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ORIGINAL ARTICLE

Postoperative Complications and Functional Outcome after Esophageal Atresia Repair: Results from Longitudinal Single-Center Follow-Up

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Abstract

Background Esophageal atresia (EA) and tracheoesophageal fistula (TEF) represent major therapeutic challenges, frequently associated with serious morbidities following surgical repair. The aim of this longitudinal study was to assess temporal changes in morbidity and mortality of patients with EA/TEF treated in a tertiary-level center, focusing on postoperative complications and their impact on long-term gastroesophageal function.

Methods One hundred nine consecutive patients with EA/TEF born between 1975 and 2011 were followed for a median of 9.6 years (range, 3–27 years). Comparative statistics were used to evaluate temporal changes between an early (1975–1989) and late (1990–2011) study period.

Results Gross types of EA were A ($n = 6$), B ($n = 5$), C ($n = 89$), D ($n = 7$), and E ($n = 2$). Seventy (64.2%) patients had coexisting anomalies, 13 (11.9%) of whom died before EA correction was completed. In the remaining 96 infants, surgical repair was primary ($n = 66$) or delayed ($n = 25$) anastomosis, closure of TEF in EA type E ($n = 2$), and esophageal replacement with colon interposition (n=2) or gastric transposition (n=1). Long-gap EA was diagnosed in 23 (24.0%) cases. Postoperative mortality was 4/96 (4.2%). Overall survival increased significantly between the two study periods (42/55 vs. 50/54; $P = 0.03$). Sixty-nine (71.9%) patients presented postoperatively with anastomotic strictures requiring a median of 3 (range, 1–15) dilatations. Revisional surgery was required for anastomotic leakage ($n = 5$), recurrent TEF with ($n = 1$) or without (n=9) anastomotic stricture, undetected proximal TEF ($n = 4$), and refractory anastomotic strictures with ($n = 1$) or without ($n = 2$) fistula. Normal dietary intake was achieved in 89 (96.7%) patients, while 3 (3.3%) remained dependent on gastrostomy feedings. Manometry showed esophageal dysmotility in 78 (84.8%) infants at 1 year of age, increasing to 100% at 10-year follow-up. Fifty-six (60.9%) patients suffered from dysphagia with need for endoscopic foreign body removal in 12 (13.0%) cases. Anti-reflux medication was required in 43 (46.7%) children and 30 (32.6%) underwent fundoplication. The rate of gastroesophageal reflux increased significantly between the two study periods (29/42 vs. 44/50; $P = 0.04$). Twenty-two (23.9%) cases of endoscopic esophagitis and one Barrett's esophagus were identified.

Conclusions Postoperative complications after EA/TEF repair are common and should be expertly managed to reduce the risk of long-term morbidity. Regular multidisciplinary surveillance with transitional care into adulthood is recommended in all patients with EA/TEF.

Keywords Esophageal atresia · Tracheoesophageal fistula · Complications · Follow-up · Outcome · Gastroesophageal function

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Introduction

Esophageal atresia (EA) and tracheoesophageal fistula (TEF) represent a spectrum of relatively rare and complex congenital

malformations, resulting from disruptions during normal foregut separation.[1] International prevalence rates of EA/TEF currently range between 1.27 and 4.55 per 10,000 births.[2–4] Due to the complex nature and infrequency of cases, EA/TEF management remains a major therapeutic challenge for most pediatric surgeons and other involved specialists.[5, 6] In most of the current reports, prematurity, low birth weight, and additional congenital anomalies are associated with higher mortality and further complicate the care of these patients,[7, 8] whereas survival rates in full-term infants with no other abnormalities can approach 100% after EA/TEF surgery.[9, 10] Today, improved survival of newborns with EA/TEF is likely related to multiple factors including advances in neonatal intensive care and anesthesia, refined surgical techniques, parenteral nutrition, and antibiotics.[11, 12] However, early[13–15] and late[16–18] postoperative morbidities frequently occur after initial repair of EA/TEF despite excellent surgical and neonatal management, and can be associated with impaired outcomes. Early recognition and treatment of potential complications is therefore essential in order to prevent poor long-term results.[19–22] At present, there is limited published data from large series of EA/TEF patients following surgery with regard to adverse events and their influence on functional outcome later in life.[24] Thus, the aim of this longitudinal study was to assess temporal changes in morbidity and mortality of patients with EA/TEF treated in a tertiary-level center, focusing on postoperative complications and their impact on long-term gastroesophageal function.

Patients and Methods

Study Population and Design

This was a longitudinal cohort study of all patients with EA/TEF that were born in a tertiary-level children's hospital between 1 January 1975 and 31 December 2011. Each patient was identified by using the hospital inpatient enquiry system and relevant data was extracted from the individual medical and operative records. No patient was excluded from this study, which followed institutional ethical committee approval (EK 27–259 ex 14/15). In 1990, a new head of department was employed, who established a specialized pediatric surgical intensive care unit including new staff members with increased expertise in the management of newborns with complex congenital malformations. In order to compare potential changes over time, cases were divided into an early (1975–1989) and late (1990–2011) study period.

General patients' characteristics were collected on gender, maternal age, prenatal findings, gestational age, birth weight (BW), mode of delivery, and coexisting anomalies. Initial postnatal management included stabilizing procedures, intravenous fluid resuscitation, and drainage of the upper esophageal pouch using an 8F or 10F Replogle suction tube. Preoperative assessment for associated anomalies composed of a full physical examination, plain chest and abdominal x-ray, and in more recent years abdominal ultrasound and echocardiography were included into the routine diagnostic workup. All pediatric surgeons that operated during the study period followed a standard practice protocol. In general, surgery was scheduled within 48 h after birth except in unstable neonates with respiratory distress that required emergency TEF ligation. Prior to surgical repair, a tracheobronchoscopy was performed in order to ascertain the presence and exact location of a proximal/distal fistula or other anticipated defects. The standard operative approach was a right posterolateral thoracotomy via the 4th intercostal space adopting an extrapleural access, whereas in cases where a right-sided aortic arch was found preoperatively, a left thoracotomy was chosen. The type of EA was classified according to the Gross classification depending on the pre- and intraoperative anatomy (Fig. 1). Long-gap EA was defined as a gap between the proximal and distal segments under tension of greater than four vertebral bodies. In EA types C and D, following initial TEF ligation and mobilization of both esophageal ends, a primary single-layer esophagoesophagostomy was attempted. Patients with EA types A and B, and those cases in which a primary anastomosis was not achievable, received a feeding gastrostomy on the first or second day of life. After a period of continuous upper pouch suction with or without serial bougienage of the upper and lower pouch, a delayed primary repair was performed where possible. In those infants, where an end-to-end anastomosis was still not feasible, esophageal replacement was undertaken. In neonates with EA type E, the isolated TEF was closed through a right cervical incision.

Early postoperative complications and late sequelae after EA/TEF repair were reviewed and where possible defined according to an international consensus paper,[25] and conservative or surgical treatment used was recorded. Standardized follow-up was undertaken in a specialized EA/TEF clinic consisting of regular physical examination as well as esophageal manometry, 24-h pH monitoring, contrast swallow study, and upper gastrointestinal endoscopy at least once within the first year of life. All examinations were repeated at 5-year intervals. A manometry catheter with 36 solid-state sensors was used, and after a 5-min resting period, ten wet swallows were performed with the patient in supine position. Integrity of esophageal peristalsis and contraction pattern was categorized as intact (i.e. propagating), weak, or absent, and lower esophageal sphincter pressure was assessed. A pH probe was positioned 3 cm above the upper boarder of the lower esophageal sphincter and connected to a recorder system. Gastroesophageal reflux disease (GERD) was defined as reflux of gastric contents causing troublesome symptoms such as recurrent regurgitation with or without vomiting, poor weight gain, irritability, heartburn, or coughing with confirmation of acidic reflux episodes on 24-h pH monitoring

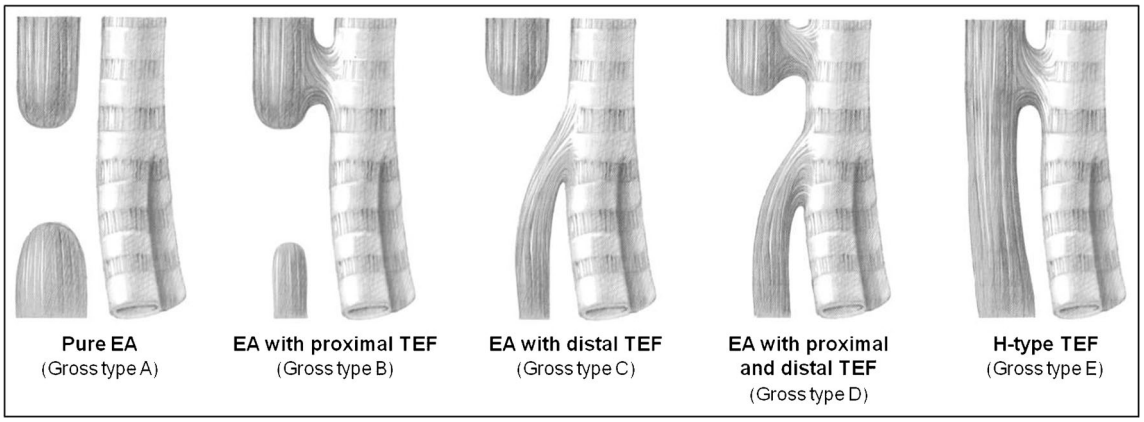

Fig. 1 Types of esophageal atresia (EA) and tracheoesophageal fistula (TEF) according to the Gross classification. Reproduced and modified with permission of Springer from[23]

(intraesophageal pH < 4.0) and upper gastrointestinal endoscopy with biopsy. The 2009 NASPGHAN/ESPGHAN guidelines were used as cutoff (i.e. a reflux index >4% was considered as abnormal).[26]

Those patients with GERD, recurrent respiratory infections, or other conditions such as swallowing disorders, neurological impairment, or coexisting anomalies were seen as often as required, and additional surveillance was arranged by the appropriate specialties.

Statistical Analysis

All data was extracted into an electronic spreadsheet and statistical analysis was performed using PASW Statistics 18.0 software application (SPSS Inc., Chicago, USA). Results are presented as median (range) or mean ± SE. Statistical differences between the two study periods were analyzed using χ^2, Fisher's Exact, or Mann-Whitney *U* test where appropriate. A *P* value of <0.05 was considered statistically significant.

Results

General Patients' Characteristics

Overall, 109 consecutive patients with EA types A (*n* = 6; 5.5%), B (*n* = 5; 4.6%), C (*n* = 89; 81.7%), D (*n* = 7; 6.4%), and E (*n* = 2; 1.8%) were observed in this study. Sixty-two (56.9%) were male and 47 (43.1%) female. Median maternal age was 27 years (range, 18–47 years) with presence of polyhydramnios in 46 (42.2%) cases. Median gestational age was 37 weeks (range, 26–43 weeks) with 58 (53.2%) infants born prematurely. Delivery was vaginal in 67 (61.5%) cases and 42 (38.5%) underwent Cesarean section. Median BW was 2480 g (range, 700–3860 g) with 17 (15.6%) neonates having a BW <1500 g. Coexisting anomalies were found in 70 (64.2%) patients and are illustrated in Table 1. Forty-two (38.5%) had major cardiac defects that required medical, surgical, or palliative treatment. A VACTERL association with at least three congenital malformations was diagnosed in a total of 11 (10.1%) newborns. There were no statistical differences in the incidence of BW <1500 g (10/55 vs. 7/54; *P* = 0.5989) and major cardiac defects (20/55 vs. 22/54; *P* = 0.6962) between the two study periods.

Survival

Overall survival was 92/109 (84.4%) with a significant increase between the early and late study period (Table 2). In total, 13 newborns died before esophageal anastomosis or replacement could be performed. One was a preterm neonate with EA type C and multiple malformations that died on the first day of life and did not receive any surgical treatment. The remaining 12 newborns had low or very low birth weight and received gastrostomy insertion, but died before esophageal continuity could be achieved at a median age of 3 days (range, 1–33 days) due to severe cardiac defects (*n* = 7), cerebrovascular hemorrhage (*n* = 3), and respiratory failure (*n* = 2). Four (4.2%) of the 96 patients that underwent final surgical repair died of cardiac failure (*n* = 2), severe aspiration pneumonia owing to a recurrent TEF (*n* = 1), and peritonitis with subsequent multi-organ failure resulting from a bowel perforation (*n* = 1) within a median time of 106 days (range, 84–529 days) after successful primary (*n* = 2) or delayed (*n* = 2) esophageal anastomosis. All deceased infants were born prematurely and had additional anomalies. There were no statistical differences in postoperative mortality rates between the two study periods (3/45 vs. 1/51; *P* = 0.3379) (Table 3).

Surgical Management

The final surgical repair of 96 patients operated for EA/TEF is displayed in Table 4. Ninety-one newborns underwent

Table 1 Coexisting anomalies, defects, and syndromes in 109 patients with EA/TEF[a]

Cardiovascular malformations (n = 74)	Gastrointestinal malformations (n = 18)
Atrial septal defect (ASD) (n = 18)	Duodenal atresia (n = 9)
Ventricular septal defect (VSD) (n = 13)	Malrotation (n = 8)
Right descending aorta (n = 13)	Omphalocele (n = 1)
Pulmonary stenosis (n = 10)	
ASD + VSD (n = 4)	Anorectal malformations (n = 13)
Tetralogy of Fallot (n = 4)	Imperforate anus without fistula (n = 8)
Single atrium (n = 3)	Recto-perineal fistula (n = 5)
Coarctation of the aorta (n = 2)	
Hypoplastic left heart syndrome (n = 2)	Airway or palate malformations (n = 9)
Hypoplastic right heart syndrome (n = 1)	Congenital diaphragmatic hernia (n = 3)
Persistent truncus arteriosus (n = 1)	Cleft palate (n = 3)
Single ventricle (n = 1)	Tracheoesophageal cleft (n = 2)
Tricuspid atresia (n = 1)	Mandibulofacial dysostosis (n = 1)
Dextrocardia (n = 1)	
	Neurological defects (n = 8)
Skeletal abnormalities (n = 41)	
Vertebral or rip defects (n = 25)	Chromosomal anomalies and syndromes (n = 8)
Limb anomalies:	Trisomy 21 (n = 3)
Radial aplasia (n = 6)	Trisomy 18 (n = 2)
Supernumerary digit (n = 4)	Pierre Robin syndrome (n = 1)
Club foot (n = 4)	Potter's syndrome (n = 1)
Thumb deformity (n = 2)	Treacher Collins syndrome (n = 1)
Genitourinary anomalies (n = 41)	

[a] Patients may have had multiple malformations

primary (n = 66; 68.8%) or delayed (n = 25; 26.0%) end-to-end esophageal anastomosis. Indications for 18 of the 25 delayed primary repairs were long-gap EA types A (n = 4), B (n = 5), C (n = 8), and D (n = 1), which were carried out after a median period of 53 days (range, 14–175 days) with (n = 6) or without (n = 12) longitudinal bougienage of upper and lower pouch. The remaining seven patients were preterm neonates with EA types C (n = 6) and D (n = 1) that were physiologically unstable with severe respiratory distress requiring ventilator support. In these cases, an emergency TEF ligation and gastrostomy insertion was performed, followed by a delayed primary anastomosis after a median stabilization time of 7 days (range, 3–9 days). Two newborns with EA type E had elective division and suture closure of their isolated TEF through a right cervical incision on day 13 and 39, respectively. Long-gap EA was diagnosed in a total of 23 (24.0%) patients with Gross types A (n = 5), B (n = 5), C (n = 9), and D (n = 4). A primary esophagoesophagostomy was possible in 3 of the 23 cases with long-gap EA, 18 underwent delayed primary repair, and 2 required esophageal replacement. Overall, three infants had esophageal replacement with colonic interposition (n = 2) or gastric transposition (n = 1) at a median age of 387 days (range, 86–552 days). Indications were long-gap EA types A (n = 1), C (n = 1), and recurrent TEF with mediastinal abscess and anastomotic stricture in an infant with EA type C after primary repair. No chyle leak, conduit necrosis, or vocal cord injury occurred. The median length of initial hospitalization was 59 days (range, 10–351 days), which decreased significantly between the two study periods (108 ± 13 vs. 59 ± 5 days; P = 0.0160).

Table 2 Survival rates of all 109 patients with EA/TEF according to the Spitz classification

Group	Definition	1975–1989 (n = 55)	1990–2011 (n = 54)	P value
I	BW > 1500 g, no major cardiac anomaly	33/35 (94.3%)	31/31 (100%)	0.49
II	BW < 1500 g or major cardiac anomaly	7/10 (70.0%)	16/17 (94.1%)	0.13
III	BW < 1500 g and major cardiac anomaly	2/10 (20.0%)	3/6 (50.0%)	0.30
Overall survival:		42/55 (76.4%)	50/54 (92.5%)	0.03

Table 3 Mortality rates in 96 operated patients with EA/TEF according to the Spitz classification

Group	Definition	1975–1989 (n = 45)	1990–2011 (n = 51)	P value
I	BW > 1500 g, no major cardiac anomaly	1/34 (2.9%)	0/31 (0.0%)	1.00
II	BW < 1500 g or major cardiac anomaly	1/8 (12.5%)	1/17 (5.9%)	1.00
III	BW < 1500 g and major cardiac anomaly	1/3 (33.3%)	0/3 (0.0%)	1.00
Postoperative mortality:		3/45 (6.7%)	1/51 (2.0%)	0.34

Postoperative Complications

Anastomotic Leakage

Anastomotic leakage was suspected in 11 (11.5%) patients following primary (n = 8) or delayed (n = 3) esophageal anastomosis and was eventually confirmed by chest x-ray with oral contrast: five in the early and six in the late study period, respectively. Six of these were localized defects not requiring surgical revision and healed spontaneously following conservative treatment with chest drainage, broad-spectrum antibiotics, and parenteral nutrition support. The remaining five were considered as major leaks with partial disruption of the esophagoesophagostomy and tension pneumothorax, and were identified after a median time of 2 days (range, 1–5 days) postoperatively. In these cases, a rethoracotomy and suture of the end-to-end esophageal anastomosis was performed. Overall, eight children with conservatively (n = 5) and surgically (n = 3) treated leaks later developed further complications: anastomotic strictures (n = 6) and recurrent distal TEF with (n = 1) or without (n = 1) anastomotic stricture.

Recurrent Distal TEF

A recurrent distal TEF was identified in ten (10.4%) infants with EA types C (n = 8) and D (n = 2): six in the early and four in the late study period, respectively. They presented with feeding difficulties and respiratory symptoms ranging from coughing to cyanotic attacks due to recurrent respiratory infections at a median time of 86 days (range, 43–217 days) after initial surgical repair. Two of these suffered from severe complications. One boy with EA type C, who had previously been operated on for dehiscence of the primary esophageal anastomosis, developed a recurrent distal fistula with mediastinal abscess and anastomotic stricture. He required open revision with cervical esophagostomy, feeding jejunostomy, and later underwent esophageal replacement with colonic interposition at the age of 17 months. The other one was a premature girl with EA type D and initially missed but then closed proximal fistula that died 106 days after primary esophageal repair of aspiration pneumonia before renewed surgical closure of a recurrent distal TEF could be performed. The remaining eight patients had successful reoperation by thoracotomy and returned to normal dietary feeding following a failed attempt of endoscopic treatment with Histoacryl or fibrin glue in five cases. Seven of these subsequently presented again with anastomotic strictures.

Table 4 Final surgical repair in 96 patients with EA/TEF

	Gross type of EA/TEF				
	A	B	C	D	E
Primary anastomosis (n = 66)	–	–	62	4	–
Delayed primary anastomosis (n = 25)	4	5	14	2	–
Closure of TEF (n = 2)	–	–	–	–	2
Esophageal replacement (n = 3)					
Colonic interposition (n = 2)	–	–	2	–	–
Gastric transposition (n = 1)	1	–	–	–	–

Undiagnosed Proximal TEF

An initially undiagnosed proximal fistula was found in four (4.2%) patients after primary anastomosis for supposed EA type C (n = 3) and following delayed primary repair for supposed EA type A (n = 1) at a median of 74 days (range, 7–122 days) postoperatively. The proximal TEF was not identified during the initial tracheobronchoscopy preceding the esophagoesophagostomy in three newborns, and in one no tracheobronchoscopy was performed. Each case of missed upper fistula or recurrent distal TEF was confirmed by repeat esophago-/tracheobronchoscopy and if necessary injection of diluted methylene blue. The initial diagnosis was reverted accordingly and all infants underwent open closure of the previously undiagnosed proximal fistula through a cervical incision. All regained full oral intake afterwards.

Anastomotic Stricture

Postoperative esophageal strictures at the anastomotic site were endoscopically confirmed in 69 (71.9%) symptomatic children with dysphagia or respiratory distress during oral feeding and were treated by hydrostatic balloon dilatations or bougienage: 39 in the early and 30 in the late study period, respectively (P = 0.0030). The median number of dilatations was 3 (range, 1–15) with the last dilatation performed at a

median age of 177 days (range, 16 days to 12.8 years). Between 1975 and 1989, 23 (59.0%) patients had <5 dilatations and 16 (41.0%) required >5 dilatations. Since 1990, only 8 (26.7%) children underwent >5 dilatations. All cases of long-gap EA developed an anastomotic stricture with need for frequent dilatations. In two infants with EA types A (n = 1) and C (n = 1), the stricture was recalcitrant to repeated dilatations and resection with end-to-end reanastomosis became necessary 10 and 12 months, respectively, following delayed primary repair. One premature boy with EA type A developed a fistula at the suture line with severe anastomostic stricture 2 months after delayed primary anastomosis with Rehbein's bougienage. He underwent open reoperation with resection of the stricture and esophageal reanastomosis. In total, GERD-associated anastomotic strictures were diagnosed in 59 (85.5%) of these patients and fundoplication ultimately became necessary in 26 cases.

Functional Follow-Up

The median age at most recent follow-up was 9.6 years (range, 3–27 years). A total of 71 (74.0%) infants were readmitted more than once in the first year of life and a median of 5 (range, 1–26) hospitalizations with or without surgical interventions were required until the age of 3 years. Eighty-nine (96.7%) of the currently living 92 patients are thriving with normal oral feeds. In 80 (89.9%) of these, full dietary intake without any supplemental feeding gastrostomy or nasogastric tube was achieved within 3 months following surgery, whereas the remaining 9 (10.1%) had prolonged dependence due to various postoperative complications: anastomotic strictures (n = 3), recurrent fistula (n = 2), or coexisting anomalies including congenital heart defects (n = 2) and syndromic disorders (n = 2). At present, three (3.3%) children remain dependent on feeding gastro- or jejunostomy. All of these have neurological impairment and suffer from severe dysphagia with high aspiration risk. Esophageal manometry showed no propagating swallows with reduced pressure of the lower esophageal sphincter and proven GERD on 24-h pH monitoring.

Weak or absent esophageal peristalsis with impaired or absent contraction pattern was found postoperatively in a total of 78 (84.8%) infants at 1 year of age, deteriorating to 100% proven dysmotility at 10-year follow-up manometry. Fifty-six (60.9%) suffered from varying degrees of swallowing difficulties. In 12 (13.0%) cases, there was at least one episode of esophageal food or foreign body impaction requiring endoscopic removal. An underlying anastomotic stricture associated with GERD and need for repeat dilatation was identified in eight of these. All of them eventually had anti-reflux surgery.

Overall, GERD was diagnosed in 73 (79.3%) patients after EA/TEF repair and all exhibited weak or absent peristalsis of the distal esophageal segment with reduced pressure of the lower esophageal sphincter, causing increased frequency of acidic reflux episodes as a result of a balance created between the intraesophageal and intragastric pressure. Forty-three (58.9%) were on intermittent or permanent anti-reflux medications, whereas the remaining 30 (41.1%) children did not respond to any conservative therapy and ultimately underwent fundoplication at a median age of 26 months (range, 31 days to 10.3 years). Types of fundoplication procedures were Nissen (n = 17), Thal (n = 5), Toupet (n = 4), and Guarner (n = 4).

Upper gastrointestinal endoscopy revealed moderate or severe esophagitis in 22 (23.9%) cases at a median time of 15 years (range, 8–22 years) after initial surgical repair, which was associated with a significant increase in GERD since the introduction of routine pH monitoring in 1990 (29/42 vs. 44/50; P = 0.0377). Barrett's mucosa without dysplasia was found in one patient at 20-year follow-up.

Recurrent respiratory infections following EA/TEF surgery occurred in 59 (64.1%) children, decreasing significantly in frequency and duration during the first 5 years of life. All of these demonstrated esophageal dysmotility and GERD. Relevant tracheomalacia was diagnosed in 29 (31.5%) cases based on tracheobronchoscopic findings after a median postoperative time of 131 days (range, 31 days to 4.1 years). The majority (n = 21) had mild symptoms and were successfully treated with non-operative conservative therapy. Eight patients, which all presented with recurrent dyspnea, dying spells, and significant tracheal collapse, eventually required surgical intervention with aortopexy (n = 6) or tracheal stenting (n = 2).

Discussion

Since the first successful primary repair of a newborn with EA/TEF in 1941, survival rates have significantly improved throughout the world and the majority of today's patients will reach adulthood.[17, 27] Although there was a significant increase in overall survival between the early and late study period in our series, no statistical differences between postoperative mortality rates were found. These findings suggest considerable improvements in neonatal resuscitation and intensive care, thus allowing for more severely ill and complex neonates with EA/TEF (i.e. Spitz group II and III) to survive and eventually undergo surgical repair. The overall mortality following surgery for EA/TEF was low at 4.2% and appears within international results.[3, 9–11, 28] In general, the postoperative mortality seems to be more reflective of a center's overall neonatal expertise rather than the operative management itself as recently demonstrated by a nationwide study of 3479 children with EA/TEF across the United States.[8]

Because of its rarity and complex nature, EA/TEF represents one of the major therapeutic challenges not only in modern pediatric surgery but also for other specialties involved due to serious short- and long-term morbidities.[13–18] Our results were consistent with previous studies indicating that despite precise esophageal reconstruction and excellent postoperative care, early and late complications frequently occur and must be dealt with.[19–22] The definition of possible complications is however lacking standardization, which makes an exact comparison with the literature difficult and thus results in highly variable incidence rates.[13, 14] It can be assumed that the development of complications after initial EA/TEF repair is most likely a multifactorial process that depends on applied surgical techniques, peri-/postoperative care, and individual patient factors.[29]

Early complications in our cohort included minor (6.3%) or major (5.2%) anastomotic leaks, recurrent TEF with (1.0%) or without (9.4%) anastomotic stricture, initially missed proximal fistula (4.2%) and refractory anastomotic strictures with (1.0%) or without (2.1%) fistula.

Severe anastomotic leakage due to partial disruption of the esophageal anastomosis is one of the most serious and potentially fatal complications following EA/TEF surgery, which should be immediately operated on before inflammation and necrosis renders the esophageal wall unsuitable for resuturing.[30] Almost 75% of the successfully treated patients in our series with an anastomotic leak developed afterwards a recurrent distal TEF or stricture, which is in accordance with a recent study from Helsinki that identified anastomotic leakage as a significant risk factor for recurrent TEF and stricture formation.[30] It is therefore recommended that all infants with EA/TEF and a previous history of anastomotic leakage, who suffer from nonspecific symptoms like recurrent respiratory issues or feeding difficulties, should be investigated by contrast study and esophago-/tracheobronchoscopy with methylene blue test.[31]

Similar to other authors,[29] our experience was that despite multiple applications, endoscopic administration of tissue adhesive substances was not very effective in the treatment of recurrent TEF, whereas we had good success rates with an open approach, careful surgical separation and interposition of vascularized pericardial or pleural tissue even in cases with severe adhesion or infection at the primary TEF site. Furthermore, a recurrent distal TEF should be distinguished from a previously unidentified proximal fistula, which is very rare but can be missed, especially when the gap between the upper and lower esophageal pouch is small without need for extensive mobilization.[32, 33] In approximately 4% of our cases with EA/TEF, an initially undiagnosed fistula above the esophagoesophagostomy was found during reoperation without much adhesion and successfully closed through an cervical incision. Nevertheless, the fact that three proximal TEFs were missed despite preoperative tracheobronchoscopy highlights the necessity to carefully inspect the posterior tracheal wall. Today, we are using a slightly bent tip of a 3F ureteral catheter to search for potential small opening pits in the posterior tracheal membrane.

Anastomotic strictures are one of the most frequent problems after EA/TEF repair and can significantly complicate the further outcome.[34] The majority usually respond well to repeated dilatations with bougies or hydrostatic balloons without need for further intervention. Only 24 (25.0%) children in our series with a stricture had more than five anastomotic dilatations. However, two of the strictures were recalcitrant and patients ultimately underwent resection with end-to-end reanastomosis. A study from the United Kingdom recently suggested that resection of an anastomotic stricture following EA/TEF surgery should be considered if more than ten balloon dilatations are required.[35] Significant tension on the anastomotic site due to long-gap disease, previous history of anastomotic leakage, and recurrent GERD are known risk factors for stricture formation.[30, 34] Unsurprisingly, all of our long-gap cases, and seven patients with a preceding leak, later developed an anastomotic stricture. In addition, most of our infants with EA/TEF that presented with recurrent strictures also had GERD, and in almost half of these a fundoplication became necessary around the age of 2 years. GERD is a common issue after EA/TEF repair that does not tend to improve over time. It most likely originates from the esophageal malformation itself, abnormal innervation patterns of the distal esophageal segment with insufficient propulsive peristalsis and deficient function of the lower esophageal sphincter, thus causing a long acid exposure time after each reflux episode.[36]

The present series concurs with a recent nationwide survey from Italy, demonstrating that the treatment of long-gap EA can be challenging as nearly all of these patients will experience some sort of postoperative difficulties.[37] Furthermore, we identified a high rate of gastroesophageal problems in our cohort including dysphagia, impaired esophageal peristalsis, and GERD, often persisting into adulthood. As patients with EA/TEF have experienced these symptoms since infancy, most have likely adapted them into their lifestyle and would not necessarily report them spontaneously. It has been pointed out that these cases may have an increased risk of malignancy of the esophagus later in life, which is why regular endoscopy and combined impedance/pH monitoring has been recommended for EA/TEF.[21] On the other hand, a recent study of 209 patients with a median follow-up of 12 years discovered only esophagitis and metaplasia, but no dysplasia or cancer after surgery for EA/TEF.[38] Thus, these findings indicate that routine endoscopic surveillance seems to have limited benefit during childhood, but is crucial from adolescence onwards. The exact cause of the underlying abnormal esophageal function in EA/TEF is, however, still not fully understood, and the correlation between symptoms, investigational findings, and later outcome often appears to be poor.[39]

In general, patients with EA/TEF needed complex and frequent hospital-based care as recently also shown by a multidisciplinary team from Toronto.[40] If a revision of the accomplished esophagoesophagostomy unfortunately becomes necessary, one has to deal with very difficult and complex cases that may still require further surgical interventions to ultimately regain esophageal continuity. In comparison with other large series,[10, 41] replacement of native esophagus in our cohort was with 3% very low, which is probably associated with the high rate of delayed primary repair. It has been reported that with regard to gastroesophageal function, delayed primary anastomosis generally provides good results, especially in the management of long-gap EA.[42] Permanent dependence on gastro-/jejunostomy feedings in this series only occurred in three neurologically impaired infants with severe swallowing disorders, whereas more than 95% enjoyed full oral intake despite existing esophageal dysmotility. According to recently published data from 90 children and adults with EA/TEF registered in a German patient support group, the health-related quality of life after complex and/or complicated surgery appears to be excellent.[43]

All 96 cases in our cohort operated for EA/TEF were managed with open surgery. Although thoracoscopic EA/TEF repair was described more than 10 years ago, this approach is currently performed at only a few centers due to technical difficulties associated with the minimally invasive access, related learning curve, and long operative time. Thoracoscopic correction of EA/TEF trends toward increased anastomotic leakage, and greater need for fundoplication.[44] Results published by surgeons who are pioneers in minimally invasive EA/TEF repair may not be generalizable and the complication rate from centers with less experience is likely underreported in the literature.[45] Furthermore, a recent randomized controlled trial reported that thoracoscopic EA/TEF repair can be associated with worse intraoperative acidosis and hypercapnia compared with open management.[46] However, in selected patients and with experienced teams, thoracoscopic correction of EA/TEF is appropriate.

The limitations of this study lie in its follow-up design and thus reliance on individually written chart records. Not reported confounding factors could not necessarily be ruled out, which may have caused a potential result bias.

Conclusion

The overall outcome following EA/TEF surgery was characterized by a low mortality rate with the vast majority of cases achieving normal dietary intake. Postoperative complications were successfully treated in nearly all patients with EA/TEF, but had a significant impact on later esophageal function. Potential problems should be early recognized and competently managed in order to reduce the risk of long-term morbidity. A multidisciplinary follow-up with proper transitional care into adulthood is therefore highly recommended.

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Data acquisition, analysis, and interpretation: F.F., B.K., A.H.-Z., P.S., H.T., H.S., M.E.H.
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Agreement to be accountable for all aspects of the work: F.F., B.K., A.H.-Z., P.S., H.T., H.S., M.E.H.

Compliance with Ethical Standards

Author Disclosure Statement The authors declare that this study was conducted in the absence of any commercial or financial relationships that could be constructed as a potential conflict of interest.

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