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ORIGINAL ARTICLE

Endoscopic Management of Esophagorespiratory Fistulas: A Multicenter Retrospective Study of Techniques and Outcomes

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Abstract
Background and Aims Esophagorespiratory fistulas (ERF) are a devastating complication of benign and malignant etiologies. ERF are associated with high mortality, short survival, and poor quality of life. We performed a multicenter analysis of patients with ERF undergoing endoscopic treatment.
Methods Multicentre retrospective study.
Results We analyzed 25 patients undergoing 35 procedures over an 8-year period. Our data showed high technical success rates (97.1% of procedures) and with good, but not ideal, clinical success rates (60% of procedures, 80% of patients), which were defined as fistula closure confirmed by radiographic or repeat endoscopic evaluation and/or a lack of recurrent episodes of clinical aspiration to focus on durable ERF closure as opposed to only initial success. Proximal ERF were the most difficult to manage with the lowest overall clinical success rates, highest rates of recurrent aspiration despite endoscopic therapy, highest adverse events, and shortest survival times. Adverse events occurred in 40.0% of our patients and were all minor. Treatment allowed for diet advancement in 75% of patients.
Conclusion This represents the largest recent collection of US data and the first multicenter study evaluating the clinical success of multiple treatment modalities while stratifying data by fistula etiology and esophageal location. The endoscopic approaches detailed in this study offer a minimally invasive and safe choice for intervention with the potential to improve quality of life despite overall suboptimal clinical success and survivorship rates for in with ERF.

Keywords Fistula · TE fistula · Tracheoesophageal · Stent · Clip · Suture · Esophagorespiratory

Introduction

Esophagorespiratory fistulas (ERF) are a pathologic communication between the esophagus and the airway and can be a devastating complication of mediastinal malignancies. They occur in 5–15% of patients with mediastinal or esophageal malignancies, but may also be secondary to benign etiologies such as surgery, stent placement, trauma, and airway cuff-related injury [1]. They have high mortality and poor mean survival due to recurrent aspiration and eventual subsequent lethal pulmonary infections. With supportive care alone, survival is reported as 1–6 weeks [2]. Quality of life is also significantly reduced due to a reduced ability of safe oral intake. Sealing the fistula can reduce aspiration, improve quality of life, and even improve survival. Multiple endoscopic techniques are now utilized to manage ERF including stents, TTS clips, and OTSClips; with or without concomitant airway stents. There are currently limited outcome data in the literature to guide clinical decision making, and studies are largely limited to case reports and small series which often focus on initial success or are based on outdated technology [3, 4]. The aim of this study is to present and analyze the largest recent collection of US data and the first multicenter

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study evaluating the clinical success of multiple treatment modalities while stratifying data by fistula etiology and esophageal location. Outcomes of particular interest included identifying the rates of technical success, clinical success, and adverse events.

Methods

We performed a multicenter, retrospective study of patients with esophagorespiratory fistulae (ERF) who presented to the University of Utah Health Science Center in Salt Lake City, Utah, and Jefferson University School of Medicine in Philadelphia, Pennsylvania. Medical records, endoscopy reports, radiologic studies, pathology reports, and other records were reviewed for patients with ERF between November 2006 and June 2015.

Inclusion criteria were as follows: (1) age 18 years and over and (2) the presence of a confirmed ERF that underwent endoscopic intervention. Patients were excluded if they were a minor, pregnant, or a prisoner. Data were collected on demographic characteristics, fistula location, fistula etiology, and history of aspiration events (both prior to and after endoscopic intervention). All patients meeting inclusion criteria with fistulas who were referred to our institutions during the study period and seen by gastroenterology were included in this study.

Outcome data included type and nature of endoscopic interventions, technical success clinical success, evidence of post-procedure aspiration, diet, need for repeat procedures, and adverse events. Technical success was defined as completion of a therapeutic intervention with accurate deployment of a device (suture, clip, stent, etc.) in the desired position without immediate complication and with apparent endoscopic closure or isolation of the fistula. Clinical success was defined as fistula closure as confirmed by radiographic or repeat endoscopic evaluation and/or a lack of recurrent episodes of clinical aspiration. Survival time or time to last documented contact from the initial intervention was recorded. This study was IRB approved at both centers.

Results

Overview of Fistula Patients

A total of 25 patients (15 males and 10 females) were identified. The mean patient age was 65.4 (range 37–81) years. A total of 23 patients were white and 2 patients were African-American (Table 1).

14/25 (56%) fistulas were secondary to active malignancy. The cancers that contributed to fistulas were: esophageal cancer including 4 adenocarcinomas and 3 squamous cell cancers (7/25, 28%), lung cancer (4/25, 16%), large B cell non-Hodgkin lymphoma (2/25, 8%), and small cell neuroendocrine tumor (1/25, 4%). 11/25 (44%) fistulas were seen in patients with a history of malignancy that were presumed to be cured at the time of their fistula presentation (referred to as "benign" fistula in subsequent text); in these patients, the fistulas were felt to arise as a consequence of oncologic treatment including surgery (6/25, 24%), chemotherapy and/or radiation therapy (1/25, 4%), or a combination of surgery and chemoradiation therapy (4/25, 16%). Fistulas were localized to the proximal esophagus in 12/25 (48%) patients, the mid-esophagus in 5/25 (20%) patients and the distal esophagus in 6/25 (24%) patients. Two patients (2/25, 8%) had multiple fistulas occurring in the proximal and mid-esophagus and in the mid- and distal esophagus, respectively. Twenty (80%) patients experienced at least one documented aspiration event prior to intervention. Speech therapy evaluations or dietary information was available for 12 patients. Of these patients, 10 were dependant on tube feeds, 6 were strict no oral intake of food and fluids (5 of whom were already on tube feeds), and one patient was able to take thick liquids prior to any intervention.

Table 1 Patient demographics

Total number of patients	25
Gender	
Male	15 (60%)
Female	10 (40%)
Ethnicity	
Caucasian	23 (92%)
African-American	2 (8%)
Mean age in years (range)	65.4 years (37–81 years)
Etiology of fistula	
Malignant	14 (56%)
Esophageal	7
Lung	4
Other	3
Benign	11 (44%)
Post-surgical	6
Post-chemoradiation	1
Post-surgical + post-chemoradiation	4
Location of fistula	
Proximal esophagus	12 (48%)
Mid-esophagus	5 (20%)
Distal esophagus	6 (24%)
Multiple fistulas	2 (8%)
Total number of procedures	35

Results by Treatment Modality for Esophagorespiratory Fistulas

Esophageal Stents

Esophageal stents were the most frequently employed treatment modality to treat ERF and were utilized in 23/25 (92%) patients and in 30/35(85.7%) procedures. The stents used were as follows: 11 Endomaxx (Merit), 11 Wallflex (Boston Scientific), 5 Polyflex (Boston Scientific), and 3 Evolution (Cook Endoscopy) were used. All but three esophageal stents were fully covered. The partially covered self-expanding metal stents were utilized in patients with unresectable esophageal squamous cell cancer that had already invaded into the trachea; stents were used for palliation in these instances. Stents ranged in size from 18 mm diameter × 90 mm length to 25 mm diameter × 150 mm length. All esophageal stents were placed under general anesthesia and the majority (16/18, 88.9%) used fluoroscopic guidance.

Treatment of Fistulas with Esophageal Stent Monotherapy

Esophageal stents were used as initial monotherapy in 13/25 patients (52%). These fistulas were localized to the proximal esophagus in 6 patients, the mid-esophagus in 3 patients, the distal esophagus in 3 patients, and 1 patient had separate fistulas in both the mid- and distal esophagus. The technical success rate for fistulae treated with esophageal stents as monotherapy was 12/13 (92.3%). In one patient with a benign proximal stricture, the diameter of the deployed stent was too small to completely cover the fistulous open, therefore ultimately requiring the stent to be exchanged for a stent with a larger diameter.

The clinical success rate for esophageal stents monotherapy to treat ERF was 7/13 (53.8%). Aspiration was documented in 5 patients while the stents remained in situ. The average survival/time to last contact was 6.0 months in this group with stents left in situ. In the 6 patients for whom dietary data were available, 3/6 (50%) were able to resume oral intake after esophageal stent placement, with two patients advancing from tube feeds to a mechanical soft diet and one patient advancing from thick liquids to regular liquids and solids.

Repeat procedures were required for 5/13 (38.5%) of these patients. The indications for repeat procedures were ongoing aspiration while the stent remained in situ (3), stent migration with subsequent aspiration (1), and persistent fistula without documented recurrent aspiration (1). A variety of therapeutic interventions were utilized for these patients that failed initial esophageal stent monotherapy, including (1) placement of new esophageal stents only (in three patients), (2) closure of the fistula with an over-the-scope clip (OTSC), (3) combination of closure of the fistula with an over-the-scope clip, placement of a new esophageal stent and an airway Y stent. Clinical success in the 5 patients that failed initial stent monotherapy was eventually achieved in 4/5 (80%) of these patients after one or two further follow-up procedures (Table 2).

Treatment of Fistulas with Esophageal Stents and Concomitant Airway Stents

Esophageal stents were combined with airway stents as initial therapy in 6/25 (24%) patients. Two Y stents and six tracheal stents were utilized. The Y stents were used to treat proximal fistulas, whereas the tracheal stents were used for fistula located in the proximal, middle, and distal esophagus. All airway stents were placed under general anesthesia. The technical success rate for the initial treatment of fistulae with concomitant esophageal and airway stents was 6/6 (100%) while the clinical success rate was 2/6 (33.3%). Recurrent aspiration occurred in 3/6 (50%) patients. The average survival/time to last contact was 3.0 months in this group. In patients for whom dietary data were available, 3/3 (100%) were able in advance their PO intake from NPO and/or tube feeds to a mechanical soft diet.

The indication for repeat procedures was repositioning of the esophageal stent after recurrent aspiration and dysphagia in the first patient and stent migration with recurrent aspiration in the second patient. In both cases, repeat procedures also utilized esophageal stents combined with airway stents and did not achieve clinical success (Table 2).

OTSClips

OTSClips were used in a total of 5 procedures. A single OTSClip was used for each of the procedures. All procedures were technically successful. OTSClips were used in combination with esophageal stents as the initial intervention of three patients with fistulas, including a proximal malignant fistula and two distal benign fistulas. There was no documented aspiration post-procedure, and clinical success was achieved in all three patients. The average survival/time to last contact was 7.33 months.

OTSClips were used in the follow-up procedures of two patients with persistent fistulas after initial therapy with esophageal stents. One OTSClip was used as monotherapy for a benign mid-esophageal fistula. The other procedure used an OTSClip in combination with an esophageal stent and concomitant Y airway stent for a proximal benign fistula. Both patients had persistent aspiration post-procedure and neither intervention achieved clinical success.

Table 2 Clinical success in the eight patients requiring repeat procedures

Patient #	Initial intervention	Second intervention	Clinical success (second procedure)	Third intervention	Clinical success (third procedure)
1	Esophageal stent	Esophageal stent	Yes		
2	Esophageal stent	Esophageal stent	Yes		
3	Esophageal stent	Endoscopic stent	No		
4	Esophageal stent	OTSClip	No	Clip and APC	Yes
5	Esophageal stent	Esophageal stent and OTSClip and airway Y stent	No	Esophageal stent and bronchoscopic guided cautery and an ENT placed suture across the fistula	Yes
6	Esophageal stent and airway stent	Esophageal stent and airway stent	No		
7	Esophageal stent and airway stent	Esophageal stent and airway stent	No		
8	Endoscopic clip	Endoscopic clip	Yes		

Other Interventions

Other interventions utilized included endoscopic clips, esophageal stent combined with an endoscopic suture, esophageal stent in combination with bronchoscopic guided cautery and a suture placed across the fistula (by an ENT surgeon), endoscopic clip combined with APC, and isolated Y airway stent (Table 3).

The technical and clinical success rates for each treatment modality are summarized in Table 4.

Results by Fistula Type

Benign

There were 11 patients with benign fistulas. The therapeutic interventions performed included esophageal stents (8), esophageal clips (2), OTSClip (1), airway stent (1), esophageal stent and airway stent (1), esophageal stent and OTSClip and airway stent (1), esophageal stent and OTSClip (1), esophageal stent and OTSClip and suture (1),

Table 3 Outcomes in the six patients who received treatments beyond stents or over-the-scope clips

Patient #	Interventions in a specific patient	Initial or repeat procedure	Fistula type	Fistula location	Technical success	Clinical success	Diet before	Diet after	Average survival/time to last contact (months)
1	Endoscopic clip (×4)	Initial	Benign	Proximal	Yes	No	Tube feeds	Tube feeds	5.5
2	Endoscopic clip (×3)	Repeat	Benign	Proximal	Yes	Yes	Tube feeds	Regular diet	2.8
3	Esophageal stent + suture	Initial	Malignant	Mid	Yes	Yes	NA	NA	6.8
4	Esophageal stent + bronchoscopic guided cautery + a suture placed across the fistula (by ENT surgeon)	Repeat	Benign	Proximal	Yes	Yes	NPO, tube feeds	NPO, tube feeds	0.23
5	Endoscopic clip + APC	Repeat	Benign	Mid	Yes	Yes	Mechanical soft	Regular diet	4.8
6	Isolated Y airway stent	Initial	Benign	Proximal	Yes	Yes	Tube feeds	Regular diet	4.1

NA = data not available

Table 4 Overall outcomes by intervention

Intervention	Number of procedures	Technical success	Clinical success
Esophageal stent monotherapy	16	15/16 (93.4%)	9/16 (56.3%)
Esophageal stent + airway stent	8	8/8 (100%)	3/8 (37.5%)
Esophageal stent + OTSClip	2	2/2 (100%)	2/2 (100%)
TTS clips	2	2/2 (100%)	1/2 (50%)
Esophageal stent + OTSClip + airway stent	1	1/1 (100%)	0/1 (0%)
Esophageal stent + OTSClip + endoscopic suture	1	1/1 (100%)	1/1 (100%)
Esophageal stent + endoscopic suture	1	1/1 (100%)	1/1 (100%)
Esophageal stent + bronchoscopic guided cautery + a suture placed across the fistula (by ENT surgeon)	1	1/1 (100%)	1/1 (100%)
OTSClip	1	1/1 (100%)	0/1 (0%)
TTS clip + APC	1	1/1 (100%)	1/1 (100%)
Isolated airway stent	1	1/1 (100%)	1/1 (100%)

endoscopic clip and APC (1), and esophageal stent and bronchoscopic guided cautery and a surgical suture placed across the fistula by an ENT surgeon (1). Technical success was achieved in 17/18 (94.4%) procedures. At least one episode of aspiration occurred in 5 patients. Durable clinical success was ultimately achieved in 10/11 (90.1%) patients with benign fistulas. The average survival/time to last contact was 6.8 months for this group.

Malignant

Seventeen procedures were performed in 14 patients with fistulas due to confirmed active malignancy. Therapeutic interventions included esophageal stents (8), an esophageal stent combined with an airway stent (7), an esophageal stent and an OTSClip (1), and an esophageal stent combined with an endoscopic suture (1). All procedures (17/17, 100%) were technically successful. Aspiration occurred in 4 patients. Clinical success was ultimately achieved for 10/14 (71.4%) patients with active malignancy. The average survival/time to last contact was 3.3 months for patients with fistulas secondary to active malignancy.

Results by Fistula Location

Proximal Esophagus

Fistulas were located in the proximal esophagus in 12 patients, and these patients underwent a total of 20 procedures. A plurality was managed with esophageal stents alone (9/20 procedures, 45%), followed by combined esophageal and airway stenting (5/20 procedures, 25%), esophageal stent and OTSClip (2), endoscopic clips (2), an airway stent alone (1), and esophageal stent and bronchoscopic guided cautery and an ENT placed suture across the fistula (1). The technical success for therapy of proximal fistulas was 95%. Aspiration was documented after initial intervention in 6 patients; however, durable clinical success was ultimately achieved in 75% patients with proximal fistula after their final intervention. The average survival/time to last contact was 4.2 months.

Mid-esophagus

Five patients had a fistula located in the mid-esophagus and underwent a total of 7 procedures. Interventions included esophageal stents (3), esophageal and airway stent (1), OTSClip (1), esophageal stent and suture (1), and clip and APC (1). The technical success rate was 100%. Clinical success was ultimately achieved in 5/5 (100%) of patients with mid-esophageal fistula. The average survival/time to last contact was 6.0 months.

Distal Esophagus

Fistulas were localized to the distal esophagus in 6 patients, and these patients underwent a total of 6 procedures. Therapeutic interventions included esophageal stents (3), esophageal and airway stents (1), esophageal stent and OTSClip (1), and esophageal stent and OTSClip and suture (1). Two of the three patients managed with esophageal stents required the placement of two stents to treat the single distal fistula. All the interventions were technically and clinically successful. The average survival/time to last contact was 7.8 months.

Multiple Fistula

Two patients had two fistulas occurring simultaneously. One patient had fistulas present in the proximal and mid-

esophagus that was managed with an esophageal stent and concomitant airway stent. The procedure was technically successful; however, aspiration was documented post-procedure and clinical success was not achieved. The second patient had fistulas localized to the mid- and distal esophagus, and both technical and clinical success were achieved with a single esophageal stent. The average survival/time to last contact was 0.07 months (2 days) and 3 months for these patients, respectively.

Adverse Events

Adverse events occurred in 10/25 (40.0%) patients. Documented adverse events included stent migration (5), pain (4), dysphagia (1), fistula site bleeding (1), reflux (1), pneumonia (1), stent infolding (1), and foreign body sensation (1) (Table 5).

Adverse events occurred in 6/16 (37.5%) procedures using esophageal stents and in 3/8 (37.5%) of procedures using concomitant esophageal and airway stents. One adverse event occurred after intervention with an esophageal stent and OTSClip.

Adverse events occurred in 6/14 (42.9%) patients with a malignant fistula and in 4/11 (36.4%) patients with a benign fistula.

Adverse events occurred in 7/12 (58.3%) patients with a proximal fistula, 1/5 (20%) patients with a mid-esophageal fistula, and 1/6 (16.7%) patients with a distal fistula. Additionally, 1 adverse event occurred in a patient with multiple fistula occurring in the proximal and mid-esophagus.

Clinical success was ultimately achieved in only 5/10 (50%) of patients after an adverse event. The average survival/time to last contact was 5.4 months in patients who experienced adverse events, compared to 4.9 months if there was no adverse event.

Table 5 Adverse events

Total adverse events	15
Stent migration	5 (33.3%)
Pain	4 (26.7%)
Dysphagia	1 (6.7%)
Fistula site bleeding	1 (6.7%)
Reflux	1 (6.7%)
Pneumonia	1 (6.7%)
Stent infolding	1 (6.7%)
Foreign body sensation	1 (6.7%)

Discussion

The present study is, to our knowledge, the largest recent collection of US data and the first multicenter study evaluating the clinical success of multiple treatment modalities for the endoscopic management of esophagorespiratory fistulas while also stratifying data by fistula etiology and location.

In patients with esophagorespiratory fistulas, endoscopic interventions are used in an attempt to create a seal between the lumen of the esophagus and the airway so as to reduce bronchial contamination and enable safe enteral feeding [5]. Our data demonstrate a high technical success rates (97.1% of procedures) for endoscopic management of ERF. Similar high technical success rates are described in the literature with rates of up to 100% for esophageal and/or airway stents [5, 6].

Although adverse events occurred in 40.0% of our patients, they were all minor. These rates of adverse events in patients with ERF are in concordance with other trials where AEs were 37% for patients treated with esophageal stents, 15% (combined stenting), 43% (esophageal, airway or combined) [6–8]. There were, however, no *significant* procedural complications directly related to the placement of a therapeutic device in our population, whereas other studies have reported these rates of 0–17% [9]. Significant procedure-related complications reported in prior studies include tracheal compression following esophageal stent placement in 7–10% of patients, respiratory failure requiring transient ventilation in 6% of patients, perforation or massive bleeding due to stent placement, and procedure-related death in up to 15.9% of patients [5, 8–11]. The use of concomitant airway stents in our study did not increase the rates of adverse events or the aforementioned significant procedure-related complications, but they also did have lower overall clinical success rates compared to esophageal stent monotherapy (33.3 vs 53.8%).

The high technical success rate combined with the low morbidity of endoscopic procedures in our study supports their role in the management of ERF. Furthermore, 75% of patients were able to advance their oral intake after treatment of their fistula. Since the majority of these patients have a poor survival, the ability to safely engage in per oral intake is an important quality of life measure.

It should be noted that technical success does not necessarily translate to clinical success in patients with ERF. Our data show the endotherapy has good, albeit not ideal, clinical success of 80%. Some fistulas are simply too large or too complex to be fully treated by any currently available means. Rates of fistula closure with esophageal and/or airway stents vary from 67 to 100% within the literature, although these results are generally based on studies of

relatively few patients without documentation of longer-term follow-up of fistula occlusion [1, 6, 10, 12–17]. Our definition of clinical success required confirmation by radiographic or repeat endoscopic evaluation and/or a lack of recurrent episodes of clinical aspiration and focused on durable ERF closure as opposed to initial success. The discrepancy between initial closure and durable clinical success is prominent in our data. Similar findings were also noted in a 2004 single-center Korean study that focused on the use of covered expandable metallic stents to treat ERF. The Korean study showed an 80% (49/61) initial clinical success rate, but over a mean follow-up of 13.4 weeks 35% fistulas was no longer felt to be sealed, and therefore, durable clinical success was only achieved in 47.5% of patients [6]. Other reported rates of fistulas reopening after initial closure are as high as 20% [6, 10]. The main cause of clinical failure reported in the literature is spillage of contrast medium through a gap between the proximal stent margin and the esophageal wall despite an adequate positioned stent, aka the so-called funnel phenomena [6, 11]. Some authors have thus advocated that a repeat esophagogram should routinely be performed at 1 week and then every 1–2 months to evaluate for persistent fistula closure [13].

Our results represent the first multicenter study to report how clinical outcomes vary with regards to the esophageal location of the fistula. Proximal ERF were the most difficult to manage, and these lesions had the lowest overall clinical success rates and the highest rates of recurrent airway aspiration despite endoscopic therapy. Additionally, patients with proximal ERF had the highest rates of adverse events. A 2001 study has also noted increased complications with proximal malignant obstructions and fistula, although they described relatively high rates of adverse events including a 15.9% death rate from complications directly related to stent placement [11]. Our study also showed distal fistulas were associated with longer survival times and mid-esophageal fistula had intermediate survival, suggesting that fistulae involving the trachea are the most ominous. A single-center European study has also described outcomes based on tracheobronchial location and showed that fistula located in the carina, left main bronchus and trachea had higher survival than those in the right main bronchus [5]. The authors suggested that the trachea and left main stem bronchus have more anatomic proximity to the esophagus and therefore right main bronchus fistula reflects more severe disease given the "reach" involved to create the fistula. The poor outcomes seen with proximal fistulas in our data may reflect the potential for widespread contamination of both lung fields that occurs when aspirated contents enter into the trachea and can infect both bronchi. On the other hand, inflammation is likely to be more localized with distal ERF where contamination occurs further down the respiratory tree and may be confined to one lung field. Furthermore, endoscopic treatment of fistulas in the proximal esophagus may be complicated and limited by proximity to the UES, especially with stents as some ERF are too close to the UES to allow safe and/or symptomatically tolerable stent placement.

This is also the first study to analyze the association between fistula etiology and clinical outcomes. As expected, survival times were lower for malignant fistula after intervention compared with benign fistula (3.3 vs 6.8 months mean survival). Clinical success rates were also lower for malignant fistula (70.4 vs 90.1%), a finding that has not been reported previously.

There is a grade C recommendation in the 2003 American College of Chest Physician guidelines that stenting of both the tracheobronchial tree and the esophagus yields the best overall results for symptom relief, although the data supporting this is not robust [18]. Despite this recommendation, dual stenting is not standard in clinical practice, possibly due to limited access to interventional pulmonologists. Interestingly, clinical success rates were lower with concomitant esophageal and airway stents compared to esophageal stent monotherapy. Our success rate with dual therapy was only 33.3%, compared to a 2013 study showing that fistula occlusion was achieved in 70% of patients with dual therapy [8]. This may be a reflection of combined stenting being utilized for larger, more complex fistula, i.e., combined stenting may be a surrogate marker for more severe patient illness and/or more severe ERF. Furthermore, 6/8 of these procedures using concomitant stenting involved proximal fistula, which we have now shown to be more challenging to manage. In our data, survival was twice as long with esophageal stent monotherapy compared to combined esophageal and airway management. This difference was not as marked in other studies (esophageal stents 262.8 days vs combined stents 252.9 days), but likely reflects the unfavorable characteristics of the fistulas that were felt to warrant combined esophageal and airway management [5].

With regards to recommendations for physicians attempting to close esophagorespiratory fistulas, we can make several points. First, recognize at the outset of treatment that these patients are seriously ill and may need significant ongoing care with frequent repeat procedures and/or imaging studies. Second, recognize that treatment must be individualized based on the type, size, and location, and number of esophagorespiratory fistula in a given patient. Definitive steps to close a fistula, i.e., suturing, OTSC clipping, are advantageous if they can be applied effectively. Some fistulas are simply too large to be sutured or clipped or the tissue surrounding the fistula is too fibrotic or friable to allow these maneuvers to be performed. Stents (despite their ease of use their ability to rapidly cover a

fistula) can be used to cover large fistulas and can help to reduce the frequency and severity of aspiration, but often do not allow the fistula to truly heal. While a full and formal algorithm is difficult to make in these patients, we would favor definitive methods to close fistulas such as clips if possible as a first line therapy recognizing that many patients will require stenting for large or complex fistulas.

Our study has several limitations. Although this is a multicenter study with relatively large numbers compared to the existing literature, the sample size is still modest. In addition, treatments for these patients are nonstandardized and highly individualized, making our dataset somewhat complex. Efforts were made to identify all long-term outcomes and adverse events, but given the retrospective nature of the study some of this data may not have been available to us despite the fact that our EMR allows for access to patient data from other hospitals in our regions.

Overall, endoscopic therapy for ERF offers a minimally invasive and safe choice for intervention with the potential to improve quality of life despite overall suboptimal clinical success and survival. Future prospective studies are required to define which interventions specific ERF are best suited for.

Compliance with ethical standards

Conflict of interest Dr. Adler is a consultant to Merit Medical and Boston Scientific. Ali Siddiqui is a consultant to Boston Scientific. The other authors have no disclosures.

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