



Diagnose and treatment for Type D congenital esophageal atresia with tracheoesophageal fistula

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ABSTRACT

Importance: Type D esophageal atresia (EA) with tracheoesophageal fistula (TEF) is characterized by EA with both proximal and distal TEFs. It is a rare congenital anomaly with a very low incidence.

Objective: To investigate diagnostic and treatment strategies for this rare condition.

Methods: We retrospectively reviewed the clinicopathological features of patients with EA/TEF treated at our institution between January 2007 and September 2021.

Results: Among 386 patients with EA/TEF, 14 (3.6%) had type D EA/TEF. Only two patients were diagnosed with proximal TEF preoperatively. Seven patients were diagnosed intraoperatively. Five patients were missed for diagnosis during the initial surgery but was later confirmed by bronchoscopy. During the neonatal period, seven patients underwent a one-stage repair of proximal and distal TEF via thoracoscopy or thoracotomy. Due to missed diagnosis and other reasons, the other 7 patients underwent two-stage surgery for repair of the proximal TEF, including cervical incision and thoracoscopy. Ten of the 14 patients experienced postoperative complications including anastomotic leakage, pneumothorax, esophageal stricture, and recurrence. Patients who underwent one-stage repair of distal and proximal TEF during the neonatal period showed a higher incidence of anastomotic leak (4/7). In contrast, only one of seven patients with two-stage repair of the proximal TEF developed an anastomotic leak.

Interpretation: Type D EA/TEF is a rare condition, and proximal TEFs are easily missed. Bronchoscopy may aim to diagnose and determine the correct surgical approach. A cervical approach may be more suitable for repairing the proximal TEF.

KEYWORDS

Diagnosis, Therapy, Tracheoesophageal fistula, Type D congenital esophageal atresia

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INTRODUCTION

Esophageal atresia (EA) and tracheoesophageal fistula (TEF) are rare congenital anomalies that have attracted the attention of pediatric surgeons.^{1–4} Type D EA, the least common type, is characterized by EA with both proximal and distal TEFs and has been reported to occur in less than 1% of EA cases.⁵ Only a few articles have reported this rare anomaly.^{6–8} Most studies on the condition, management, and outcomes of type D EA/TEF are published in the form of case reports.^{9–11} As the incidence of type D EA/TEF is low, most institutions lack clinical, diagnostic, and treatment experiences. Therefore, we aimed to evaluate effective diagnostic and treatment strategies for type D EA/TEF by retrospectively analyzing the clinical characteristics and management of affected patients admitted to our center. To our knowledge, this retrospective cohort of 14 patients with type D EA/TEF is the largest series to date.

METHODS

Ethics approval

This study was approved by the Ethics Committee of Beijing Children's Hospital (2019-k-333), and the patient informed consent requirements were waived.

Data collection

A retrospective analysis was performed on patients with type D EA/TEF who were treated at Beijing Children's Hospital between January 2007 and September 2021. Five of the 14 patients with type D EA/TEF had their initial neonatal surgery at different hospitals, while the remaining nine were treated at our center. Clinicopathological data for all cases were recorded, including age, sex, birth weight, combined anomalies, diagnosis, surgical conditions, postoperative complications, and follow-up data.

Surgical method

During the initial surgery, all patients had thoracoscopy or thoracotomy to restore esophageal continuity in the newborn period. At preoperative bronchoscopy, the light source at the front end of the bronchoscope was used to project onto the body surface to help locate the TEF. A guide wire was then placed under direct visualization of the bronchoscope. The location of the TEF was identified from an intraoperative X-ray examination. If the proximal TEF was located at or above the level of T2, a cervical approach was warranted; if the proximal TEF was located below the level of T2, thoracoscopy or thoracotomy was chosen. The thoracoscopic approach is routinely performed from the right side. A 5 mm Trocar was placed at the 5th intercostal space on the right subscapular line, and two 3 mm

Trocars were placed at the 3rd and 6th intercostal space on the midaxillary line. The intrathoracic pressure was maintained at 6–8 mmHg. Ligate the Azygos vein first. Then, careful dissection was performed to expose the distal TEF, and both the tracheal and esophageal ends of the fistula were sutured. The blind end of the proximal esophagus was fully mobilized. The tracheal and esophageal ends were sutured in cases where proximal TEFs were found. The primary anastomosis was considered safe in cases where the proximal and distal blind ends could be brought close enough to overlap. During thoracotomy, an incision was made at the right 4th intercostal space, and the rest of the steps were the same as described above for the thoracoscopic approach. Five children with proximal TEF located at or above the level of T2 underwent surgical repair with a cervical approach. The right supraclavicular cervical crease incision was chosen for the cervical approach. The trachea and esophagus can be exposed freely after separating the sternocleidomastoid muscle. The fistula was then located and ligated, followed by repair of the trachea and esophagus. A free prevertebral fascia or muscle flap was placed between the fistula tracts to prevent recurrence. Relevant surgical steps can be found in our previously published studies.^{12,13}

Postoperative follow-up

Follow-up was routinely performed after surgery. Routine esophageal radiography was performed 7 and 14 days postoperatively. Outpatient follow-up was scheduled every 3 months during the first 1 year after surgery and every 6 months thereafter. All patients were followed up until the end of June 2023. Patients in this study underwent one or more stages of surgery, therefore complication rates were calculated as the sum of all complications occurring after both surgeries.

RESULTS

Characteristics of patient

Among 386 patients with EA/TEF at our institution between January 2007 and September 2021, 14 were identified with type D EA/TEF (3.6%; eight male and six female patients). The median gestational age was 38 weeks (range: 37–40 weeks); the median birth weight was 3100 g (range: 1800–3600 g). Nine patients (64.3%) were preoperatively or intraoperatively (during the first surgery after birth) diagnosed with type D EA/TEF. The most common symptom of these nine patients before initial surgery was vomiting with feeding, which was similar to other types of EA. In the other five patients (35.7%) whose proximal fistulas were missed after the neonatal surgery, the common symptoms after the initial surgery were coughing with feeding (5/5) and recurrent pneumonia (3/5).

TABLE 1 Clinical baseline data for all type D esophageal atresia/tracheoesophageal fistula patients

Patient	Gender	Gestational age (weeks)	Birth weight (kg)	Gap distance (cm)	Combined deformity	Preoperative diagnosis	Missed diagnosis	Diagnostic method of proximal fistula	Follow-up (months)
1	M	40	3.2	1.5	Vertebral deformities	Type C	Yes	Bronchoscopy	26.5
2	M	37	1.8	1.2	Polydactyly; Pyloric stenosis	Type C	Yes	Bronchoscopy	23.3
3	M	37	3.0	1.0	Hiatal hernia	Type C	Yes	Bronchoscopy	16.5
4	M	38	3.1	1.5	None	Type C	Yes	Bronchoscopy	19.8
5	F	38	3.0	2.5	None	Type C	Yes	Bronchoscopy	27.5
6	F	37	3.1	1.5	PDA; Atrial septal defect; Down syndrome	Type D	No	Bronchoscopy	Abandon
7	F	39	3.1	1.2	None	Type C	No	Intraoperative discovery	Lost
8	M	40	3.0	1.5	None	Type D	No	Radiography	92.0
9	M	38	3.6	1.5	PDA; Diaphragmatic eventration	Type C	No	Intraoperative discovery	Abandon
10	M	38	2.9	1.0	PDA	Type C	No	Intraoperative discovery	Lost
11	F	39	2.6	2.0	None	Type C	No	Intraoperative discovery	Abandon
12	F	37	3.1	2.5	PDA	Type C	No	Intraoperative discovery	61.5
13	M	37	3.4	1.5	PDA; Duplex kidney	Type C	No	Intraoperative discovery	27.0
14	F	38	3.1	1.5	Pyloric stenosis; Vertebral deformities	Type C	No	Intraoperative discovery	12.3

Abbreviations: F, female; M, male; PDA, patent ductus arteriosus.

Five patients had isolated EA/TEF without other anomalies, and the other nine patients had malformations of other systems. Down syndrome was diagnosed in one patient (7.1%), including abnormal facial features, atrial septal defect, and patent ductus arteriosus (PDA). Additionally, four patients had PDA (28.6%), and two of them also had diaphragmatic eventration and duplex kidneys. Other malformations included pyloric stenosis (two cases), vertebral deformities (two cases), polydactyly (one case), and hiatal hernia (one case). Except for three patients who abandoned treatment during the perioperative period of the initial surgery, the other 11 patients were routinely followed up postoperatively for 12–92 months, during which two were lost to follow-up while the other nine demonstrated adequate oral intake and age-appropriate growth and weight gain. General and clinical data are summarized in Table 1.

Diagnosis of proximal tracheoesophageal fistula

The age at diagnosis of type D EA/TEF varied from 2 to 55 months. Esophagography was performed in all

14 patients, including nine neonates and five patients referred to our center for missed proximal TEF. Only one proximal TEF of the neonate was initially detected preoperatively on esophagography (Figure 1A, B). However, esophagography showed that the proximal blind-ending pouch in these patients appeared less dilated than that in type C. These proximal TEFs in seven patients (50.0%) were finally diagnosed during the first surgery either by thoracoscopy or thoracotomy. Six patients underwent bronchoscopy, including one neonate, who was initially diagnosed preoperatively by bronchoscopy. Other five patients' TEFs were missed during the initial surgery performed at other hospitals but were later confirmed on bronchoscopy.

Surgical treatment and postoperative complications

The age at initial surgery ranged from 2 to 11 days, with a median age of 4 days. During the neonatal period, seven patients with proximal and distal fistulas underwent a one-stage thoracoscopic repair (2/7) or thoracotomy (5/7).

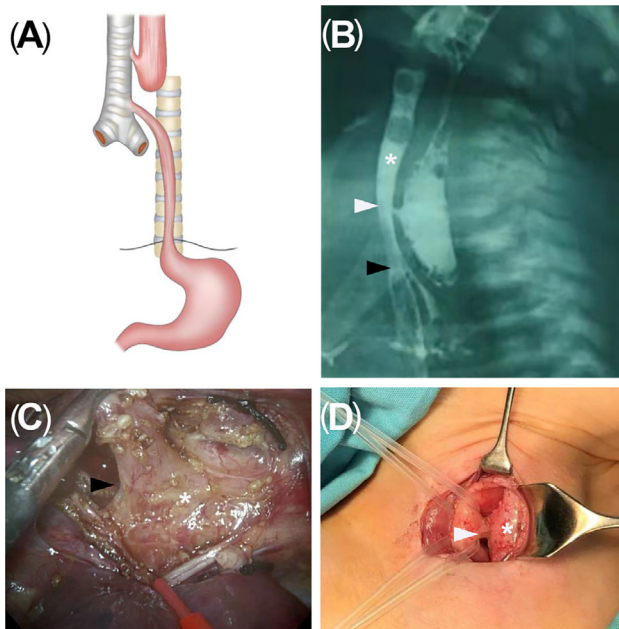


FIGURE 1 Diagnostic and treatment methods for distal and proximal TEFs in patient 8. (A) Revised illustration of the Gross classification of anatomical patterns of type D EA/TEF. (B) Esophagography showing distal and proximal TEF. (C) Initial neonatal thoracoscopic repair of the distal TEF. (D) Two-stage repair of proximal TEF by cervical incision. The white arrow indicated proximal TEF; the black arrow indicated distal TEF; the asterisk indicated trachea. EA, esophageal atresia; TEF, tracheoesophageal fistula.

In two patients, the distal fistulas were repaired using a thoracoscopic technique during the neonatal period, and the proximal fistulas located at or above the level of T2 were intraoperatively diagnosed and later repaired surgically using a cervical approach (Figure 1C, D). Proximal fistulas were missed in five patients at the initial surgery performed at different hospitals. Then, two-stage surgeries were performed to repair the missed proximal fistulas in these five patients, including cervical incision (3/5) and thoracoscopy (2/5). The age at the last surgery ranged from 2 to 55 months.

Ten of the 14 patients (71.4%) experienced postoperative complications [early postoperative complications: anastomotic leakage (5), pneumothorax (3); late postoperative complications: esophageal stricture (7), recurrence (3)]. Most of the perioperative complications were managed by conservative treatment. However, three patients gave up treatment after the operation because of the following conditions: Down syndrome (one patient) and severe postoperative complications (two patients: one with anastomotic leakage with severe empyema and one patient failed to extubate due to diaphragmatic eventration complicated with severe pneumonia and dyspnea). Seven patients with esophageal stricture were managed by routine endoscopic esophageal balloon dilation. Three

patients with recurrence underwent surgical repair, and two with recurrent distal TEFs underwent thoracoscopic repair. In another patient, recurrent proximal and distal fistulas were repaired through cervical and thoracoscopic approaches, respectively.

This cohort of patients had a high incidence of perioperative complications. Notably, patients who underwent one-stage repair of distal and proximal TEFs during the neonatal period showed a higher incidence of anastomotic leak (4/7, 57.1%). In contrast, only one of the other seven patients who underwent two-stage repair of the proximal TEF developed an anastomotic leak (14.3%). Of those five patients who underwent repair of the proximal TEF via a cervical approach, three developed esophageal strictures and one had a recurrence, but no anastomotic leakage was noted. The distance from the proximal TEF to the blind end of the esophagus was greater than 1 cm in three of these four patients who developed anastomotic leakage after one-stage surgery. This suggests that a gap greater than 1 cm may increase the complication rate after repair of proximal TEFs with thoracoscopy or thoracotomy. The surgical and perioperative characteristics of the patients are presented in Table 2.

DISCUSSION

EA/TEF is a serious congenital malformation of the digestive tract during the neonatal period, with an incidence of 1/2500–1/4500.^{1–4} Type D EA/TEF refers to EA combined with distal and proximal TEFs, and it accounts for less than 1% of all EA types.⁵ In recent years, the incidence of type D EA/TEF has been reported to be between 0% and 6.42% in several large cohort studies.^{4,6–8,14,15} In a study by Conforti et al.,¹⁴ including 180 patients with EA, none were type D, and only one (0.49%) of 204 EA cases reported by Parolini et al.⁶ was type D. In another study involving 396 patients with EA, the incidence of type D was 2.0% (8/396).⁷ Friedmacher et al.⁸ found seven type D cases in their study of 109 EA cases, reporting the highest incidence of 6.42%. The proportion of type D reached 3.63% in our sample of 386 EA cases, which is slightly higher than the incidence reported in most prior investigations. This may be explained by the fact that our center serves as the Chinese National Children's Medical Center, which also serves as a national referral center for EA cases. Most type C cases can be managed well at other institutions, while type D cases could be misdiagnosed as type C and later referred to our center.

The common symptoms of type D are choking and regurgitation after feeding, accompanied by cyanosis and dyspnea.^{9,16} Compared with other EA/TEF types, the clinical manifestations of type D lack specificity, which also leads to high misdiagnosis rates.⁹ Several studies have

TABLE 2 Surgery-related information for all type D esophageal atresia/tracheoesophageal fistula patients

Patient	Age at first surgery	Age at last surgery	Number of operations	Surgical method	Complications
1	5 d	55 m	3	1. Thoracotomy repair of distal TEF 2. Thoracoscopy repair of recurrence TEF 3. Cervical incision repair of proximal TEF	Esophageal stricture; Recurrence
2	3 d	10 m	2	1. Thoracotomy repair of distal TEF 2. Thoracoscopy repair of proximal TEF	Anastomotic leakage; Pneumothorax
3	4 d	5 m	3	1. Thoracotomy repair of distal TEF 2. Cervical incision repair of proximal TEF 3. Thoracoscopy repair of recurrence TEF	Esophageal stricture; Recurrence
4	2 d	9 m	2	1. Thoracotomy repair of distal TEF 2. Cervical incision repair of proximal TEF	Esophageal stricture
5	3 d	4 m	2	1. Thoracoscopy repair of distal TEF 2. Thoracoscopy repair of proximal TEF	Esophageal stricture
6	3 d	3 d	1	1. Thoracotomy repair of distal and proximal TEFs	None
7	10 d	12 m	2	1. Thoracotomy repair of distal and proximal TEFs 2. Thoracotomy resection of esophageal stenosis	Anastomotic leakage; Esophageal stricture; Vocal cord paralysis
8	2 d	3 m	2	1. Thoracoscopy repair of distal TEF 2. Cervical incision repair of proximal TEF	None
9	5 d	5 d	1	1. Thoracotomy repair of distal and proximal TEFs	Pneumonia
10	6 d	6 d	1	1. Thoracotomy repair of distal and proximal TEFs	Anastomotic leakage; Esophageal stricture
11	11 d	11 d	1	1. Thoracoscopy repair of distal and proximal TEFs	Anastomotic leakage; Pneumothorax; Pleural empyema
12	3 d	3 d	1	1. Thoracotomy repair of distal and proximal TEFs	Pneumothorax
13	8 d	3 m	2	1. Thoracoscopy repair of distal TEF 2. Cervical incision repair of proximal TEF	None
14	4 d	7 m	3	1. Thoracoscopy repair of distal and proximal TEFs 2. Cervical incision repair of proximal recurrence TEF 3. Thoracoscopy repair of distal recurrence TEF	Anastomotic leakage; Esophageal stricture; Recurrence

Abbreviations: d, days; m, months; TEF, tracheoesophageal fistula.

found that preoperative diagnosis of type D is difficult, and most cases are misdiagnosed as type C before surgery.^{9,17,18} Only two of the 14 cases in this study were diagnosed preoperatively. Seven patients were diagnosed with type D during the initial surgery. The proximal fistula was missed during the initial surgery in five cases (35.7%), resulting in misdiagnosis as type C. This led to repeated coughing and pneumonia after surgery. The five cases of missed proximal fistulas were finally diagnosed from bronchoscopy.

Chest radiography, esophagography, and bronchoscopy are commonly used for diagnosis of EA/TEF.^{1,3} However, for type D EA/TEF, esophagography cannot reliably detect proximal TEFs, and risks such as aspiration of contrast medium and radiation overdose cannot be excluded.⁹ In our study, only one patient (7.1%) was diagnosed with type D EA by esophagography before surgery, which indicated that the diagnostic value of esophagography for type D EA was

limited. Although the proximal TEF is difficult to visualize on esophagography, the proximal blind-ending pouch in type D appears less dilated than that in type C.¹⁹ The narrow-shaped remnant in type D patients was opposed to the fluid-filled proximal pouch in type C patients. Seven cases of proximal fistula were confirmed during surgery, and another six cases of proximal TEF were definitively diagnosed from bronchoscopy. In five of these children, the diagnosis of proximal TEF was missed during the initial surgery at other hospitals. After admission to our center, bronchoscopy revealed an abnormal fistula in the posterior tracheal wall and a positive methylene blue test. Another patient was suspected of having a proximal TEF during preoperative esophagography in the neonatal period and underwent preoperative bronchoscopy to confirm the diagnosis of type D EA/TEF. In this study, we found that bronchoscopy combined with a nasogastric tube infusion of methylene blue is a reliable method for detecting

abnormal fistulas. Some studies have reported that placing a guidewire through the fistula under the guidance of a bronchoscope may help surgeons accurately locate the fistula by pulling the guidewire during surgery.²⁰ The light source of the bronchoscope can be projected on the body surface. The placement of a guidewire can help to locate the proximal TEF and determine the surgical approach. Bronchoscopy can also detect tracheal malformations such as tracheomalacia, laryngeal clefts, and preoperative vocal cord dysfunction.^{11,21} Although studies have suggested that some factors limit routine preoperative bronchoscopy in the neonatal period, including low incidence of D-type EA/TEF, poor tolerance in neonates, and relatively hidden proximal fistula requiring experienced endoscopists.^{9,17,22} We still recommend that routine preoperative bronchoscopy be considered in the neonatal period if the facility has adequate medical resources. Especially, in patients with a narrow proximal blind-ending pouch on esophagography, or when the surgeon lacks sufficient experience.

With the development of thoracoscopy technology, an increasing number of pediatric surgeons have started using the thoroscopic approach to treat EA/TEF, which has the advantages of minimal invasiveness and adequate visualization.^{12,13,23–26} However, studies on the surgical treatment of type D EA/TEF with a definite preoperative diagnosis are lacking.^{9–11} Some researchers believe that for EA/TEF with a preoperative diagnosis of type C, proximal TEF should be highly suspected in cases when a large amount of gas leaks from the proximal esophagus during intraoperative esophageal anastomosis.¹⁶ In half of the patients in this study, proximal TEF was found intraoperatively. Rothenberg²⁵ suggested that thoroscopic surgery was the first choice for isolated H-type TEF, which has the advantages of minimal invasiveness, adequate visualization, and minimal recurrent laryngeal nerve injury; however, suturing the proximal fistula under thoracoscopy was extremely difficult. In this study, we found that a two-stage cervical invasion repair of the proximal TEF had a lower rate of serious complications compared with a one-stage thoracic or thoroscopic repair of both distal and proximal TEFs in the neonatal period. As for the surgical approach to the repair of proximal TEF, thoracic or thoroscopic approaches have a higher rate of anastomotic leakage than cervical invasion. There would be multiple simultaneous anastomoses in a one-stage surgery. Increases in the number of anastomoses might also increase the incidence of complications such as anastomotic leakage. Notably, the distance from the proximal TEF to the blind end of the esophagus greater than 1 cm might increase the complication rate of proximal TEF repair by thoroscopic approach or thoracotomy. For high-positioned proximal TEFs, blindly and widely dissecting the proximal esophageal pouch to find the proximal TEF so as to

achieve a one-stage thoracotomy or thoroscopic repair in the neonatal period might adversely increase the incidence of serious complications. Thus, we recommend a two-stage cervical approach for patients diagnosed preoperatively with type D EA with a proximal TEF located at or above the level of T2. For proximal TEF below the level of T2, both proximal and distal TEF can be treated in a one-stage operation. For patients diagnosed with type-D EA during surgery, it is recommended to dissect about 1 cm from the blind end of the proximal esophagus to locate and repair the proximal TEF. In case no proximal TEF is identified within 1 cm of the blind end of the proximal esophagus, a second surgery to repair the proximal TEF using a cervical approach is recommended. The proximal fistula ascends from the anterior esophageal wall to the posterior aspect of the trachea. This anatomical structure results in relatively mild clinical symptoms arising from isolated proximal TEF. Feeding requirements before a two-stage surgery can be ensured by placing an upper esophageal vacuum suction and a gastric feeding tube. For missed proximal TEFs, the treatment principle was similar to that of H-type EA/TEF, and a cervical approach should be the first choice.

This study has the following limitations. First, not all primary surgeries in our cohort were performed at our center, which may have resulted in bias. Second, as a descriptive study, this study cannot give statistical results. Additionally, due to the lower incidence of type D EA/TEF, the sample size of our cohort was insufficient. Our diagnosis and treatment recommendations were based on a comprehensive consideration of the results and the surgeon's experience. These recommendations need to be validated in future studies with larger sample sizes.

In conclusion, type D EA/TEF is rare and easily misdiagnosed, and bronchoscopy may help confirm the diagnosis. The surgical strategy of proximal TEFs would depend on the location of the proximal TEF to determine whether to perform one-stage thoroscopic surgery or two-stage repair with a cervical approach. Early definitive diagnosis and standard treatment ensure that most patients would have a good prognosis.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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