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TRACHEOESOPHAGEAL FISTULAS: AN EPIDEMIC IN THE SARS COV2 PANDEMIC: CASE REPORT

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TRACHEOESOPHAGEAL FISTULAS: AN EPIDEMIC WITHIN THE SARS COV2 PANDEMIC. A CASE SERIES

Tracheoesophageal fistulas (TEFs) can described as a pathological communication between the trachea and the esophagus. According to their origin they may be classified as benign or malignant. Benign TEFs occur mostly as a consequence of prolonged mechanical ventilation, particularly among patients exposed to endotracheal cuff overinflation. During the SARS CoV2 pandemic, the amount of patients requiring prolonged ventilation rised, which in turn increased the incidence of TEFs.

Summary of the cases: We report the cases of 14 patients with different comorbidities such as being overweight, or having been diagnosed with diabetes mellitus or systemic hypertension. The most common symptoms on arrival were dyspnea and cough. In all cases, the diagnosis of TEFs was made through upper endoscopy. Depending on the location and size of each fistula, either endoscopic or surgical treatment was provided. Eight patients were treated endoscopically. Successful closure of the defect was achieved through over the scope clips in 2 patients, while 3 of them required endoscopic metal stenting. A hemoclip was used to successfully treat 1 patient, and it was used temporarily for another patient pended surgery.

Surgical treatment was performed in patients with failed endoscopic management, leading to successful defect correction. Two patients died before receiving corrective treatment and 4 died later on in their clinical course due to infectious complications.

Conclusions: The incidence of TEFs increased during the COVID-19 pandemic (from 0.5% to 1.5%). We believe endoscopic treatment should be considered as an option for this group of patients, since evidence reported in literature is still a growing area. Therefore, we propose an algorithm to lead intervention in patients presenting with TEFs due to prolonged intubation.

Keywords: case report, tracheoesophageal fistula, COVID-19, endoscopy/therapy, gastroenterology/therapy

Core Tip: Due to the significant increase in tracheoesophageal fistulas presenting in patients with severe pneumonia due to COVID-19, we recommend early identification and correction of risk factors for TEFs in this group of patients. For instance, it should become a standard of care to frequently measure endotracheal cuff pressure and, if possible, to periodically evaluate the tracheal mucous through bronchoscopy in order to identify early lesions that could lead to TEFs. Regarding treatment, we recommend providing initial endoscopic treatment until optimal conditions for surgical management are achieved, whenever technically possible due to size and location of the fistula**.**

Tracheoesophageal fistulas (TEFs) are defined as abnormal communications between the esophagus and the trachea or bronchi, leading to the passage of oral and gastric secretions into the respiratory tract.[1] TEFs can be classified into two main categories: congenital or acquired. The congenital form is frequently associated with type C esophageal atresia (85%), presenting in an isolate manner in 4% of cases. Characteristically, clinical manifestations of this condition develop early in life.[2,3,4]. On the other hand, acquired TEFs mainly affect adults and are most frequently found in the cervicothoracic junction. TEFs can be malignant or benign. Each type constitutes approximately half of the acquired cases. [4]

Malignant TEFs are a catastrophic complication of invasive neoplasms of the esophagus (squamous cell carcinoma), trachea, lung, or mediastinum[4,5,6]**.** On the other hand, benign fistulas mainly develop due to prolonged mechanical ventilation (through an endotracheal tube or tracheostomy); blunt trauma to the neck and chest; traumatic or surgical injury of the esophagus, granulomatous mediastinal infections; previous esophageal stents, or ingestion of foreign bodies/corrosives[5]. In patients undergoing invasive mechanical ventilation, some of the risk factors for TEFs include prolonged intubation, endotracheal cuff overinflation, excessive movement of the endotracheal tube (prone positioning), hypotension, diabetes mellitus, previous respiratory tract infections, use of steroids and requiring nasogastric tube feeding, among others[7,8].

The most common clinical presentation of TEFs includes respiratory distress, dysphagia, cough after swallowing (ONO sign), malnutrition and recurrent pulmonary infections. The severity of symptoms largely depends on their size and location[8,9]. A diagnosis should be made by combining characteristic findings on thoracic imaging (esophagogram, chest tomography with 3D reconstruction) and those on endoscopic studies such as bronchoscopy and upper endoscopy. These studies are also essential when planning the best treatment option for each patient[1,8,10,11].

The mean survival reported for patients with TEFs is less than 3 months from the time of diagnosis. As such, adequate treatment should include an immediate multidisciplinary approach, including specialists in critical care, interventional pulmonology, gastroenterology, and thoracic surgery. Currently there are few case reports regarding TEFs due to prolonged intubation in patients with COVID-19[12,13,14,15,16]. We herein present a case series on patients with COVID-19 who develop TEFs, while discussing diagnostic and therapeutic approaches.

Case presentations

Before creating this case series, we obtained informed consent from each patient or their legal guardians. We included patients who were admitted to a university hospital in the city of Bogotá, Colombia in the period comprised between November 2020 and December 2021. We identified 14 adult patients with severe SARS CoV2 pneumonia who developed TEFs as a complication of prolonged mechanical ventilation.

We present the sociodemographic variables of the patients and relevant information on their past medical histories in **Table 1**. The average age was 53.5 years (range 38-72 years). Half of the sample was composed by men. Comorbidities were found in 85.7% of the patients, the most frequent being obesity/overweight, diabetes mellitus and systemic hypertension.

Table 1. Characteristics of patients with tracheoesofageal fistulas 2020-2021

Case	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Total n (%)
Age (years)	60	58	72	52	46	63	56	46	41	61	49	39	69	38	
Sex	M	F	M	F	F	F	F	F	M	M	M	M	M	F	
BMI	25.1	34.3	23.9	28.6	32	19.1	28	27	26	29.5	23	32	27.1	23.4	
Past medical history															
Diabetes mellitus	-	X	-	-	X	-	X	X	-	-	-	X	X	-	6 (42.8)
Systemic hypertension	-	-	X	-	-	X	X	X	-	-	-	X	X	-	6 (42.8)
Obesity/Overweight	X	X	-	X	X	-	X	X	X	X	-	X	X	-	10 (71.4)
Other	-	-	PC	-	-	H	-	-	H	AF	-	-	-	-	

M: Male F: Female BMI: Body mass index PC: Prostate cancer H: Hypothyroidism AF: Atrial Fibrillation

The clinical characteristics of the patients are shown in **Table 2**. The most common symptoms, which lead all patients to attend the emergency room were cough and dyspnea. All of the subjects were diagnosed with severe pneumonia due to COVID-19. At least 64.2% presented with septic shock, requiring vasoactive support. All patients required invasive mechanical ventilation for more than 14 days. ARDS was documented in 13 patients, this variable was no available for assessment in one patient. All patients were treated with steroids (Dexamethasone: 6 mg SC OD. for 10 days), steroids were prematurely stopped in one patient due to diabetic ketoacidosis during treatment. All patients received enteral nutrition through nasoenteral tubes.

The pressure of the endotracheal cuff was measured in only 2 patients (14.2%), being greater than 35cmH2O in both cases. TEFs were documented by endoscopic study of the upper digestive tract (100%) and in some cases with three-dimensional reconstruction neck computed tomography (71.4%). All TEFs were found in the proximal esophagus, with an average distance of 16.7cm from the dental arch, and the average diameter was 18.2mm (3-40mm). **Fig 1**

Table 2. Characteristics of patients with tracheoesophageal fistula 2020-2021

Case	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Total n (%)
Reason for consultation															
Fever	X	-	X	X	X	X	-	X	X	-	X	X	X	-	10 (71.4)
Cough	X	X	X	X	X	X	X	X	X	X	X	X	X	X	14 (100)
Dyspnea	X	X	X	X	X	X	X	X	X	X	X	X	X	X	14 (100)
Clinical findings															
Viral pneumonia SARS CoV2	X	X	X	X	X	X	X	X	X	X	X	X	X	X	14 (100)
SOFA	2	6	SD	4	8	SD	SD	10	SD	SD	SD	SD	6	SD	
Clinical course															
Invasive mechanical ventilation	X	X	X	X	X	X	X	X	X	X	X	X	X	X	14 (100)
ARDS	X	X	SD	X	X	X	X	X	X	X	X	X	X	X	
Vasoactive	X	X	SD	X	X	X	SD	X	X	X	SD	SD	X	SD	
Shock	X	X	SD	X	X	X	SD	X	X	X	SD	SD	X	SD	
Steroids	X	X	X	X	X	X	X	X	X	X	X	X	X	X	14 (100)
Dispositivo vía esofagica	X	X	X	X	X	X	X	X	X	X	X	X	X	X	14 (100)
Cuff pressure measurement	-	-	-	X	-	-	-	-	X	-	-	-	-	-	2 (14.2)
Tracheostomy	X	X	-	X	-	-	X	-	X	X	X	X	-	X	9 (64.2)
Gastrostomy	X	-	-	X	-	X	X	-	X	X	X	X	-	X	9 (64.2)
Diagnosis															
Upper gastrointestinal endoscopy	X	X	X	X	X	X	X	X	X	X	X	X	X	X	14 (100)
Computed axial tomography of the neck	X	X	X	X	X	X	N	X	-	N	X	X	N	X	13 (92.8)
Complications															
Tracheitis	X	-	-	-	-	-	-	-	-	-	-	X	X	-	3 (21.4)
Pneumonia	-	-	X	X	X	X	X	X	X	X	-	-	-	X	9 (64.2)
Bacteremia	-	X	-	-	-	-	-	-	-	-	X	-	-	X	3 (21.4)
Clostridioidal infection	-	-	X	-	-	-	-	-	-	-	-	-	-	X	2 (14.2)
Acute kidney injury	-	X	-	-	-	-	-	X	X	X	X	-	X	-	6 (42.8)
Treatment															
Ovesco Clip (OTS clip)	X	-	X	X	-	-	X	-	-	-	-	-	-	-	4 (28.5)
Hemoclip (TTS endoclip)	-	-	-	-	-	-	X	-	-	X	-	-	-	-	2 (14.2)
Self-expanding metallic stent	-	X	-	-	-	-	-	X	-	-	-	X	-	-	3 (21.4)
Surgery	X	-	-	X	-	X	-	-	X	-	X	X	-	X	7 (50)

ND: No data; SOFA: Sepsis Organ Failure Assessment; ARDS: Acute Respiratory Distress Syndrome; N: No fistula detected

All of the patients had bacterial infectious complications, including tracheitis (21.4%), pneumonia (64.2%) and bacteremia (21.4%). Therefore, they required treatment with broad-spectrum antibiotics leading to Clostridioides difficile infection in 14.2% of the sample. Six patients developed terminal acute kidney injury requiring renal replacement therapy. For the closure of TEFs, 8 patients were taken to temporary or definitive endoscopic treatment: 4 patients needed over the scope clips (OTS clip), achieving successful endoscopic closure in 2 patients. Clip placement failed in one of the patients due to tissue fibrosis; a recurring defect was documented in another patient. Three patients received temporary management with a fully coated metallic stent (SEMS), managing to completely cover the defect. Hemoclips (TTS endoclips) were used in 2 patients. In one patient, with a 3mm

TEF, adequate closure of the defect was achieved; while in another patient temporary reduction in diameter was achieved, allowing further management with an OTS clip **Fig 1**. In 6 patients, a surgical approach was indicated given the location and size of the fistula. Surgical management was also provided to the patient with failure to therapy with the OTS clip, achieving successful correction of the defect. On follow-up, recurrence of TEFs was observed in only one patient treated with an OTS clip, and an increase in the size of the fistula was detected, for which surgical therapy was considered, successfully closing the defect. Despite the efforts made, 42.8% (6/14) died due to infectious complications, two patients died before receiving surgical management.

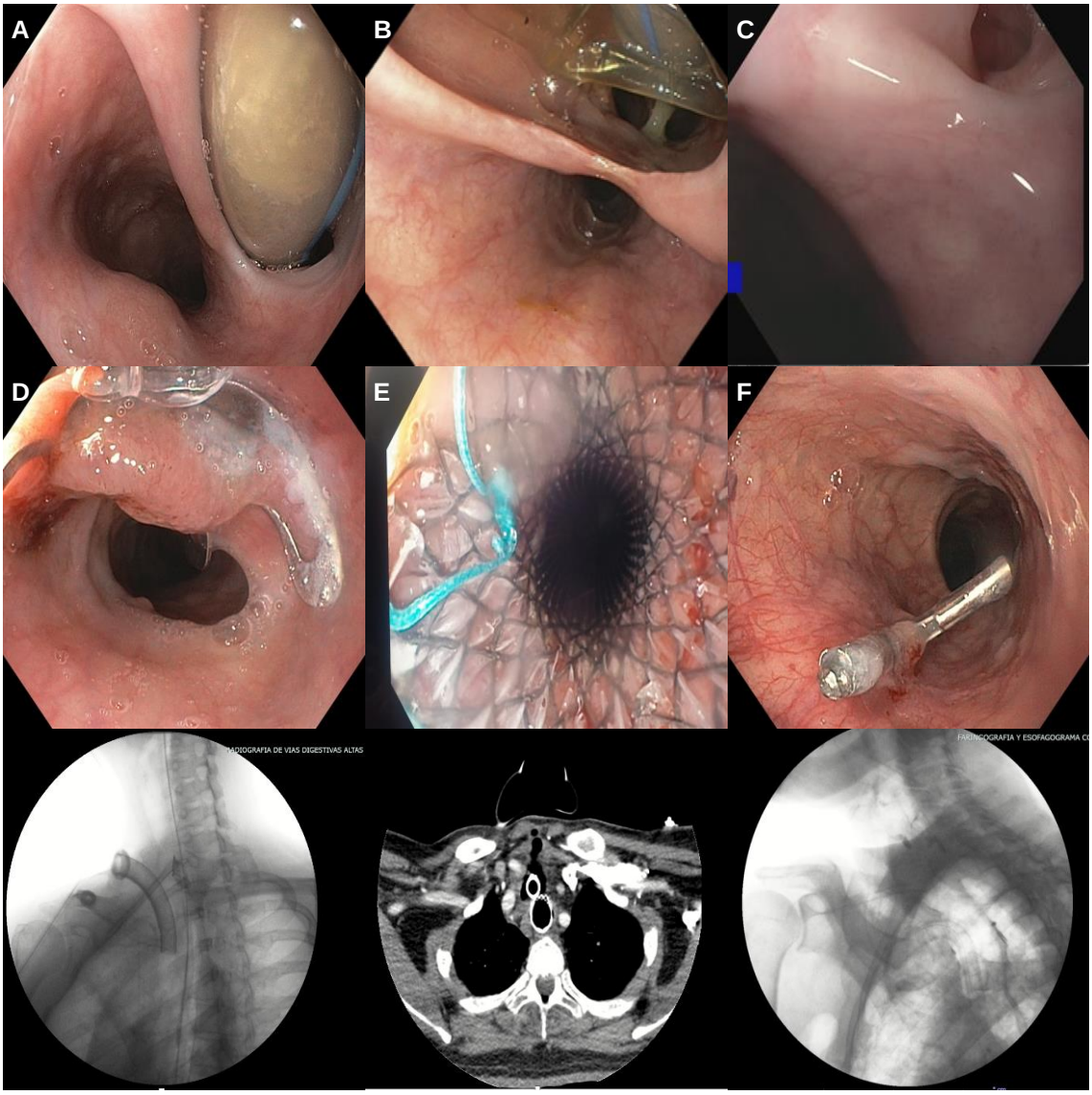

Fig. 1 A: 20mm TEF; B: 30mm TEF; C: 3mm TEF; Endoscopic treatment D: OTS clip closure; E: Closure with a partially coated self-expanding metal stent; F: Closure with a TTS endoclip; G: Esophagogram without leakage- OTS clip therapy; H Computerized axial tomography showing closure of TEF with fully covered SEMS; I: Esophagogram displaying TEF closure through TTS endoclips, with aspiration due to deglutition disorder. (Further pictures and videos may be found as supplementary material)

Discussion

Acquired tracheoesophageal fistulas are a rare clinical entity, with incidence rates approaching 0.5%. Up to 75% of cases are due to trauma related to endotracheal cuff overinflation or prolonged mechanical ventilation[4,8,17]. The pressure exerted by the endotracheal tube cuff erodes the tracheal mucosa, leading to ischemic destruction of the tracheal cartilage, which creates a communication with the esophageal wall[4,8].

The current health situation, due to the SARS Cov2 pandemic, which significantly increased cases of severe pneumonia and ARDS, led to a parallel increase in TEFs associated with prolonged endotracheal intubation. We found that 14 out of 894 patients undergoing mechanical ventilation for severe COVID-19 pneumonia, developed TEFs (incidence 1.56%). In most patients, several risk factors were simultaneously found; these included prolonged mechanical ventilation, hypotension, steroid use, diabetes mellitus, obesity, excessive movement of the endotracheal tube due to frequent position changes (supine-prone) [18]. We hypothesize that monitorization of the endotracheal cuff pressure was insufficient; possibly due to overcrowding in critical care units, as well as the exhaustion, anxiety, and depression developed by healthcare workers during the pandemic.[19,20,21]

Spontaneous closure of tracheoesophageal fistulas is rare, and therefore requires the use of different treatment approaches, including endoscopic and surgical options[4,23,24]. Among the endoscopic options is the use of fully coated metallic stents (SEMS), OTS clips, TTS endoclips and suture systems among others[25,26,27,28]; These procedures have allowed for high success rates (73-83%) regarding closure of perforations, leaks and gastrointestinal fistulas[29]. However, due to TEFs low incidence, no consensus guidelines on the management of this entity currently exist, particularly concerning patients with SARS CoV2 infection. It has been reported that mechanical ventilation increases the risk for suture dehiscence. Furthermore, comorbidities and the critical condition of patients with severe COVID-19 pneumonia usually leads to deferral of surgical procedures until after mechanical ventilation withdrawal. This is why considering endoscopic interventions as initial management in critically ill patients with tracheoesophageal fistula associated with mechanical ventilation due to Covid 19 should be sought.

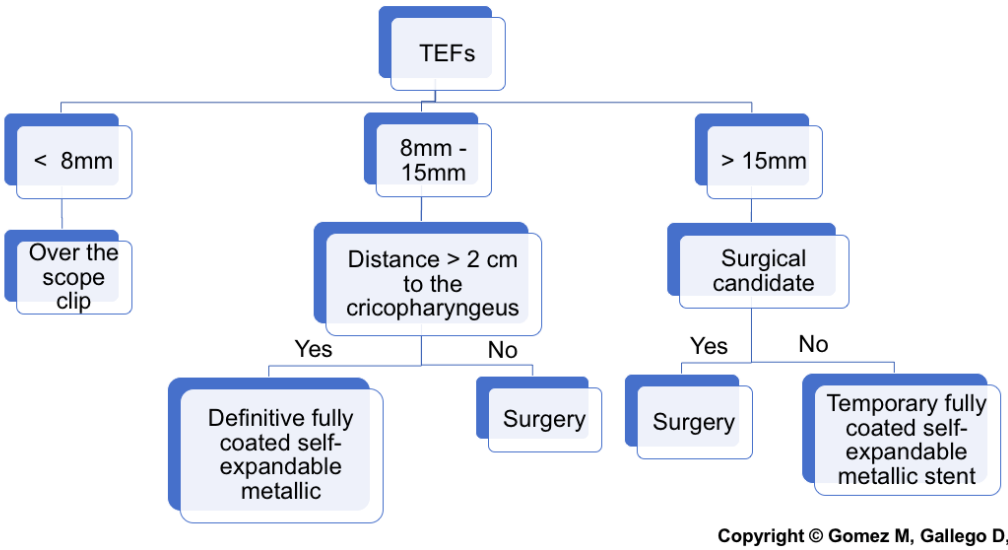

Fig. 3 Suggested treatment algorithm

We present a treatment algorithm for this group of patients in **Figure 3.** Our approach is determined by the size and location of the fistula, using OTS clips for defects below the size of 8mm. For lesions between 8 and 15mm we suggest to use SEMS as long as the fistula is more than 2 cm distal to the cricopharyngeus where the stent can be properly fixed. In lesions larger than 15 mm, we propose upfront surgical treatment, as well as when the fistulas are less than 2 cm from the cricopharyngeus (because at this distance the stent may lead to foreign body sensation). When the patient is not a good surgical candidate and has lesions larger than 15mm located more than 2cm away from the cricopharyngeus, a fully SEMS can be placed as bridging therapy, while the patient becomes stable and in better condition for surgical treatment. Although we have a small sample size, to the best of our knowledge this is the first study to illustrate the management of this type of patients in the context of the coronavirus pandemic.

Conclusion

Due to the significant increase in diagnosis of TEFs in patients with severe pneumonia due to COVID-19, and the high frequency of risk factors for TEFs in these patients, we recommend early identification prevention of these conditions, in addition to frequent measurement of the endotracheal cuff pressure. If possible, we recommend periodic evaluation of the tracheal mucosa with bronchoscopy to identify early lesions that could lead to the development of tracheoesophageal fistulas. Regarding treatment, we suggest providing initial endoscopic management in small fistulas (below 15mm) or until optimal conditions for surgical management are met (if larger than 15mm). Definitive endoscopic treatment may be offered according to the size and location of the fistula.

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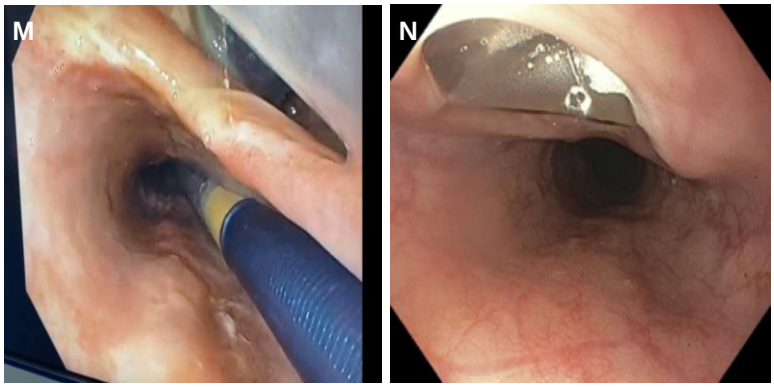
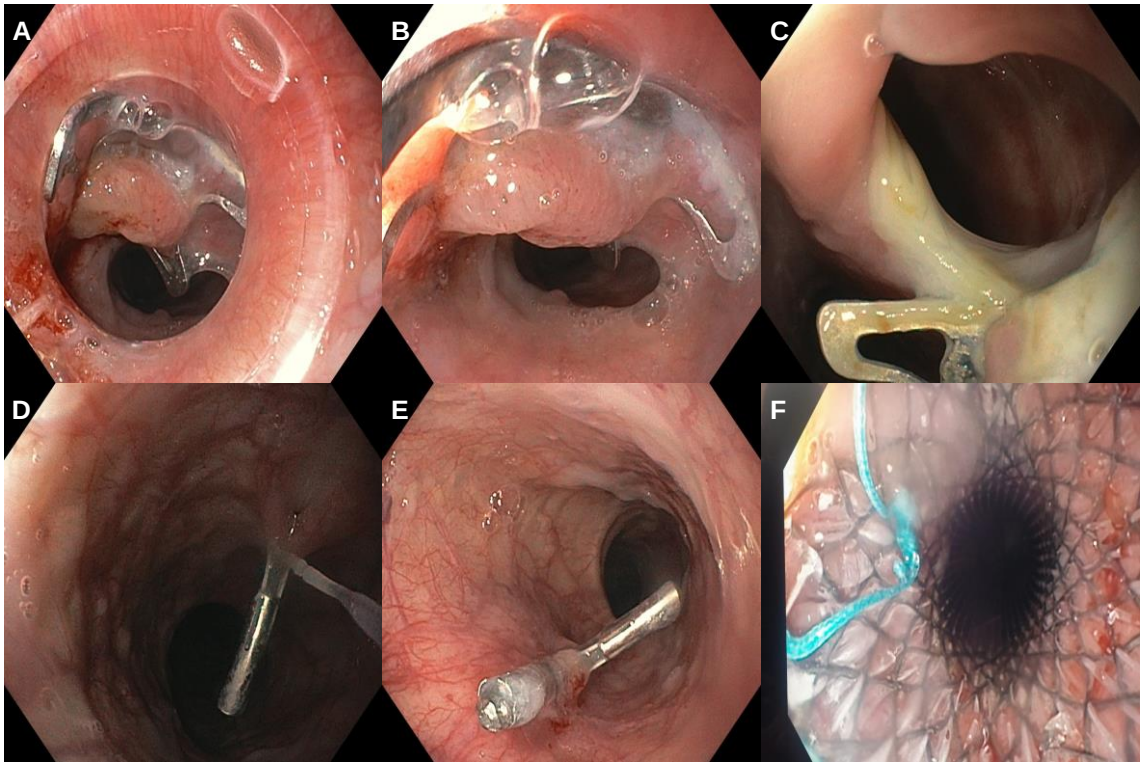
Supplementary Material

Supplementary Figure 1. Tracheoesofageal fistulas



Supplementary Figure 1. A: 10mm TEF; B: 15mm TEF; C: 2mm TEF; D: 20mm TEF; E: 20mm TEF; F: 20mm TEF; G: 3mm TEF; H 40mm TEF; I: 10mm TEF; J: 3mm TEF; K: 20mm TEF; L: 30mm TEF; M 25mm TEF; N: 20mm TEF

Supplementary Figure 2. Endoscopic treatment of TEFs



Supplementary figure 2. Endoscopic treatment of TEFs A: Closure with OTS clip; B: Closure with OTS clip ; C: Closure with OTS clip with defect recurrence ; D: Closure with TTS endoclip; E: Closure with TTS endoclip; F: Closure with partially coated self-expanding metallic stent