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Treatment of isolated and recurrent tracheoesophageal fistula in children: a case series and literature review

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ABSTRACT

Background Despite improvements in the treatment of esophageal atresia with tracheoesophageal fistula (TEF) in recent decades, complications still exist. The rate of fistula recanalization after surgical repair is ~5% in large cohorts. However, there is controversy regarding the gold standard of treatment. This research aimed to evaluate the efficacy of treatment of pediatric patients with isolated (H-type) and recurrent TEF in our clinic.

Methods We retrospectively analyzed 12 patients (7 boys, 5 girls) aged 35 days–14.6 years. The median age of our patients was 632 days [95% CI (confident interval) 120.1 to 2118.7]; the mean birth weight was 2713 g (95% CI 2258 to 3169; median: 2763 g); and the mean gestational age was 37.1 weeks (95% CI 35.4 to 38.8; median: 37 weeks). All patients were managed for isolated or recurrent TEF between January 1, 2015 and December 31, 2020 using endoscopy (laser de-epithelialization).

Results Laser de-epithelialization alone was effective in 8 of 12 patients (66.67%), with a mean number of de-epithelializations of 2.25 (range: 1–4). After one attempt at de-epithelialization, success was achieved in only two patients (n=16.67%). The mortality rate was 0%. The median follow-up for patients who received endoscopic treatment exclusively (n=8) was 3.7 years (95% CI 1.38 to 4.87) after the last stage of de-epithelialization.

Conclusion Flexible endoscopy is an alternative treatment to open surgical repair of isolated and recurrent TEF in children. The effectiveness of endoscopic laser de-epithelialization alone with subsequent fistula obliteration was 66.7%, with a median follow-up of 3.7 years.

Key messages

What is already known about this subject?

- There are no generally used gold standards for diagnosis and treatment of isolated and recurrent tracheoesophageal fistula (TEF).
- Endoscopy can be an effective treatment option in some patients with isolated and recurrent TEF.
- The effectiveness of endoscopic treatment depends on patient selection and on the chosen endoscopic method.

What are the new findings?

- This study clearly shows the importance and need for standardizing approaches.
- The overall efficiency of endoscopic laser de-epithelialization alone in isolated/recurrent TEF was 66.67% in our study, whereas the efficiency after one attempt was only 16.67%.
- Patient selection is primarily based on fistula size and carrying out the procedure in several stages can be a decisive factor for increasing the effectiveness of endoscopic treatment.

How might it impact on clinical practice in the foreseeable future?

- This publication contributes to the literature in terms of minimal surgical intervention for isolated/recurrent TEF.
- We hope that our personal experience and external collective data will be useful in developing standardized solutions.

INTRODUCTION

Tracheoesophageal fistula (TEF) is an abnormal communication between the posterior tracheal wall and the anterior esophageal wall.[1] This topic is of interest owing to the high prevalence of esophageal atresia (EA) with TEF (~1:2500–1:4500 live births)[2 3] and to the lack of consensus on the gold standard of treatment. Despite improvements in the treatment of EA with TEF in recent decades, complications still exist. The rate of fistula recanalization after surgical repair is ~5% in large cohorts.[4–6]

The most common reason for recanalization is tissue injury in the poorly vascularized anastomotic area.[7] Factors leading to tissue injury and/or affecting the recurrence of TEF include the following: (1) technically inadequate fistula disconnection, (2) complications from the esophageal anastomosis (high tissue tension, mechanical trauma due to early balloon dilatations), (3) tracheal injury during the initial surgery, (4) juxtaposition of the esophageal and tracheal suture line, (5) gastroesophageal reflux disease, and (6) missed proximal fistula.[7 8] Premature infants, as well as children with low birth weight, tend to experience recurrent TEF more frequently.[9] Fistula recanalization usually occurs in the first 18 months after the initial surgery, except in rare cases where it may occur years later.[10]

Clinical manifestations include symptoms such as choking and coughing, first on liquids and then on mushy and solid foods, and cyanosis with eating, particularly when the patient is in a recumbent position.[8] Moreover, there was a high incidence of recurrent respiratory diseases in this group. Patients who had recurrent TEF had significantly more hospitalizations for respiratory symptoms and had significantly more episodes of clinical bronchiolitis per patient. In addition, patients with recurrent TEF had significantly more episodes of positive PCR for viruses.[11]

Aworanti and Awadalla[12] observed that a prone esophagram performed by injecting the contrast under pressure through an nasogastric tube while withdrawing the tube is the most sensitive investigation with the least false negatives. Conversely, Richter *et al*[13] assert the opposite, stating that false negatives reach up to 50% with this method. Others propose that bronchography with bronchoscopic probing is the most sensitive method.[14] Esophagoscopy and bronchoscopy, including Fogarty's catheter probing and probing with methylene blue, are important diagnostic options for recurrent TEF,[9 12] and Daniel and Smith[15] consider it to be the gold standard for fistula identification.

There is no consistent approach regarding bronchoscopy type. Some authors consider that rigid bronchoscopy is a routine procedure for preoperative evaluation[15] and is the instrument of choice for fistula visualization and delivery of the obliterating agent.[7] Other authors believe that it is possible to use both of these methods (rigid and flexible endoscopy) in diagnostics,[14 16] whereas another study favored flexible bronchoscopy for that purpose.[17]

METHODS

We retrospectively analyzed 12 patients (7 boys and 5 girls) who underwent endoscopic treatment for isolated and recurrent TEF between January 1, 2015 and December 31, 2020 (table 1), with age ranging from 35 days to 14.6 years. The median age of our patients at the time when fistula or recanalization was detected was 632 days (95% CI 120.1 to 2118.7); the mean birth weight was 2713 g (95% CI 2258 to 3169; median: 2763 g); and the mean gestational age was 37.1 weeks (95% CI 35.4 to 38.8; median: 37 weeks). Seven patients underwent surgery for EA gross type C at birth, one patient underwent surgery in two steps for EA gross type A (esophagostomy, gastrostomy, and esophagocoloplasty), and four patients had EA gross type E (isolated TEF, H-type fistula). After diagnostic tracheoscopy and esophagoscopy with identification of the size and form of the fistula, indications for endoscopic treatment were determined (figure 1).

To assess fistula patency, we used three different diagnostic tools: (1) methylene blue test, (2) insertion of the soft guidewire into the TEF and visualization of the distal part in the esophagus, and (3) obturation of the TEF orifice with a balloon catheter and radiopaque medium administration.

The main indication for laser de-epithelialization was a fistula diameter ≤3 mm.

De-epithelialization was performed using a MULTILINE laser (neodymium-doped yttrium aluminum garnet [ND: YAG] Wavelenght [L]=1064 nm, Power [P]=20 W and ND: YAG L=1340 nm, P=15 W). The manipulation was performed from the esophagus in seven patients, from the trachea in three patients, and from both the esophagus and the trachea in two patients (figure 2).

We used flexible bronchoscopes BF-XP190 (diameter: 2.8 mm with instrumental channel 1.2 mm), BF-P190

Table 1 Clinical characteristics of patients with isolated and recurrent TEF

Patient's code	Sex	Birth weight (g)	Gestational age (weeks)	Gross type of EA	First treatment option for isolated or recurrent TEF	Number of de-epithelializations performed	Last manipulation for treatment	Follow-up (from date of last hospitalization) (years)
1	M	3790	39	C	De-epithelialization	4	De-epithelialization	3.6
2	M	3000	N/A	E	De-epithelialization	3	De-epithelialization	4.5
3	M	1750	36	C	De-epithelialization	2	De-epithelialization	5.2
4	F	2850	40	C	De-epithelialization	2	De-epithelialization	4.8
5	M	1820	33	C	De-epithelialization	2	De-epithelialization	3.8
6	F	2650	36	E	De-epithelialization	4	Thoracotomy	–
7	M	3470	40	C	De-epithelialization	1	Thoracotomy	–
8*	M	3720	38	E	Thoracotomy, closure	1	Rethoracotomy	–
9	F	2675	37	C	De-epithelialization	1	De-epithelialization	2.9
10	M	2850	40	E	De-epithelialization	1	Thoracotomy	–
11	F	1870	34	A	De-epithelialization	3	De-epithelialization	1.4
12	F	2120	35	C	De-epithelialization	1	De-epithelialization	1.3

*Patient 8 underwent thoracotomy with a separation of the trachea and esophagus at birth; subsequently, recurrent TEF occurred and one attempt of laser de-epithelialization was made. Due to the ineffectiveness of the procedure, repeated thoracotomy was performed.
EA, esophageal atresia; F, female; M, male; N/A, not applicable; TEF, tracheoesophageal fistula.

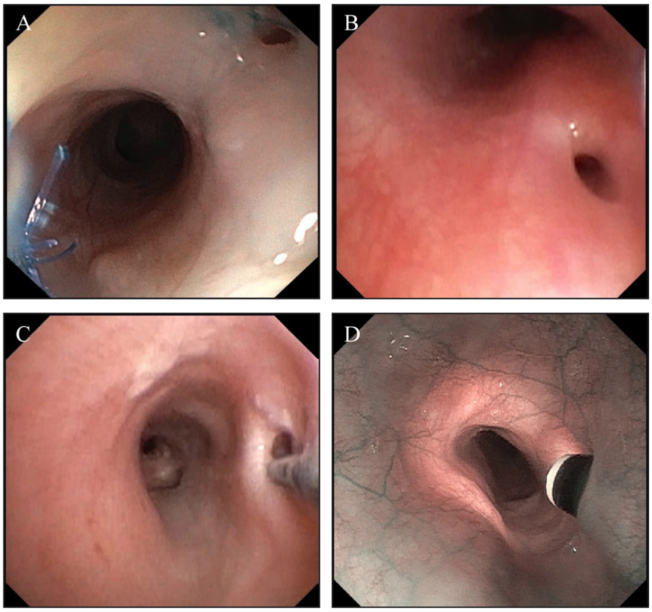

Figure 1 Diagnostic tracheoscopy and esophagoscopy. (A) Recanalization of tracheoesophageal fistula: visualization from the esophagus. (B) Recanalization of tracheoesophageal fistula: visualization from the trachea. (C) Soft guidewire is inserted into the tracheoesophageal fistula orifice from the trachea. (D) View from the esophagus: a 2.8 mm bronchoscope is inserted through the tracheoesophageal fistula (TEF) in the esophagus. Such a TEF diameter is not appropriate for endoscopic de-epithelialization.

(4.0/2.0mm), and esophagogastroscopes GIF-XP 190 (5.4/2.0 mm) by Olympus (Japan) in all cases.

RESULTS

The total number of endoscopic interventions (diagnostic and therapeutic) for isolated or recurrent TEF was 105 in our cohort, of which 67 were esophagogastroscopies and 38 were bronchoscopies. On average, 8.8 (95% CI 5.9 to 11.8; median: 8; range: 4–17) endoscopic procedures were performed for each patient with isolated or recurrent TEF, including control studies.

Patients underwent several procedures of de-epithelialization for recurrent/isolated TEF, with a mean number of 2.08 (95% CI 1.34 to 2.82; range: 1–4). Out of 11 patients, 4 underwent surgery (thoracotomy and plastic surgery of the trachea) due to failure of endoscopic treatment. In 3 patients, surgery was performed after only one attempt at endoscopic treatment. The endoscopic method of laser de-epithelialization alone was effective for isolated/recurrent TEF in 8 of 12 patients (66.67%), including 6 patients after surgical treatment of EA gross type C, 1 patient after surgical treatment of EA gross type A, and 1 patient with isolated TEF, with a mean number of de-epithelializations of 2.25 (range: 1–4). After one attempt at de-epithelialization, success was achieved in only two patients (16.67%). The mortality rate was 0%. The median follow-up period for patients who exclusively received endoscopic treatment (n=8) was 3.7 (95% CI 1.38 to 4.87, with a normal distribution) years after the last stage of de-epithelialization.

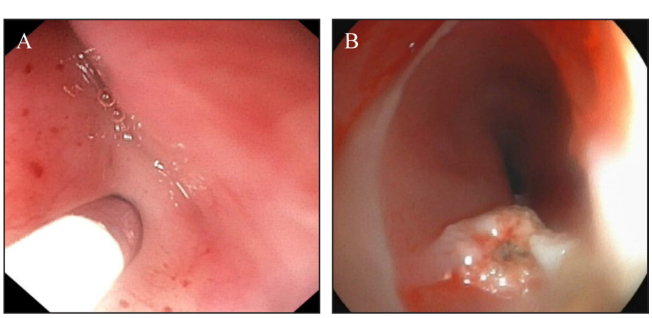

Figure 2 De-epithelialization findings. (A) Laser waveguide is inserted into the tracheoesophageal fistula from the esophagus for de-epithelialization. (B) Fistula orifice after laser de-epithelialization (view from the esophagus).

DISCUSSION

Choosing between surgical and endoscopic treatment is a topical issue for treating many different kinds of diseases in pediatric surgery and, in particular, for isolated/recurrent TEF.

Although endoscopic treatment methods are a less invasive alternative to open surgery, the recurrence rate is higher, and a few attempts are usually required for complete fistula closure.[3 12] There are three main options for endoscopic treatment of TEF in children: tissue adhesives/sclerosants, de-epithelialization, and a combination of these methods.[12]

Substances that can be injected into the fistula tract include n-butyl cyanoacrylate (enbucrilate, histoacryl), n-butyl cyanoacrylate and lipiodol, fibrin glue intraluminal or submucosal, and fibrin glue + added aprotinin submucosal injection of dextranomer/hyaluronic acid copolymer (Deflux). The underlying mechanism of action for this group of substances is the induction of an inflammatory response, leading to foreign body granuloma formation and fibrosis.[8 15]

Briganti *et al*[18] described the clinical experience of using a submucosal injection of dextranomer/hyaluronic acid copolymer (Deflux) in four children. In three of the children, respiratory disorders were eliminated as a result of such treatment; however, the fistula was not completely closed, and after a few months open surgical interventions were performed.

De-epithelialization can be performed in several ways: fulguration of the fistula mucosa with diathermy, laser or argon plasma coagulation probe, mechanical (bronchial brush, biopsy forceps, suction) and chemical (silver nitrate bead, 50% trichloroacetic acid) abrasion, and submucosal sclerosant injections (30% sodium chloride, 0.5% polidocanol).[15]

It should also be remembered that, although the methods listed above seem to be of highly promising and safe, some authors[18] do not recommend methods such as electrocoagulation due to high risk of perforation, at

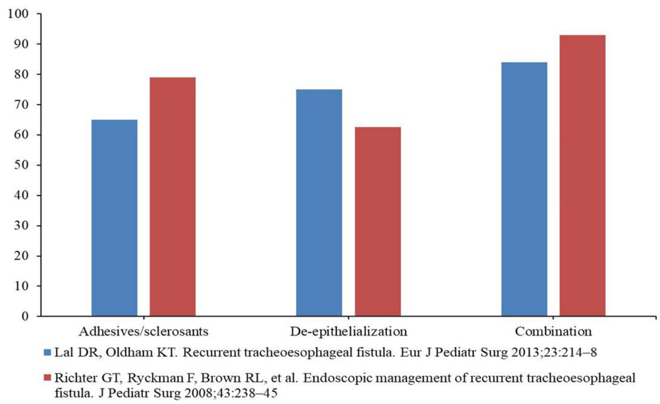

Figure 3 Rate of successful treatment of recurrent tracheoesophageal fistula by different methods from literature review.

least with thin fistula walls; therefore, endoscopic procedures also have potential threatening complications, such as perforation of the tracheal wall and adhesive aspiration.[12]

Some studies have reported that the best outcomes can be achieved using a combined method[8 13] (figure 3). Tzifa *et al*[19] highlighted the importance of de-epithelialization before adhesive/sclerosant injection. According to the authors' data, the effectiveness of the combined method based on systematic reviews was 84%[1] and 93.3%.[13]

There is some controversy concerning the superiority and indications of endoscopic and surgical intervention, and as mentioned previously there is currently no consensus on the choice of method. Some authors[12 18] believe that open surgery is the treatment of choice for recurrent TEF, and others[20] consider endoscopy a preferable choice, particularly in cases of small and slender fistulas that are easily exposed.[16] It is believed by some that the endoscopic approach should be the first-line therapy for children with low birth weight and small isolated fistulae.[21]

Small-sized fistulae (≤4 mm) have a higher probability of successful occlusion than large-sized fistulae.[18] In one of the studies,[13] the indication for endoscopic treatment was a narrow fistula (<2 mm) with diagonal tracts where a cuffed tube can be placed beyond the fistula site. Postoperative intubation beyond the repaired fistula for 2 days to prevent inadvertent mechanical recannulation was recommended.[13]

As previously noted, some authors[3 12 20] believe that a few attempts are required for complete endoscopic fistula closure. A systematic review by Aworanti and Awadalla[12] reported successful single endoscopic treatments in 37% of patients, with the mean number of treatments required for complete closure being 2.1, whereas Asik *et al*[16] permitted two to three attempts of endoscopic treatment before switching to open surgery.

In conclusion, endoscopic methods (flexible endoscopy) are an alternative to open surgery for treatment of isolated and recurrent TEF in children. The effectiveness of endoscopic laser de-epithelialization alone with subsequent fistula obliteration was 66.7% in our group, with a median follow-up of 3.7 years. Fistula size, particularly the diameter, is one of the most important criteria for determining the initial treatment choice. At least two attempts are required for optimal assessment of treatment efficacy.

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Data availability statement The data that support the findings of this study are available from the corresponding author, upon reasonable request.

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