Development of a multidisciplinary program to expedite care of esophageal emergencies

Running Title: Esophageal Emergency Program

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Presented at 29th Annual General Thoracic Surgical Club Poster Session

Tucson, AZ March 10-13, 2016

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Key words: esophageal perforation, obstruction emergency

Word count: 2833

Abstract

Background

Level-one programs have improved outcomes by expediting multidisciplinary care of critically ill patients. We established a novel level-one program for the management of esophageal emergencies.

Methods

Following IRB approval, we performed a retrospective analysis of patients referred to our level-one esophageal emergency program from April 2013 through November 2015. A historical comparison group of patients treated for the same diagnosis the prior two years was used.

Results

Eighty patients were referred and transported an average distance of 56 miles (range 1-163). Median time from referral to arrival was 2.4 (range 0.4-12.9) hours. Referrals included six (7%) patients with esophageal obstruction and 71 (89%) with suspected esophageal perforation. Of the patients with suspected esophageal perforation, etiologies included iatrogenic (n=26), Boerhaave's syndrome (n=32), and other (n=13). Forty-six percent (n=33) of patients were referred due to pneumomediastinum but perforation could not be subsequently demonstrated. Initial management of patients with documented esophageal perforation included surgery (n=25), and endoscopic intervention (n=8), and supportive care (n=5). Retrospective analysis demonstrated a statistically significant difference in mean Pittsburgh severity index scores between

esophageal perforation treatment groups ($p<0.01$). In patients with confirmed perforations, there were 3 three (8%) mortalities within 30 days. More patients in the esophageal one program were transferred to our institution in <24 hrs following diagnosis than in the historical comparison group ($p<0.01$).

Conclusions

Development of an esophageal emergency referral program has facilitated multidisciplinary care at a high-volume institution and early outcomes appear favorable.

Abstract word count: 239

Introduction

Level-one clinical programs have been created for the treatment of trauma and cardiovascular emergencies to improve outcomes by expediting multidisciplinary care of critically ill patients. Esophageal perforation and other esophageal emergencies remain challenging with high morbidity and mortality. Meta-analyses have reported overall operative mortality rates for esophageal perforation to range between 12% and 19%.[1, 2] Management delay in these cases has additionally been associated with adverse outcomes.[3, 4] In 2013, using the preexisting infrastructure of our institution's level-one cardiovascular and high-volume esophageal cancer programs, we established a novel level-one program designed exclusively to facilitate management of esophageal emergencies. We sought to review referral details, treatment strategies, and outcomes after the first 30 months of this program's initiation. We compared the program results to a historical control group to determine whether the initiation of our program was successful at expediting the care of patients with esophageal emergencies.

Patients and Methods

We established a novel level-one esophageal emergency hotline using our institution's preexisting level-one patient transfer center. A record of all patients referred to this program was prospectively collected. Following institutional review board approval, we

performed a retrospective review of referred patients from the program's inception in April 2013 through November 2015. We also retrospectively reviewed the medical records of patients treated at our institution for the same diagnoses (esophageal perforation, esophageal obstruction) the two years prior to the initiation of our program as a historical comparison group. All data was managed using Research Electronic Data Capture (REDCap) tool hosted at Indiana University School of Medicine.[5] Collected data included demographic information (age, gender, race), transfer logistics (origination hospital, mode of transportation (ground/ambulance, air/helicopter), time from referral to arrival at our institution, medical co-morbidities (cardiac history, diabetes, chronic obstructive pulmonary disease, previous esophageal disorder), clinical status, type of esophageal emergency and if perforation, etiology and location of injury, treatment type (supportive care, endoscopic management, surgery) and outcomes (hospital length of stay, need for re-intervention, complications, and 30-day mortality).

Patients were initially triaged by already existing infrastructure (from a previously existing cardiovascular emergency program) according to an esophageal emergency algorithm that was developed by our multidisciplinary team consisting of esophageal specialists in thoracic surgery, gastroenterology, and radiology (Figure 1). In brief, upon receiving a referral, transfer center operators conference call the referring physician to the on-call thoracic surgeon and/or gastroenterologist, and radiologist. Operating room and endoscopy charge nurses are also included in the teleconference as indicated. Concurrently, the transfer center operators fax initial resuscitation and antibiotic orders to the referring hospital, assure pertinent radiographic images obtained at the referring

hospital are uploaded onto a radiology cloud server, and arrange for transportation. Upon acceptance of the patient, the patient is transferred via ground or air depending on the patient's clinical status and distance from the referring hospital. The patient is admitted to the step-down unit for further evaluation or supportive care, surgical intensive care unit for further evaluation or supportive care, operating room, or endoscopy suite as determined by the disposition established during the teleconference. The patient is then managed per the accepting on-call thoracic surgeon and/or gastroenterologist.

Unpaired student's t tests were used to compare continuous data, Fisher's exact tests for dichotomous data, and Chi-square for categorical variables. A two-tailed p value of less than 0.05 was considered significant. Data are presented as mean $\pm$ standard error of the mean unless otherwise noted.

Results

From the program's inception on April 1, 2013 through November 30, 2015, 80 patients were referred for an esophageal emergency (Figure 2). Referrals were received from 45 different hospitals. Patients were transported a mean distance of 56 miles (range 1-163) to our institution. Median time from referral to institution arrival was 2.4 (range 0.4-12.9) hours. Twenty percent (n=16) of patients were transported by air while 80% (n=64) of patients transported by ground. Patient demographics and comorbidities are given in Table 1. The median age of referred patients was 52 years (range 18-97); 46%

(n=37) of patients were female and 54% (n=43) were male. Forty-four percent (n=35) of referred patients had a prior history of an esophageal disorder with esophageal stricture (n=8), gastroesophageal reflux (n=6), esophageal malignancy (n=5), eosinophilic esophagitis (n=4), and Barrett's esophagus (n=4) comprising the majority of pre-existing disorders. Comorbidities were prevalent and found in slightly over half of referred patients including 11% (n=9) with a cardiac history, 15% (n=12) diabetes, 16% (n=13) chronic obstructive pulmonary disease, 4% (n=3) renal insufficiency, and 4% (n=3) with cirrhosis.

Figure 2 depicts the reasons for referral to the program and initial treatment delivered. In summary, the reasons for referral included 6 (7%) patients with esophageal obstruction, 71 (89%) patients with suspected esophageal perforation, and 3 (4%) previously established patients (2 complications after esophagectomy and 1 recurrent bleeding esophageal varices). Five patients with esophageal obstruction due to food impaction (n=4) or foreign body (n=1) were successfully managed with endoscopic extraction by gastroenterology. Four of these patients were discharged the day following intervention and one patient had a longer hospitalization due to a pre-existing psychiatric disorder. Another patient with a psychiatric disorder who ingested a fluorescent light bulb was taken directly to surgery for a right thoracotomy and esophagotomy after a failed endoscopic removal attempt at the referring hospital.

Of the seventy-one patients referred for suspected esophageal perforation, etiologies included iatrogenic (n=26), Boerhaave's syndrome (n=32), and other (n=13) (Table 2). Other causes for perforation included incarcerated paraesophageal hernia (n=2), and one patient each with esophageal malignancy, caustic ingestion, foreign body ingestion, osteophyte erosion into the esophagus, and bronchoesophageal fistula. Thirty-three of these patients (46%) were referred due to pneumomediastinum, yet a frank perforation could not be demonstrated on subsequent contrast esophagram. Thirty-eight patients (54%) were confirmed to have a perforation either by referring hospital radiographic studies or additional studies obtained at our institution. The mean age of patients with pneumomediastinum but no perforation was 39 years as compared to 62 years for patients with confirmed perforations ($p<0.01$). Of patients with pneumomediastinum but no perforation, 9 (27%) had a comorbidity, versus 27 (71%) of patients with a confirmed perforation ($p<0.01$). However, there were no significant differences with respect to cardiac history (15% vs. 16%), COPD (15% vs. 18%), or history of an esophageal disorder (33% vs. 50%) respectively.

Of the thirty-eight patients confirmed to have an esophageal perforation, 4 and 34 were contained and non-contained (mediastinum, pleural, or peritoneal spaces) perforations, respectively (Table 3). All but two patients were diagnosed and transferred within 24 hours of perforation. Initial management of patients with perforation included surgery (n=25), endoscopic stent placement (n=8), and supportive care (n=5). Of the patients undergoing surgery, 16 had primary repair, 6 underwent esophagectomy with diversion, 2 had esophagectomy with acute reconstruction, and 1 underwent pleural space

debridement with concurrent stent placement. Reintervention was required in 1 (20%), 4 (50%), and 8 (32%) patients initially treated with supportive care, endoscopy, and surgery respectively, which were not statistically significant. Reintervention in the form of delayed esophagectomy was planned in an observed patient who presented with a contained intra-abdominal leak following a staging endoscopic ultrasound of an adenocarcinoma. Of the patients who underwent esophageal stenting and required reintervention, one patient proceeded to surgery after the stent incompletely excluded a bronchoesophageal fistula and another patient developed a periesophageal abscess and underwent percutaneous drainage. Two patients had repeat endoscopy for stent replacement/repositioning. Three patients undergoing primary surgical repair had persistent leaks requiring endoscopic clips (n=2) and stent placement (n=1). Reintervention in patients undergoing surgery for esophageal perforation also included thoracic duct ligation (n=1), thoracotomy with washout (n=2), repair of fascial dehiscence following a transhiatal esophagectomy (n=1), and dilation of a stricture after primary repair (n=2).

The mean Pittsburgh severity score (PSS)[6] for patients with suspected but no confirmed leak was similar to the PSS for patients with confirmed leak who received supportive care (1.5 vs. 2.0, p=NS). Average PSS for patients undergoing observation for documented leak was significantly lower than for those undergoing endoscopic intervention (6.1, $p<0.01$) or surgery (5.1, $p<0.01$, Table 3). Complications were predominately respiratory in nature and occurred in 62.5% of patients treated endoscopically and 40% of patients undergoing surgery (Table 3). Furthermore, PSS

was not significantly predictive of overall morbidity and mortality between the three categories. Patients with demonstrable perforation treated with supportive care, endoscopically, and surgically had a median hospital length of stay of 3 days, 14 days, and 13 days, respectively ($p<0.01$). In patients with confirmed perforations, there were 3 (8%) deaths within 30 days. Of note, one patient was an 80 year old with multiple comorbidities initially treated with an endoscopic stent and per family request care was withdrawn. Both mortalities in patients undergoing surgery (primary repair n=1, transhiatal esophagectomy n=1) died of cardiac disease, one with history of congestive heart failure and the other sustained a cardiac arrest after discharge while in a subacute rehabilitation facility. Of the six surviving patients undergoing esophagectomy with diversion, three have had successful reconstruction using a substernal gastric conduit. The three other patients were awaiting reconstruction.

In comparison to historical control prior to initiation of this program, 33 patients were treated at our institution for the same diagnoses from April 1, 2011 through March 31, 2013. Figure 3 depicts the change in number of patients referred for an esophageal emergency following the initiation of the esophageal one program. During this time period, referrals were received from 21 different hospitals. Patients traveled a mean distance of 43 miles (range 1-164miles; p=NS) and median time from referral to arrival was 2.7 (range 0-32.5) hours ($p=0.05$). These differences trended toward significance (Table 4). The percentage of patients who were referred who were already inpatients at our institution was 21% (n=7) during this time period, compared to 6% (n=5) following the initiation of the esophageal one program ($p=0.04$). In patients with a confirmed

perforation, non-contained leaks were more prevalent in the esophageal one group than in the historical controls (34/38 versus 18/31, $p<0.01$). Other diagnostic details (location of perforation, PSS), treatment strategy and re-intervention rates were the same between patients with confirmed perforation who were treated before and after the esophageal one program was started (Table 5). More patients in the esophageal one program were transferred to our institution in <24 hrs following diagnosis than in the historical comparison group ($p<0.01$). The mean hospital length of stay for the historical comparison group was 15 days (NS) and the 30-day mortality was 6.5% (NS).

Comment

Esophageal perforation as well as other esophageal emergencies remain a challenging assortment of clinical scenarios whereupon prompt diagnosis and treatment is paramount to successful management. Treatment options for perforation include observation if contained, endoscopic therapy (usually stent placement) if the perforation is of limited size[7-11], or surgical management when a large perforation with gross contamination is present. The basic tenets of surgical management of esophageal perforations include source control of the perforation (either primary repair, which is preferred[12], esophageal resection with concurrent reconstruction, or diversion[13] with drainage. Authors at the University of Pittsburgh developed a perforation severity score (PSS), which was subsequently validated in a separate cohort of patients and found to be predictive of the need for surgical management as well as of mortality.[6,11] A PSS of

greater than 5 is predictive of a greater than 3-fold increase in need for surgical management and carries a 27% risk of death; a PSS of greater than 9 carries 0% survival. Patients with a true esophageal perforation in whom diagnosis and time to treatment are delayed typically have a higher PSS and poorer outcome. Our data support these findings. In our cohort, patients with lower PSS were likely to be successfully treated with observation while patients with higher PSS required endoscopic or surgical management.

Improved outcomes have been demonstrated in institutions performing higher volumes of esophageal surgery as compared to lower volume centers.[14, 15] Similar to the treatment of esophageal neoplasms, optimal treatment of esophageal emergencies, such as perforation, has become a multidisciplinary process. Level-one clinical programs have been created for the treatment of trauma and cardiovascular emergencies and have demonstrated improved outcomes by expediting multidisciplinary care of critically ill patients. Therefore, we established a level one esophageal program with the intent of expediting the care of patients with esophageal emergencies using the infrastructure from the previously established level-one at our institution. In our algorithm, the initial conference call and electronically-shared radiographic images facilitated care by saving multiple conversations prior to and after patient arrival. Moreover, in our experience, a consensus was typically more quickly reached during this teleconference regarding a preliminary disposition at the time of patient arrival including the need for more testing versus immediate intervention.

Finally, the transfer center arranged rapid transport for suspected or documented perforations where time can be critical.

We present results of our level one esophageal program 30 months following its inception. During the two years prior to the establishment of the level one esophageal program, we were referred on average 8 patients with an esophageal emergency every six months. Following the establishment of the program, we have been referred on average 14 patients with an esophageal emergency every six months with the volume being consistent at this increased rate of referral throughout the existence of the program. Similarly, the number of hospitals referring patients with esophageal emergencies to our institution increased from 21 to 45 hospitals. The mean distance traveled by patients to our institution increased from 43 miles to 56 miles, with a decrease in median transportation time from 2.7 hours to 2.4 hours. Finally, in the cohort of patients with confirmed esophageal perforation, 37.5% of patients referred prior to the establishment of the esophageal one program arrived within 24hrs of perforation compared to 94.7% after the inception of our program. By increasing accessibility to care, we feel that we have positively impacted our catchment area with the development of this program. Once the patient arrived to our institution and underwent treatment, the outcomes before and after the initiation of the esophageal one program were comparable. There were no significant differences in the re-intervention, hospital length of stay, and 30-day mortality rates.

One striking and unexpected finding was the relatively large number of patients referred through this program presenting with pneumomediastinum without evidence of mediastinal or pleural fluid by CT imaging. While the volume of patients referred to our institution prior to the inception of the esophageal program was lower than the volume of patients referred following the establishment of the program, all patients referred for a concern for perforation were found to have a perforation. On the other hand, following the inception of the esophageal one program, in 46% of patients referred for a concern for perforation the diagnosis of a perforation was not confirmed by evaluation with an esophagram. These patients were significantly younger with less comorbidities than patients with demonstrable perforation. Some retrospective studies have suggested that contrast studies are unnecessary in this scenario.[16,17] However, we believe that there is little downside to obtain a contrast esophagram with a brief hospitalization for observation. Our experience is therefore in agreement with Careras and colleagues who contend that the diagnosis of a "benign spontaneous pneumomediastinum" is a diagnosis of exclusion after upper aerodigestive tract perforation has been definitely ruled out.[18] That being said, given our experience if it is possible to obtain an esophagram at the referring hospital this should be pursued. If perforation is not confirmed, the expense of transfer as well as the stress of travel on the patient and the patient's family could be avoided.

There are limitations to our data as well as limitations to this type of level one program. Precise time of perforation in some patients, specifically with Boerhaave's syndrome and incarcerated paraesophageal hernia, was not captured due to delay in either

presentation or diagnosis at the referring hospital. Although a general consensus in management was outlined at the outset of the program, individualized treatment plans by the accepting physician augments heterogeneity from case-to-case limiting the interpretation of outcomes. While transportation to our institution was rapid with a median 2.4 hours between referral to institution arrival, travel modality (ground vs. air) was individualized based on patient severity, distance from the referring facility, and in some cases weather conditions precluding helicopter evacuation which impacted travel times. Finally the relatively low incidence of esophageal emergencies may not justify an isolated stand alone level one program but adding this type of program to preexisting institutional level one programs and a high volume esophageal surgery program has required little additional resources.

Esophageal emergencies, including perforation, require rapid evaluation and treatment to optimize outcomes. Moreover, given the wide variety of etiologies and acuity of presentations, a multidisciplinary approach in specialized centers is valuable. A multidisciplinary level one program designed specifically for esophageal emergencies is feasible and in our experience has facilitated treatment of these challenging patients. Based on our experience, we intend to further streamline the care of these patients with increased awareness throughout our catchment area, improved accessibility to timely care, and more defined treatment algorithms and care plans following arrival to our facility.

Acknowledgments

The authors would like to acknowledge all other clinicians who assist in caring for esophageal emergency patients at Indiana University Health, particularly those in the Division of Gastroenterology.

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Table 1. Patient demographics and comorbidities. Patient numbers given with percentage of series in parenthesis.

Age	Median 52 years (18-97)
Gender	
Female	37 (46%)
Male	43 (54%)
Overall/any comorbidities	41 (51%)
Cardiac History	9 (11%)
Coronary artery disease	9
Myocardial infarction	3
Congestive heart failure	2
Atrial arrhythmia	4
Hypertension	30 (38%)
Hyperlipidemia	8 (10%)
Chronic obstructive pulmonary disease	13 (16%)
Diabetes	12 (15%)
Renal insufficiency (creatinine >2)	3 (4%)
Cirrhosis	3 (4%)
Prior esophageal disorder	35 (44%)
Esophageal stricture	8
Gastroesophageal reflux	6
Esophageal malignancy	5
Barrett's esophagus	4
Eosinophilic esophagitis	4
Paraesophageal hernia	2
Esophageal dysmotility	2
Esophagitis	2
Esophageal diverticulum	1
Achalasia	1

Table 2. Etiology for suspected perforation. Patient numbers given with percentage of series in parenthesis.

Boerhaave syndrome	32 (45%)
Iatrogenic	26 (37%)
Other	13 (18%)
Coughing	2
Gastric volvulus	2
Malignancy	1
Caustic ingestion	1
Foreign body ingestion	1
Osteophyte erosion into esophagus	1
Bronchoesophageal fistula	1
Unknown	4

Table 3. Outcomes in patients with confirmed esophageal perforation. Patient numbers given with percentage of initial treatment group in parenthesis.

	Supportive Care (n=5)	Endoscopic Intervention (n=8)	Surgery (n=25)	
Leak				
Contained	3	0	1	
Non-contained	2	8	24	
Location of leak				
Cervical	0	0	1	
Thoracic	3	8	14	
Abdominal	2	0	10	
Time from perforation to arrival				
<24hrs	4	7	25	
≥24hrs	1	1	0	
Pittsburgh Perforation Severity Score	2.0	6.1	5.1	p<0.01
Re-intervention required	1 (20%)	4 (50%)	8 (32%)	NS
Any complication	1 (20%)	5 (62%)	14 (56%)	NS
Respiratory complication	1 (20%)	5 (62.5%)	10 (40%)	NS
Pneumonia	0	3	2	
Atelectasis	0	0	1	
Pulmonary embolus	0	1	0	
Ventilation >48hrs	0	1	6	
Unplanned reintubation	0	0	2	
Tracheostomy	0	0	6	
Other	1	1	4	
Cardiac complication	0 (0%)	2 (25%)	6 (24%)	NS
Myocardial infarction	0	1	0	
Atrial arrhythmia	0	1	5	
Congestive heart failure	0	0	1	
Other	0	0	0	
Acute kidney injury	0 (0%)	1 (12.5%)	1 (4%)	NS
Sepsis	0 (0%)	3 (37.5%)	4 (16%)	NS
Other	0	2	6	NS
Mean hospital length of stay (days)	3	14	13	p<0.01

30-day mortality	0	1 (12.5%)	2 (8%)	NS

Figure Legends

Table 4. General referral differences between the two-year period prior to and after the establishment of the esophageal one program.

	April 2011-March 2013 (n=33)	Esophageal One (n=80)	
Mean distance travelled (miles)	43	56	p=NS
Median time from initial call to arrival (hours)	2.7	2.4	p=0.05
% inpatient referrals	21%	6.2%	p=0.04
% referred for concern for perforation	94%	89%	
% perforation confirmed	100%	54%	p<0.01
% perforation not confirmed	0%	46%	

Table 5. Diagnosis and outcomes in patients with confirmed perforation in the two-year period before and 30months after the establishment of the esophageal one program.

	April 2011-March 2013 (n=31)	Esophageal One (n=38)	
Leak			p<0.01
Contained	13	4	
Non-contained	18	34	
Location of leak			NS
Cervical	3	1	
Thoracic	23	25	
Abdominal	5	12	
Time from perforation to arrival			p<0.01
<24hrs	9	36	
≥ 24hrs	12	2	
Mean Pittsburgh Perforation Severity Score	5	4.9	NS
Intervention type			NS
Supportive care	4	5	
Endoscopic	10	8	
Surgery	17	25	
Reintervention required	14	13	NS
Mean hospital length of stay (days)	15	15	NS
30-day mortality	2	2	NS

Figure 1. Triage algorithm for patient referral.

The figure depicts the work-flow of patients being referred to our institution for an esophageal emergency.

Figure 2. Patient referral pattern and initial treatment delivered.

This chart provides the reasons for referral to our esophageal emergency program as well as initial treatment that was delivered. Eighty patients were referred for esophageal obstruction, suspected or documented perforation, and prior history of care at our institution.

Figure 3. Volume of patients referred for esophageal emergencies before and after the establishment of the esophageal one program.

This graph depicts the volume of patients referred to our institution for an esophageal emergency in six-month increments from April 2011 through November 2015. The arrow (April 2013) marks the inception of the esophageal one program. The last data point consisted of referrals during a three-month period (September 2015-November 2015).