

Endoscopy esophageal mucosal circumferential resection followed by bypass surgery to treat tracheoesophageal fistula



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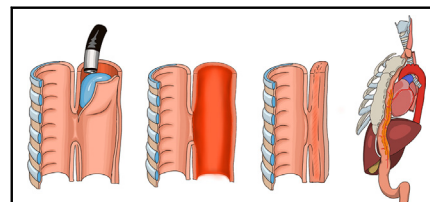
ABSTRACT

Objective: Tracheoesophageal fistula (TEF) is a severe complication often associated with advanced thoracic malignancies or chemoradiotherapy. This study introduces an innovative approach combining endoscopic submucosal dissection (ESD) and esophageal bypass surgery. This retrospective study aimed to evaluate the prognosis of patients with TEF in complete clinical remission after definitive chemoradiotherapy who underwent repair with such approach.

Methods: This is a retrospective analysis of 12 patients with TEF secondary to thoracic malignancies treated between June 2021 and June 2022. Patients underwent ESD for de-epithelialization of the esophageal lumen, followed by esophageal bypass surgery. Key outcomes included survival rates, fistula closure rates, postoperative clinical outcomes, and functional status improvement assessed by Karnofsky Performance Status scores.

Results: All patients had complete clinical remission of their primary malignancies before treatment. TEF closure was achieved in 10 patients (83.3%) within 28 to 72 days post-ESD. Median duration from ESD to bypass surgery was 39 days. Kaplan-Meier analysis revealed a 1-year survival rate of 65% and a 2-year survival rate of 60%. Postoperative morbidity included 1 anastomotic leak and 1 case of esophageal mucocoeles, both successfully managed. Functional outcomes significantly improved, with 91.6% of patients achieving a Karnofsky Performance Status score >80 at 6 months.

Conclusions: The combination of ESD and esophageal bypass surgery represents a promising approach for TEF management, demonstrating high rates of fistula closure, enhanced functional outcomes, and overall survival. Future studies should aim to validate these findings in larger cohorts and explore the long-term sustainability of these outcomes. (JTCVS Techniques 2025;33:256-63)



Combination of ESD and esophageal bypass surgery used for TEF management.

CENTRAL MESSAGE

The combination of ESD and esophageal bypass surgery is a safe and promising approach for managing TEF in patients with complete clinical remission after definitive chemoradiotherapy.

PERSPECTIVE

We proposed combining ESD with esophageal bypass for TEF patients in complete clinical remission post-dCRT. As oncologic outcomes improve with targeted therapy and immunotherapy, future studies should explore broader applications of this technique, assess its durability, and define optimal patient selection criteria to integrate it effectively with the armamentarium of TEF treatment options.

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Abbreviations and Acronyms

dCRT = definitive chemoradiotherapy
 ESD = endoscopic submucosal dissection
 KPS = Karnofsky Performance status
 TEF = tracheoesophageal fistula

 Video clip is available online.

Tracheoesophageal fistula (TEF) develops in up to 15% of patients with esophageal cancer and in approximately 1% of those with lung cancer.^{1,2} This condition is often seen in advanced tumors with tracheal invasion or as an adverse event following chemoradiotherapy.³⁻⁵ The mean survival of patients diagnosed with malignant TEF was only 2.8 months from the time of diagnosis.¹

Conventional treatments, such as esophageal bypass surgery, have been employed for nearly a century to manage TEF, irrespective of its benign or malignant nature. Although it provides an alternative route for food passage and alleviates symptoms of recurrent aspiration, this procedure is still associated with high risk of esophageal mucocoeles rupture and eventual death exacerbated by aspiration.^{6,7} Previous studies have shown that surgical intervention for TEF, particularly in selected patients, can lead to improved survival.⁸ Patients with malignant TEF who exhibit a complete clinical remission are frequently neglected, prompting the inquiry of whether they should be classified as malignant or benign TEF, highlighting a significant deficiency in comprehending outcomes for this demographic.

Considering the challenges and potential benefits of this patient cohort, we propose a technical enhancement to traditional bypass surgery. In this study, we introduce a novel application of endoscopic submucosal dissection (ESD) for de-epithelializing the esophageal lumen to achieve TEF closure before bypass surgery. This process induces fibrosis and complete stenosis, promoting healing of the fistula. Several case reports have already demonstrated the effectiveness of combining ESD with clips or mesh to treat TEF.^{9,10} In patients with TEF who have achieved complete clinical remission after definitive chemoradiotherapy, the combination of ESD and esophageal bypass surgery will lead to improved prognosis.

METHODS

Patient Selection

This retrospective study aimed to evaluate the prognosis of patients with TEF in complete clinical remission after definitive chemoradiotherapy who underwent repair with ESD followed by esophageal bypass surgery

(Figure 1). Prognostic outcomes include overall survival, postoperative clinical outcomes, TEF closure rates, and functional status. Between June 2021 and June 2022, 12 consecutive patients who developed TEF following chemoradiation were included in this study. The inclusion criteria were a history of malignant chest tumors, a history of definitive concurrent chemoradiotherapy, the primary tumor evaluated as having a complete clinical response, and able to tolerate endoscopic and surgical treatment. This study was approved by the institutional review board of Shanghai Chest Hospital (IS23051; date of approval: August 9, 2023). As a retrospective study, patients' consent was waived in this study.

Tumor Evaluation

Bronchoscopy and gastroscopy were performed to exclude macroscopic residual tumors. In addition, positron emission tomography and computed tomography scan were essential for assessing primary tumors, regional lymph nodes, and distant metastases. The evaluation of complete clinical response, including no abnormal masses or lymphadenopathy on computed tomography scan, and no hypermetabolic activity in the esophagus or regional lymph nodes on positron emission tomography. For patients with suspected residual tumor, a biopsy will be performed for confirmation.

TEF Evaluation

The fistula was evaluated by bronchoscope (Olympus BF-1TQ290) and gastroscopy (Olympus GIF-260J). The location (relationship between the carina and glottis) and size (longitudinal diameter) of TEF were recorded in detail. If there was an existing esophageal stent, it would be removed firstly to facilitate ESD. ESD was typically performed 2 to 4 weeks after stent removal to allow mucosal inflammation from the indwelling stents to subside and optimize submucosal lifting. A temporary tracheal stent was inserted for individuals at high risk of aspiration before the removal of the esophageal stent to minimize aspiration risk and facilitate airway protection during anesthesia for ESD. The choice of tracheal stent depends largely on the location of the fistula. If the fistula is in the carina region, a Y-shaped stent is preferred. This tracheal stent was removed 1 to 2 weeks after ESD. A simultaneous percutaneous endoscopic gastrostomy was performed to facilitate the administration of enteral nutrition after ESD.

ESD

Double-lumen endotracheal intubation was performed to ensure satisfactory isolation of the diseased airway from the ventilated lung. Patients were positioned laterally for the procedure. ESD was performed from the thoracic inlet (approximately 20 cm from the incisors) to the esophagogastric junction to achieve complete eradication of the thoracic esophageal mucosa. Endoscopic mucosal resection was used in areas adjacent to the fistula, whereas argon plasma coagulation was applied when submucosal lifting was inadequate due to inflammation to ensure effective de-epithelialization (Figure 2 and Video 1).

After ESD, patients were instructed to spit out saliva, and a nasogastric tube was placed 20 cm from the incisors for continuous drainage. The nasogastric tube was typically removed after 1 week. One month after ESD, an endoscopic evaluation was performed, including esophagogastroduodenoscopy to assess the proximal esophagus and bronchoscopy to evaluate fistula closure. This assessment was critical in determining whether a persistent communication remained between the esophagus and trachea. Esophageal bypass surgery was performed if the TEF was closed after ESD. If the fistula remained open, patients was advised to proceed with bypass surgery first, followed by close monitoring postoperatively. In cases where a mucocoele developed, a subtotal resection of the thoracic esophagus was considered to prevent complications.

Esophageal Bypass Surgery

Firstly, the stomach was mobilized laparoscopically in the supine position. A linear stapler was then used to transect the esophagus as high as possible above the gastroesophageal junction, followed by the creation of

a stomach conduit of approximately 3 cm in width. Secondly, an oblique incision was made to expose the cervical esophagus, which was excised at the thoracic inlet to completely exclude the thoracic atresia esophagus. Finally, the stomach was pulled up through retrosternal approach, and end-to-side anastomosed with the esophagus at the neck (Video 1).

Outcomes Evaluation and Follow-Up Schedule

Patients' clinical materials were collected from a prospective database, including age, sex, functional status, and details regarding the surgical procedure. Postoperative morbidity and mortality were documented. The TEF closure was confirmed using bronchoscopy. Transnasal esophagogastroduodenoscopy

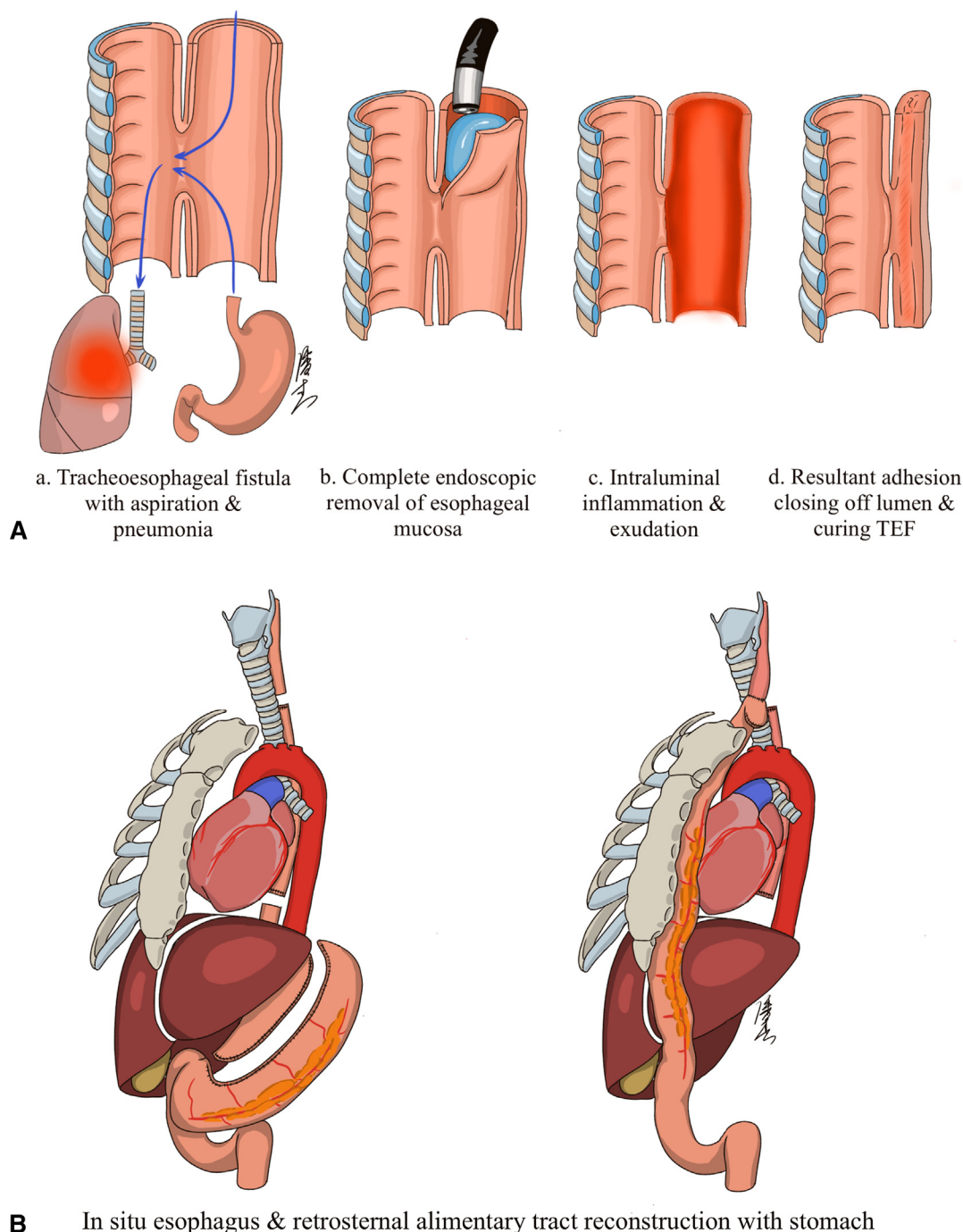


FIGURE 1. Procedure of endoscopic thoracic esophageal mucosal eradication to close the tracheoesophageal fistula (TEF) and esophageal bypass surgery. A, Endoscopic thoracic esophageal circumferential mucosal removal can lead to esophageal lumen adhesions and occlusion, thereby closing the TEF and eliminating aspiration and pneumonia. B, Replace the esophagus with substitute of stomach via the substernal route to complete the reconstruction of the digestive tract and to restore the oral intake.

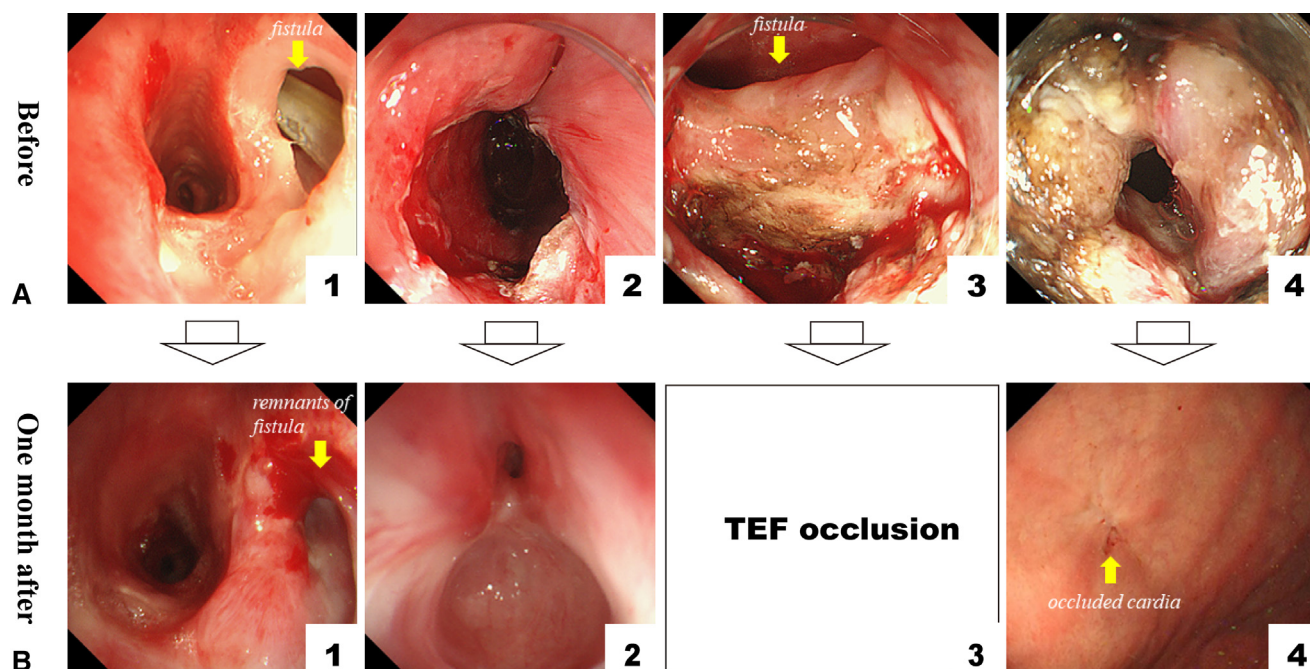


FIGURE 2. The steps of endoscopic thoracic esophageal mucosal eradication. A, The condition of tracheoesophageal fistula (TEF) before and during the surgery. A1, Bronchoscopy reveals a tracheoesophageal fistula on the left side of the carina and proximal to the left main bronchus. A2, Endoscopic circumferential resection of the esophageal mucosa to the thoracic inlet. A3, The mucosa around the tracheoesophageal fistula on the side of the esophagus is ablated and destroyed. A4, Complete resection of the thoracic esophageal mucosa up to the cardia opening. B, The condition of TEF 1 month after surgery. B1, Bronchoscopy reveals that the TEF has been occluded and the airway is isolated from the digestive tract. B2, Complete closure of the oral side of the thoracic esophagus. B3, TEF was unable to be seen on esophageal side. B4, Retrograde endoscopic observation through the gastrostomy opening reveals complete occlusion of the cardiac opening.

is routinely performed to assess anastomotic healing 1 week after surgery. The first follow-up was scheduled 1 month after surgery, every 4 months thereafter. Follow-up assessments included symptoms, regular evaluations of functional status with Karnofsky Performance Status (KPS) scores and any complications related to the surgery.¹¹

Statistical Analyses

Continuous variables were expressed as means $\pm$ standard deviations or medians (interquartile ranges) when appropriate, whereas categorical

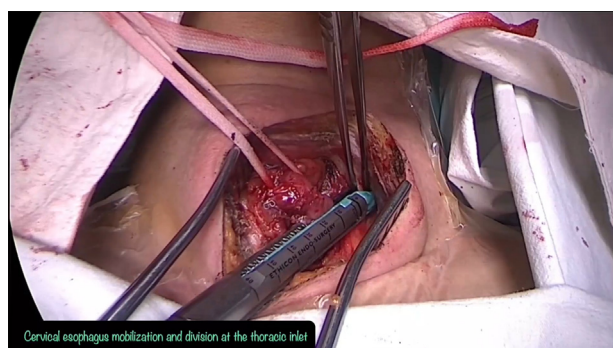
variables were described as numbers and percentages. Differences in the variables between the baseline and postbypass periods were compared using paired *t* tests. Kaplan-Meier curves were used to delineate the survival outcomes. All statistical analyses were performed using the SPSS software version 29.0 (IBM Corp.)

RESULTS

Patient Demographics

A total of 12 patients were enrolled in this study, comprising 8 men (66.7%) and 4 women (33.3%). The mean age of the participants was 56 ± 11 years. The main tumors were identified as esophageal cancers ($n = 7$ [58.3%]), lung cancers ($n = 3$ [25.0%]), and tracheal malignancy ($n = 2$ [16.7%]). All patients achieved complete clinical remission of their primary tumors after definitive chemoradiotherapy (dCRT). The median time interval from the initiation of dCRT to the onset of TEF was 13.5 months (range, 1-84 months).

Detailed radiotherapy plans could not be accurately reviewed. During this time frame, esophageal stents were placed in 7 patients (58.3%), tracheal stents in 3 patients (25.0%), and gastrointestinal occlude devices in 1 patient (8.3%). The mean body mass index of the patients was 19.4 ± 3.1 , whereas the baseline KPS score was 47.5 ± 11.4 . The 12 patients' detailed demographics are presented in Table 1.



VIDEO 1. The procedure of combination of endoscopic submucosal dissection and esophageal bypass surgery used for trachea-esophageal fistula management. EMR, Endoscopic mucosal resection. Video available at: [https://www.jtcvs.org/article/S2666-2507\(25\)00236-6/fulltext](https://www.jtcvs.org/article/S2666-2507(25)00236-6/fulltext).

TABLE 1. The detailed demographics of the 12 patients with tracheoesophageal fistula

Patient no.	Tumor stage	Fistula size (cm)	Stent history	ESD + EMR with or without ablation	Interval*	Fistula	Complications after bypass surgery
1	ycT0 N0 M0	1	None	ESD + EMR	0	Closed	
2	ycT0 N0 M0	1	Esophageal stent	ESD + EMR with ablation	0	Closed	Anastomotic leak
3	ycT0 N0 M0	1	Esophageal stent	ESD + EMR with ablation	7	Closed	
4	ycT0 N0 M0	1	Esophageal stent	ESD + EMR with ablation	5	Existing	
5	ycT0 N0 M0	1	Esophageal stent	ESD + EMR with ablation	38	Closed	
6	ycT0 N0 M1	1	Esophageal stent	ESD + EMR	36	Closed	
7	ycT0 N0 M0	1.5	No	ESD + EMR	45	Closed	Esophageal cystic dilation
8	ycT0 N0 M0	0.3	Tracheal stent	ESD + EMR	35	Closed	
9	ycT0 N0 M0	2.5	Tracheal and esophageal stent	ESD + EMR	72	Existing	
10	ycT0 N0 M0	2.5	Tracheal and esophageal stent	ESD + EMR	55	Closed	
11	ycT0 N0 M0	1	None	ESD + EMR	75	Closed	
12	ycT0 N0 M0	2	GI occluder device	ESD + EMR	45	Closed	

ESD, Endoscopic submucosal dissection; EC, esophageal cancer; EMR, endoscopic mucosal resection; GI, gastrointestinal; LC, lung cancer; TT, tracheal tumor. *Days between ESD and bypass surgery.

The median diameter of the fistula, measured via bronchoscopy, was 1.0 cm (range, 1.0-1.6 cm). Among them, 5 fistulas (41.7%) were located in the main trachea, 2 (16.7%) spanned the carina, and the remaining 5 (41.7%) were located in the main bronchus (including 1 patient with 2 fistulas located in the left and right main bronchus concomitantly). The locations of the TEF are shown in Figure 3.

ESD and Esophageal Bypass

The mean endoscopic operative time was 155 ± 81 minutes. ESD was performed in 8 (66.7%) patients and hybrid resection and ablation in the remaining 4 (33.3%). Ten patients (83.3%) underwent simultaneous PEG treatment. Following ESD, the median lengths of stays in the intensive care unit and hospital were 2 days (range, 0-3 days) and 3 days (range, 2-4 days), respectively. One patient developed upper gastrointestinal bleeding from the raw surface of dissection on day 4, which was successfully treated with endoscopic hemostasis. There were no further endoscopic-treatment-related complications.

Esophageal bypass surgeries were successfully performed in all patients, with a median interval of 39 days (range, 0-63 days) following ESD. The mean duration of the bypass operation was 183 ± 67 minutes. The bypass surgery was performed together with ESD for patients 1 and 2, whereas the surgeries for patients 3 and 4 took place 1 week later. The remaining 8 patients underwent the surgery at least 1 month following ESD.

SURGERY OUTCOMES

Complete TEF closure occurred in 10 patients within 28 to 72 days after ESD. Bronchoscopy revealed that the fistula

on the side of the trachea appeared as a shallow diverticulum (Figure 2, B1), and esophageal examination revealed that the esophagus was completely occluded approximately 20 cm from the incisors and complete occlusion of the cardiac opening (Figure 2, B2 and B4). The thoracic esophageal lumen remained open in 2 (16.7%) patients. Aerodigestive communication through the TEF remained, although the esophageal lumens were narrow and demiclosed.

Following bypass surgery, the median lengths of stay in the intensive care unit and in the hospital were 1 day (range, 1-2 days) and 9 days (range, 8-13 days), respectively. One patient (8.3%) developed anastomotic leak 1 week after bypass surgery and was successfully treated conservatively. Oral intake was resumed in all patients. One patient (8.3%) developed esophageal mucocoeles and was treated with thoracic esophagectomy.

Six months after bypass surgery, the plasma albumin levels of all patients were within the normal range and 11 patients (91.6%) had a KPS scores >80 . The body mass index ($P < .001$), serum albumin levels ($P = .007$), and KPS scores ($P < .01$) significantly improved compared with baseline levels (Figure 4).

SURVIVAL OUTCOME

The Kaplan-Meier survival analysis (Figure 5) for patients with TEF who underwent ESD followed by bypass surgery shows a 1-year overall survival rate of approximately 65%. And the 2-year overall survival rate is approximately 60%. No deaths occurred within 30 days after bypass surgery. There were no reported deaths or hospital readmissions within 90 days. All 4

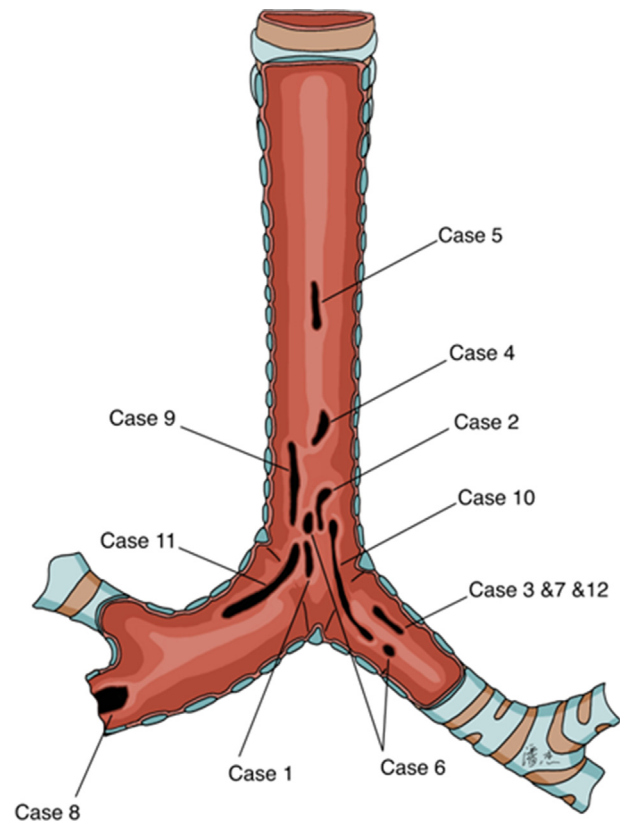


FIGURE 3. Location distribution of the tracheoesophageal fistula on the side of the airway in this study.

patients who succumbed to cancer related death were due to disease progression.

DISCUSSION

Esophageal interventions, including both ESD and EMR, are among the standard therapies for T1 N0 esophageal malignancies. However, severe stenosis or occlusion of

the esophageal lumen often occurs after extensive circumferential resection of the esophageal mucosa.¹² In this modified innovation, we exploited the complication to obliterate the esophageal lumen to eliminate the fistula. A demucosa esophagus could effectively prevent the emergence of a mucocele. This new strategy can optimize patient results; nonetheless, specific technical considerations are crucial to ensure success of the procedure.

Key technical considerations include removing all esophageal stents and thoroughly evaluating the underlying mucosa. After assessment, it may be essential to defer ESD to enable resolution of edema and inflammation to prevent the development of a cystic mucocele. A temporary tracheal stent is recommended to prevent aspiration during procedure. Also, performing a percutaneous gastrostomy before ESD is important to facilitate continuous drainage, reduce aspiration risk, and support perioperative nutrition. In addition, ESD and bypass surgery should be performed in stages to ensure complete closure of esophageal lumen. This strategy became evident in 2 instances where ESD and surgery were performed on the same day. Postoperative cough significantly increases intraluminal pressure in the esophagus, impeding TEF closure and ultimately resulting in failure.

Guan and colleagues¹³ conducted a large retrospective study on 221 patients with advanced and locally advanced esophageal cancer who developed an esophageal fistula. The study demonstrated that median overall survival of patients with esophageal cancer with an esophageal fistula was 11 months, irrespective of the treatment method (ie, stenting, surgery, or palliative care). The median survival time after being diagnosed with a fistula was 3.6 months.¹³ Similarly, Murad and colleagues¹⁴ conducted a retrospective cohort study that examined 61 patients with aerodigestive fistulas. The study reported survival rates of 31%, 11.5%, and 4.9% at 1-, 3-, and 5-years, respectively.

In contrast to the outcomes from previous trials, our reported 1-year overall survival rate was significantly higher at 65% in which the numbers plateau relatively thereafter until 2 years. This improvement highlights the effectiveness of the innovative surgical approaches implemented in our study and reinforces the need for such methods to address the unique challenges posed by TEF. Building on these promising results, future research should aim to expand the surgical indications of these findings in other contexts and to examine their long-term outcomes. Ultimately, the goal is to refine the management of TEF and offer better therapeutic alternatives, thereby improving their prognosis and overall treatment experience.

The majority of patients demonstrated significant improvement in their functional status 6 months after esophageal bypass surgery, as evidenced by KPS score. Specifically, 91.6% achieved a KPS score higher than 80, which is a significant improvement from the baseline KPS

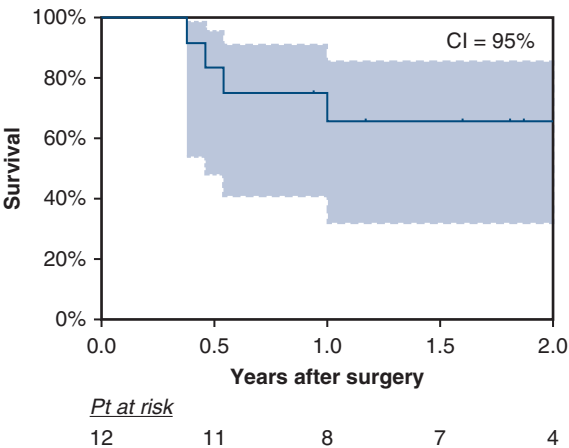


FIGURE 4. Overall survival of the patients in this study.

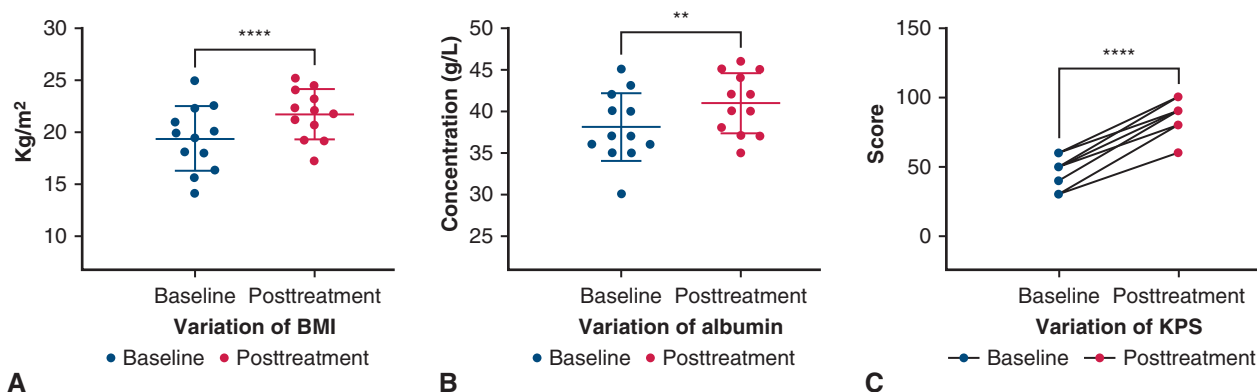


FIGURE 5. Comparisons between posttreatment at 6 months after bypass surgery and baseline levels in variation of the body mass index (BMI) (A), variation of serum albumin levels (B), and variation of the Karnofsky Performance Status (KPS) score (C). ** $P < .010$. **** $P < .001$.

score. This study highlights the positive impact of the integrated approach of bypass surgery and ESD on patients' quality of life. In addition to improved health condition, improved KPS scores showed that patients feel better and can be more engaged in daily activities. These results further support the potential of this strategy to significantly enhance patient outcomes, hence reinforcing its value in managing TEF.

Limitations

This study has several limitations that must be acknowledged. Firstly, the retrospective design combined with a relatively small sample size from a single center limits the generalizability. This study is limited to a highly selective cohort of patients with complete clinical remission after dCRT, it may not reflect the wider community of individuals with TEF, particularly those with residual or untreated malignancy. Additionally, the technical complexity of the innovative technique may limit its applicability in all clinical contexts, especially in facilities with limited experience in advanced endoscopic procedures. The requirement for specialized personnel in the fields of anesthesia and advanced endoscopy is a potential barrier for broader implementation. Lastly, the follow-up period was limited to 2 years, which is relatively short for assessing long-term overall survival and the permanent closure of the TEF. As a result, it is yet unknown whether longer-term outcomes might reveal more sustained improvements or higher rates of permanent fistula closure. Nevertheless, the patients in this study will be monitored further to evaluate these long-term outcomes.

CONCLUSIONS

This study highlights the potential of integrating ESD with esophageal bypass surgery to improve overall survival in patients with TEF resulting from chemoradiotherapy. This innovative approach not only promotes fistula closure

and restoration of oral intake but also has the potential to enhance long-term survival relative to conventional treatments. With advancement in targeted therapy and immunotherapy, an increasing number of patients may achieve complete clinical remission, creating a growing need for effective and durable TEF treatment strategies. Further research should explore broader applications of this approach and assess its long-term efficacy in diverse patient populations.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: tracheoesophageal fistula, esophageal bypass surgery, ESD, dCRT