use	7 (7.2%)	2 (9.1%)	$p = 0.68$
Charlson comorbidity index (mean)	2.8	7.1	$p = 0.0004$[a]
Presentation			
Sepsis	45 (46.4%)	18 (81.2%)	$p = 0.08$[a]
Hemodynamic instability	14 (14.4%)	4 (18.1%)	$p = 0.75$
Mechanical ventilation	16 (16.5%)	13 (59.1%)	$p = 0.006$[a]
Mean time to treatment	54.3	153.3	N/A
Median time to treatment (range)	28.5 (0–480)	36 (0.5–480)	$p = 0.52$
Treatment			
Primary repair	69 (71.1%)	8 (36.4%)	$p = 0.2$
Resection and reconstruction	4 (4.1%)	5 (22.7%)	$p = 0.9$
Diversion	10 (10.3%)	1 (4.5%)	$p = 0.9$
Drainage alone	5 (5.2%)	3 (13.6%)	$p = 0.9$
Conservative	9 (9.3%)	5 (22.7%)	$p = 0.9$

[a] $p < 0.1$.

Univariate analysis of esophageal perforations based on various factors' influence on mortality. Categoric variables were analyzed using the Fisher exact test, and continuous variables were analyzed using the Wilcoxon two-sample test.

N/A = not applicable; Preop = preoperative.

only 2 deaths in the cervical perforation group (8%), one in the abdominal group (11%), and 10 patients in the benign thoracic group (13%). The perioperative 30-day mortality of patients with malignant thoracic perforations was 63%.

The mean and median lengths of stay were considerably higher in both the malignant and benign thoracic perforations as compared with the cervical and abdominal perforations (Table 4). The median number of critical care unit days, and median number of days of mechanical ventilation during their hospital stay was lowest in the cervical perforation group (4.5 and 1.5 days, respectively) and highest in the malignant thoracic perforation group (9.5 and 8.5 days, respectively). Additionally, postoperative leak rates were highest in the malignant thoracic perforation group (43.7%), and lowest in the abdominal perforation group (0%). Only 3 of the 7 malignant thoracic perforations who leaked underwent a reoperation, as 4 of the patients and their families elected not to undergo a second operation and desired compassionate care. The median time from perforation to initial treatment for those patients subsequently presenting with a secondary leak was considerably higher in the malignant thoracic perforation group (168 hours), although the number of patients was quite small. In reviewing the initial treatment strategy for those patients who had a secondary esophageal leak, the leak in the cervical perforation group followed an initial resection and diversion procedure (distal staple line dehiscence). The primary treatments for the 18 leaks in the nonmalignant thoracic perforation group were the following: 9 primary repairs, surgical drainages with decortications, 3 resection and diversions, 1 exclusion and diversion, and 2 chest-tube drainages without surgical decortication. The primary treatments for the 7 leaks in

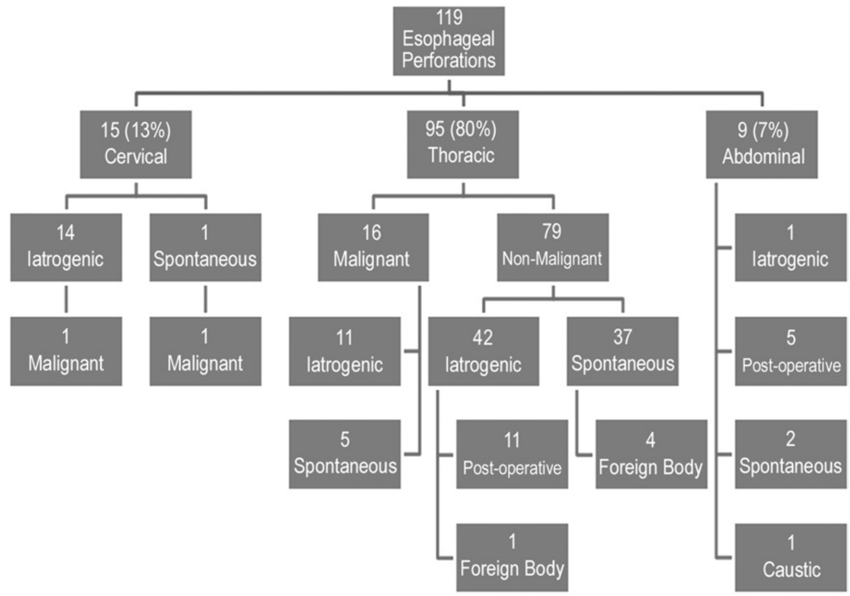

Fig 1. Esophageal perforations managed at London Health Sciences Centre from 1981 to 2007. There were 16 malignant perforations in the thoracic group, 2 malignant perforations in the cervical group, and none in the abdominal group.

the malignant thoracic perforation group were 2 primary repairs, 2 surgical drainages with decortications, and 3 resection and reconstructions.

Patients who underwent primary repair were grouped into 3 categories based on their time from perforation to treatment: First, those undergoing treatment less than or equal to 24 hours from their perforation; second, those who underwent treatment between 25 and 72 hours from their perforation; and third, those who underwent treatment greater than 72 hours from their perforation. Mortality rates between the 3 groups are virtually identical (8%, 6%, and 8% respectively).

In an attempt to determine which factors had the most influence on mortality, all patients were grouped into those that died and those who survived, and variables shown in Table 1 were analyzed as contributors to mortality by univariate and multivariate logistic regression described above. With respect to univariate analysis, malignant perforations ($p = 0.0008$), patients requiring mechanical ventilation on presentation ($p = 0.006$), patients presenting with sepsis ($p = 0.08$), and patients who had pulmonary comorbidities preoperatively ($p = 0.02$) or were severely malnourished ($p = 0.001$), all were statistically significantly associated with mortality. A higher Charlson comorbidity index was also associated with an increased risk of mortality ($p = 0.0004$). A wait time of greater than 24 hours was not associated with an increased risk of mortality ($p = 0.52$).

The multivariate logistic regression analysis revealed that patients with preoperative respiratory failure requiring mechanical ventilation had a mortality odds ratio of 32.4 (95% CI 3.1 to 272.0), followed by malignant perforations with an odds ratio of 20.2 (95% CI 5.4 to 115.6), a Charlson comorbidity index of greater than or equal to 7.1 with an odds ratio of 19.6 (95% CI 4.8 to 84.9), preexisting pulmonary comorbidities with an odds ratio of 13.9 (95% CI 2.9 to 97.4), and presentation with sepsis with an odds ratio of 3.1 (95% CI 1.0 to 10.1) (Table 5). Malnutrition was no longer significant.

Comment

The perforated esophagus continues to remain a difficult clinical entity to deal with, and a condition that carries with it a great deal of morbidity for the patient. Thus, it is imperative that approaches to and outcomes of patients

Table 2. Patient Demographics by Perforation Site

Characteristic	Cervical Perforations	Benign Thoracic Perforations	Malignant Thoracic Perforations	Abdominal Perforations
Number of patients	15	79	16	9
Age, years (mean/median/range)	67.1/69/39–85	65.6/64/8–92	65.5/64/46–84	50.5/42/22–84
Gender (male/female)	3/12	59/20	7/9	5/4
Mean ASA score	3.3	3.6	3.7	3.3
Comorbidity score (mean, score out of 9)	1.4	1.6	2.5	1
Charlson comorbidity index (mean, score out of 37)	3.7	2.8	6.3	1.8

Patients sustaining abdominal perforations were considerably younger on average than those in the other three categories were. Both the mean ASA score and the comorbidity score were highest in the malignant thoracic perforation group.

ASA = American Society of Anesthesiologists.

Table 3. Patient Presentation and Treatment by Site of Perforation

Variable	Cervical Perforations	Benign Thoracic Perforations	Malignant Thoracic Perforations	Abdominal Perforations
Number of patients	15	79	16	9
Mean/median time to treatment (hours)	36.6/10	64.8/20	128.7/45	18.8/14
Initial presentation Severity score (mean, score out of 3)	0.4	0.625	0.666	1.13
Treatment				
Primary repair	10	57	3 (2 received stents)	6
Resection & diversion	0	6	1	1
Exclusion and Diversion	0	1	1	1
Resection and Reconstruction	1	0	6	1
Surgical drainage ± decortications	2	6	2	0
Chest tubes	0	5	2	0
Compassionate care	2	4	1	0

The majority of patients with cervical, benign thoracic, and abdominal perforations were treated with primary repair. Patients with malignant thoracic perforations were treated more commonly by other methods. Resection and reconstruction represented the most common method by which these patients were managed. The initial presentation severity score is a nonvalidated score in which patients are given a single point for the presence of sepsis syndrome, respiratory failure requiring mechanical ventilation, and hemodynamic instability requiring vasopressor or inotropic support.

with esophageal ruptures continue to be analyzed to optimize our management of this highly morbid condition. We present the largest single-institution series of esophageal perforations in the literature to date in the hopes of furthering the evolution of the management of this clinical entity.

Many studies [2, 8, 16, 17] have indicated that the interval time from perforation to treatment has a significant impact on mortality, with an interval of less than 24 hours being associated with a significant reduction in morbidity and mortality [2, 16, 18–20]. In a recent review of the literature, Brinster and colleagues [2] reported that mortality increased by a factor of 2 if diagnosis, and thus treatment, was delayed by more than 24 hours. Although this has become an accepted tenet in the literature, in our analysis of 119 consecutive patients, wait time to treatment was not associated with a significant increase in mortality (Table 5). What was more critical, however, was the underlying condition of the patient at the time of presentation. The presence of pulmonary comorbidities, malignancy, preoperative sepsis, and patients requiring mechanical ventilation at time of presentation (indicative of a severe inflammatory response to the perforation) were all associated with a significant increase in the risk of mortality in patients with thoracic esophageal perforations.

Our perioperative mortality rates were influenced by both the site and underlying etiology of the esophageal perforations, facts that have been documented extensively in the literature [16, 18, 19, 21–24]. Cervical esophageal perforations, because of the containment of the contents within the fascial planes of the neck, tend to

Table 4. Length of Hospital Stay, Critical Care Unit Stay, and Number of Days Requiring Mechanical Ventilation by Perforation Site

Variable	Cervical Perforations	Benign Thoracic Perforations	Malignant Thoracic Perforations	Abdominal Perforations
Length of hospital stay (days) mean/median (range)	25.1/14 (7–83)	35.7/23 (5–200)	31.3/25 (8–93)	19.3/10 (1–72)
Number of patients requiring critical care unit	8 (53%)	61 (77%)	13 (81%)	3 (33%)
Number of critical care unit days mean/median (range)	7.0/4.5 (3–26)	16.3/6 (1–150)	15.0/9.5 (1–52)	10.3/3 (1–27)
Number of patients requiring mechanical ventilation	8	59	13	3
Number of days requiring mechanical ventilation mean/median (range)	4.75/1.5 (1–23)	13.3/5 (1–86)	14.0/8.5 (1–49)	9.0/2.0 (1–24)
Postoperative esophageal leak need for reoperation	1 (6.7%)	18 (22.8%)	7 (43.73) (18%)	0 (0%)
Median time from perforation to initial treatment for posttreatment leak (hours)	1	40	168	N/A
Reoperation	1 (6.7%)	18 (22.8%)	3 (18%)	1 (11%)
Postoperative mean morbidity score (range)	0.5 (0–4)	1.2 (0–5)	1.57 (0–4)	1.12 (0–5)

The postoperative morbidity score is a nonvalidated scoring system in which single points are given across 6 domains (sepsis, respiratory failure, myocardial infarction, arrhythmia, renal failure, hepatic failure). Reoperation rates are also shown, and were the highest for the benign thoracic group.

Table 5. Multivariate Analysis

Factor	Multivariable Odds Ratio	95% CI
Mechanical ventilation	32.4	(3.1–272.0)
Malignant perforation	20.2	(5.4–115.6)
Charlson comorbidity index ≥ 7.1	19.6	(4.8–84.9)
Pulmonary comorbidity	13.9	(2.9–97.4)
Sepsis	3.1	(1.0–10.1)

Odds ratios and 95% confidence intervals (CI) for statistically significant factors found in multivariate analysis. Preoperative malnutrition was eliminated during multivariate analysis.

incite less of a systemic inflammatory response than thoracic and abdominal perforations. Perforations occurring in these areas are not as well contained, and thus elicit more of both a local and systemic inflammatory response leading to a compromise in many organ systems, particularly respiratory function [2, 11, 13]. This logically leads to a higher morbidity and mortality rate. In our series, the mortality rate of cervical esophageal perforations was 7.6%, in keeping with the mortality rate of 6% quoted in the review by Brinster and colleagues [2]. However, when thoracic esophageal perforations were subdivided into those with a malignant or benign etiology the perioperative mortality rate in the benign thoracic perforations was similar to that of abdominal and cervical perforations, whereas the mortality rate of malignant thoracic perforations was significantly higher at more than 60%. The fact that malignant esophageal perforations carry with them a higher risk of mortality likely points to a combination of the underlying malignant disease having effects on the patient's overall preoperative status, particularly with respect to nutrition and the more extensive surgical procedures often required in their management.

The necessity for esophageal exclusion and diversion is a controversial issue. Saarnio and colleagues [25] in cases of severe mediastinal sepsis have recently advocated a two-staged repair, with initial esophageal resection and cervical esophagostomy and gastrostomy. We feel that this conclusion is somewhat premature. Clearly, a longer wait time would increase the local inflammatory response in the tissues around the perforation. However, in our retrospective review, time to treatment did not influence mortality to a statistically significant degree, nor did it obviate the possibility of performing a primary repair. Indeed, the mortality rate for patients undergoing primary repair did not increase significantly even if performed at greater than 72 hours. Furthermore, in patients presenting preoperatively with severe sepsis who ultimately survive, exposing them to a second highly morbid operation to reconstruct their gastrointestinal continuity carries with it a significant potential risk. In our series of 119 patients, exclusion and diversion was only performed a total of 11 times (Table 4). The last exclusion and diversion procedure was performed at our institution in 2000 in a patient with a T4 esophageal primary malignancy that had a spontaneous perforation while on chemotherapy and presented in septic shock, and had a grossly devitalized and friable esophagus. We feel our data demonstrate that a two-staged repair, with initial exclusion and diversion of gastrointestinal continuity is unnecessary except in rare cases when anatomically not feasible. However, the number of patients in this subgroup analysis is small, and studies that are more robust are required to adequately define the role of exclusion and diversion in the contemporary management of esophageal perforations.

We did demonstrate in our series that a higher preperforation comorbidity burden negatively influences our primary outcome. Although we did analyze individual comorbidities which we believed would be significant, we attempted to standardize this approach using a widely utilized comorbidity index developed by Charlson and colleagues [15]. Our multivariate analysis did demonstrate that a higher comorbidity index value was associated with a significantly increased risk of mortality. However, the Charlson index is weighted such that malignancy, both locoregional and metastatic, increases the patient's score more significantly than many other of the listed comorbidities. Thus, the fact that malignant perforations, as discussed above, inherently carry with them a significantly increased risk of mortality may, at least in part, explain the significance of this generalized comorbidity index as a determinant of mortality in our study.

There were a few instances where the operating surgeon attempted to primarily repair a malignant perforation using suture closure in addition to wide drainage. It was felt that this maneuver would be the most expeditious method to control the perforation and reduce mediastinal soiling. This technique was performed before esophageal stenting was widely used. Currently, unstable malignant patients would be treated with some combination of wide drainage and stenting.

We recognize that there are a few limitations to our study. First, our study is a retrospective review and not a prospective, randomized trial. Secondly, although this review represents the largest single series review of esophageal perforations, the number of subjects is still relatively small. Adding our data to the cumulative data available in the literature in the form of a systematic review would add more weight to our conclusions, and perhaps will be the scope of a future study.

We present the largest single-institutional review of patients with esophageal perforations, a clinical entity that continues to present a challenge to the thoracic surgeon. The site of perforation, the presence of an underlying malignancy, the presence of severe sepsis or need for mechanical ventilation at presentation, and the preexisting comorbidities of the patient have a significant impact on the overall patient outcome. Time to treatment is not as important to survival as the manner in which patients present, and restoration of intestinal continuity, either by primary repair or by excision and reanastomosis, can be attempted even in patients with a greater time from perforation to treatment with respectable morbidity and mortality rates.

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