Morbidity and mortality in esophageal atresia and tracheoesophageal fistula: a 20-year review

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Background **The outcome of newborns with esophageal atresia (EA) and tracheoesophageal fistula (TEF) has improved considerably. At present, the overall survival rates reported from developed countries are between 85 and 95%. This, however, is not the case from developing countries, where several factors contribute to higher morbidity and mortality rates. This study is an analysis of our experience with 158 patients of EA and TEF, with emphasis on factors contributing to morbidity and mortality.**

Patients and methods **This is a retrospective study of 158 patients with EA and TEF treated over a period of 20 years (between January 1992 and December 2011). Their records were reviewed, the study period was divided into two equal periods, and the results were analyzed accordingly.**

Results **A total of 158 patients (89 boys and 69 girls) with EA/TEF were treated. Their mean birth weight was 2.4 kg (700–3800 g). Their ages at diagnosis ranged from newborn to 8 months. Their gestational age ranged from 32 weeks to 41 weeks. Contrast study was used in 45 (28.5%) patients. Aspiration pneumonia was detected in 34.8% patients. The distribution of the number of patients according to the type of EA/TEF was as follows: 132 (83.5%) patients had EA with distal TEF, 14 (8.9%) had pure EA, five (3.2%) had EA with proximal and distal TEF, five (3.2%) had H-type TEF, and two (1.3%) had EA with proximal TEF. Forty-one (22.2%) patients had long-gap EA/TEF. Associated anomalies were seen in 82 (51.9%) patients, and 17 (10.8%) patients had severe anomalies. The postoperative complications included: anastomotic leak in 20 patients (12.7%), stricture in 22 (13.9%), gastroesophageal reflux in 18 (11.4%), tracheomalacia in two (1.3%), and recurrent TEF in one (0.6%). However, there was a marked decrease both in mortality and morbidity during the second period of the study. In our study, the overall mortality rate was 20.9%, but if those with severe associated anomalies were excluded, our postoperative mortality rate was 8.4%. Sepsis was the main cause of death.**

Conclusion **This is a relatively large series from a developing country. Although our postoperative complication rates were similar to those from developed countries, the overall mortality was higher. There was, however, a marked improvement during the second period of the study. This is attributed to a better understanding, early diagnosis, prompt referral, and better surgical techniques. Prematurity, sepsis, and associated severe malformations were the main causes of death. Once major anomalies responsible for death were excluded, our postoperative mortality rate was 8.4%. Sepsis continues to be a major cause of death, and several factors contribute to this, including prematurity and delayed diagnosis with increased incidence of aspiration pneumonia. To decrease the mortality rate, these factors should be addressed, and every effort should be made to overcome them. Patients with long-gap EA/TEF continue to be a management challenge, and every attempt should be made to preserve the native esophagus. Delayed primary repair and/or esophageal stretching are at present the preferred techniques with good long-term functional results.** ***Ann Pediatr Surg*** **9:93–98** © **2013 Annals of Pediatric Surgery.**

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Introduction

Esophageal atresia (EA) with or without tracheoesophageal fistulas (TEFs) is a fairly common congenital malformation. In 1941, Cameron Haight [1] performed the first primary repair of EA with TEF since then, the management of these patients has evolved considerably over the years. This is attributed to several factors, including early diagnosis, better perioperative management, refinements in neonatal surgical techniques, and improved anesthesia and neonatal intensive care. It is also recognized that prompt diagnosis, appropriate clinical management, and expeditious referral to a tertiary care center have had a dramatic impact on the improved survival of these infants. Estimates today suggest that, in the absence of other severe anomalies, survival rates in these infants approach 90–100% from developed countries [2–5]. This, however, may not be the case from developing countries, where several factors continue to contribute to morbidity and mortality. This report is an evaluation of our experience with 158 patients with EA/TEF seen over a 20-year period, with special emphasis on factors pertaining to the final outcome.

Patients and methods

Over a period of 20 years from January 1992 to December 2011, 158 patients with EA with or without TEF were

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Table 1 Classification of the different types of esophageal atresias (*N*=158)

Type of anomaly	*N* (%)
Esophageal atresia with a distal tracheoesophageal fistula	132 (83.5)
Pure esophageal atresia	14 (8.9)
Esophageal atresia with both proximal and distal fistulas	5 (3.2)
Esophageal atresia with a proximal fistula	2 (1.3)
H-type tracheoesophageal fistula	5 (3.2)

treated at our hospital. Their medical records were retrospectively reviewed for age at diagnosis, sex, birth weight, gestational age, associated anomalies, method of diagnosis, associated aspiration pneumonia, type of anomaly, morbidity, and mortality. The study was divided into two equal periods (January 1992–December 2001 and January 2002–December 2011), and the results were analyzed and compared in relation to these two periods. This division into two equal periods was made arbitrarily, and the aim was to observe the effects of an early diagnosis, the method of diagnosis, and early and proper transfer on the final outcome.

Results

A total of 158 patients (89 boys and 69 girls) with EA with or without TEF were treated at our hospital. The majority of our patients (80%) were referrals from other hospitals in the region and some of them were from distantly located hospitals. The mean birth weight of the patients was 2.4 kg (700–3800 g). Their gestational ages ranged from 32 to 41 weeks, and in 40 (25.3%) of them the gestational age was less than 35 weeks. In 45 (28.5%) patients, there was a positive history of polyhydramnios. Five of our patients were one of a pair of twins, and one of them had a brother with EA. Their ages at diagnosis ranged from newborn to 8 months. Contrast study to confirm the diagnosis was used in 45 (28.5%) patients, and most of these procedures were performed during the initial years of the study as well as before their referral to our hospital. Fifty-five (34.8%) patients had aspiration pneumonia at the time of admission.

The different types of EA and TEF are shown in Table 1. EA with distal TEF was the most common condition and was observed in 132 (83.5%) patients; this was followed by pure EA in 14 patients (8.9%). Five patients (3.2%) had EA with both proximal and distal TEF, five (3.2%) had H-type TEF, and two (1.3%) had EA with proximal TEF. Associated anomalies were seen in 82 (51.9%) patients as shown in Table 2. Congenital heart disease was the most common condition and was observed in 52 (33%) patients. Chromosomal abnormalities were seen in 13 (8.2%) patients; these included Edward's syndrome in eight patients and Down's syndrome in five. Two of our patients had associated agenesis of the left hemidiaphragm with severe lung hypoplasia, and nine (6%) had associated anorectal malformations. A right-sided aortic arch was seen in 11 (7%) patients, and four(2.5%) had associated intestinal atresia. Seventeen (10.8%) patients had severe associated anomalies that contributed to mortality; these included Edward' syndrome in eight patients, agenesis of the left hemidiaphragm with lung hypoplasia in two, severe congenital heart disease in five, severe hyaline membrane disease in one, and epidermolysis bullosa in one.

Table 2 Associated congenital malformations in 158 patients with esophageal atresia with or without tracheoesophageal fistulas

Associated anomaly	*N* (%)
Congenital heart disease	43 (27.2)
Right-sided aorta	11 (7)
Vertebral anomalies	11 (7)
Edward's syndrome	8 (5)
Down's syndrome	5 (3.2)
VACTERL association	2 (1.3)
Agenesis of the left hemidiaphragm	2 (1.3)
Intestinal atresia	4 (2.5)
Urological malformations	3 (1.9)
Congenital esophageal stenosis	1 (0.6)
Anorectal malformations	9 (5.7)
Hydrocephalus	3 (1.9)
Limb deformity	4 (2.5)
Others	41 (25.9)

Table 3 Comparison of results according to the two study periods

Parameters	Study period I (1989–2001)	Study period II (2002–2011)
Total number of patients	89	95
Mortality	23 (25.84)	10 (10.25)
Aspiration pneumonia	41 (46.6)	14 (14.73)
Leak	12 (13.48)	8 (8.42)
Stricture	15 (16.85)	7 (7.36)
Recurrent fistulas	1 (1.12)	0

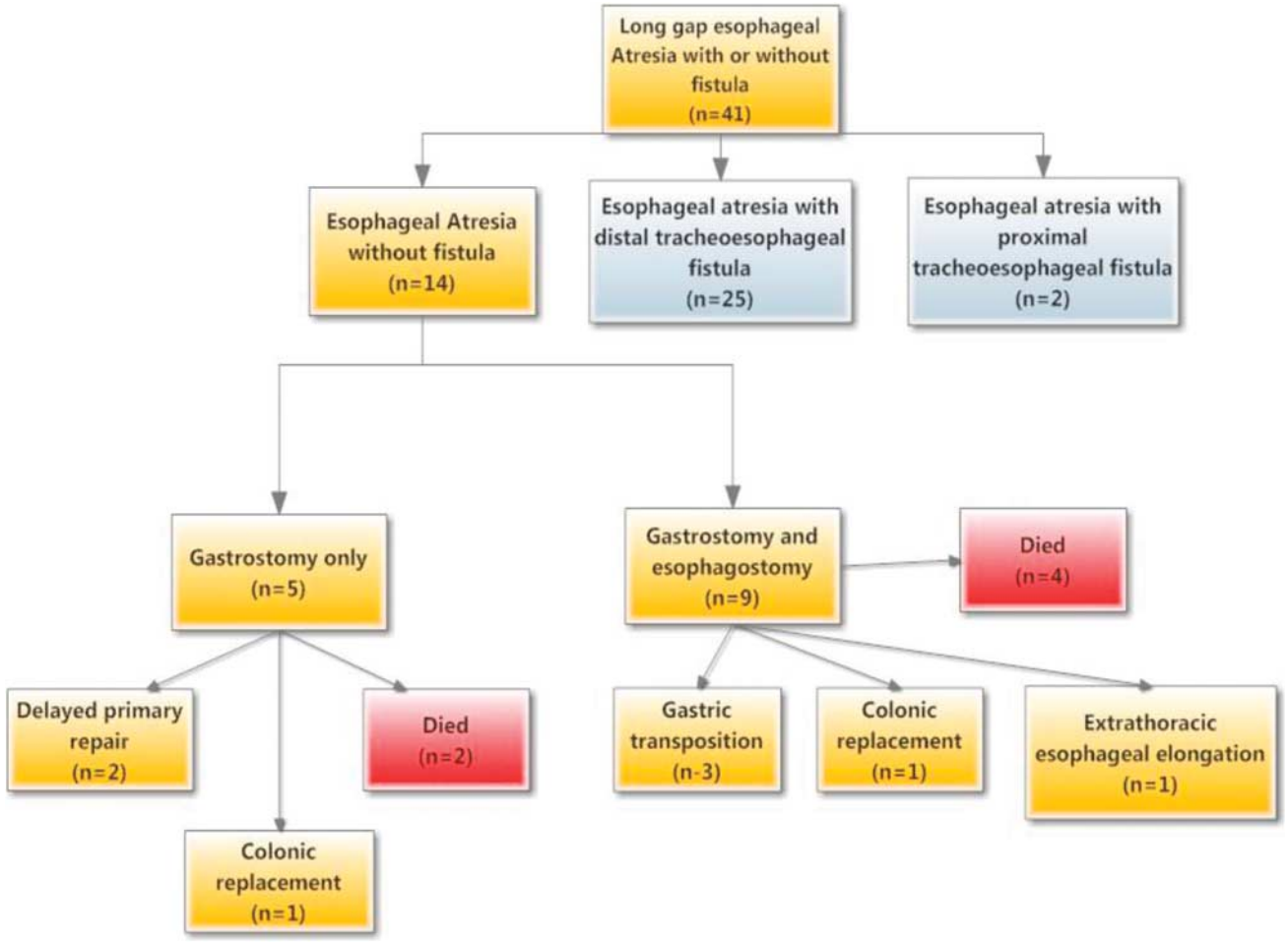
Table 4 Distribution and mortality according to Spitz's classification

Group	Number of patients	Mortality (%)
I	82	0 (0)
II	41	8 (19.5)
III	35	25 (71.4)

All our patients were operated upon, except for two who had severe associated anomalies and died before surgery. The patient distribution according to Spitz's classification [6] is shown in Table 4. In our study, postoperative complications included anastomotic leak in 20 (12.8%) patients, stricture in 22 (14%), gastroesophageal reflux in 18 (11.5%), tracheomalacia in two (1.3%), and recurrent TEF in one (0.6%). The result analysis in relation to the two study periods is shown in Table 3.

Forty-one (26.3%) of our patients had long-gap EA with or without TEF. This is arbitrarily defined as an inability to perform primary anastomosis, primary anastomosis under severe tension, or a gap between the two esophageal ends greater than three vertebral bodies. Among the patients, 25 had an EA with TEF, 14 had pure EA, and two had EA with a proximal TEF fistula. Of the 14 patients with pure EA, three underwent initial gastrostomy – two died because of sepsis and one subsequently underwent a retrosternal colonic replacement; two underwent gastrostomy and delayed primary repair – both of them developed an esophageal stricture that was dilatable; and nine underwent gastrostomy and esophagostomy – three

Fig. 1



Long-gap esophageal atresia without a fistula.

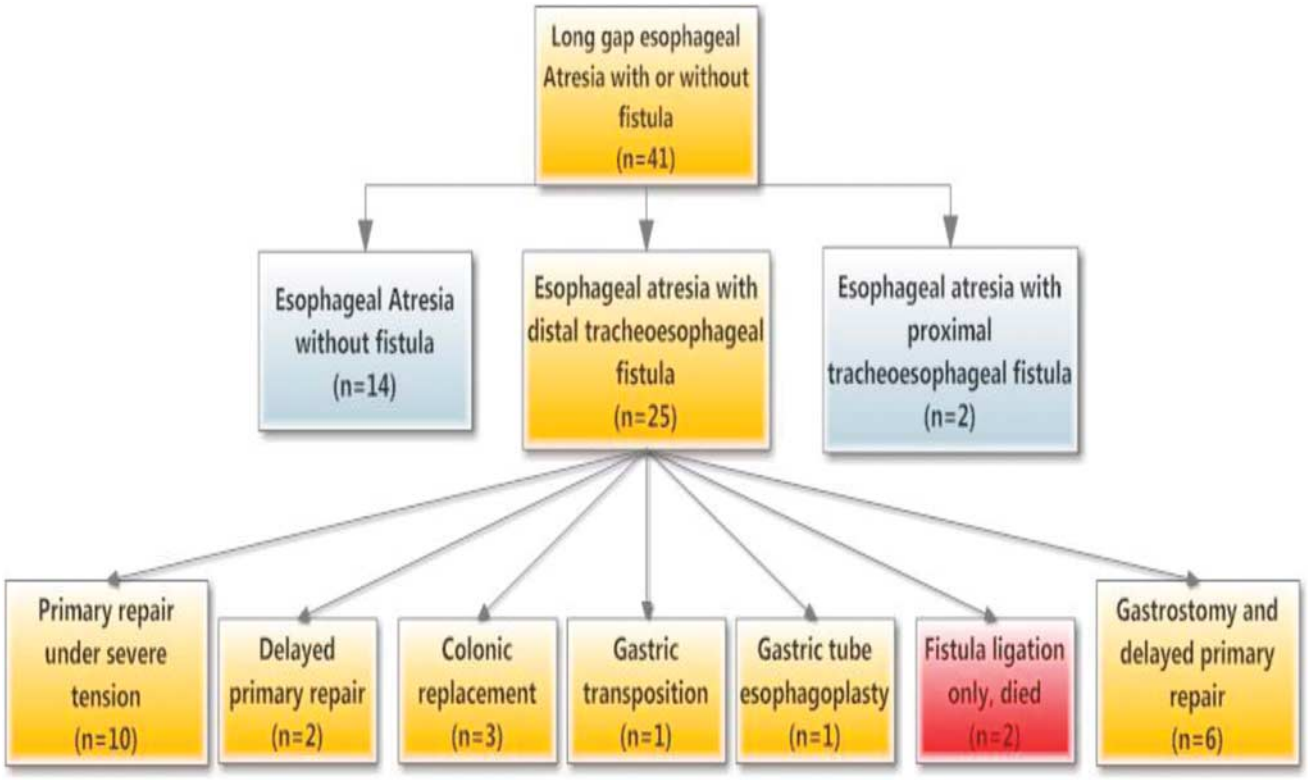
subsequently underwent gastric transposition, one underwent a retrosternal colonic replacement, one underwent an extrathoracic esophageal elongation, and four died while waiting for surgery. Twenty-five patients had EA with distal TEF; of them, 10 underwent primary repair under severe tension, and all patients developed an esophageal stricture that was dilatable, except for one who subsequently required resection of the stricture and an end-to-end anastomosis. Two patients underwent a delayed primary repair after closure of the fistula, whereas six underwent closure of the fistula, gastrostomy, and delayed primary repair. Three patients underwent gastrostomy and esophagostomy, with subsequent colonic replacement. Two patients underwent ligation of the fistula only and planned for a delayed primary repair; however, they died of sepsis. Two patients underwent ligation of the fistula as well as gastrostomy and planned for a delayed primary repair; however, there was no significant growth of the esophageal ends, and subsequently one of them underwent a gastric transposition and the other underwent gastric tube replacement. Two patients had EA with proximal TEF; both of them underwent gastrostomy and esophagostomy – one patient subsequently underwent gastric tube esophagoplasty and the other underwent gastric transposition (Figs 1–3).

Thirty-three of our patients died, resulting in an overall mortality rate of 20.9%. This is relatively high, but if we exclude those with severe congenital anomalies (eight patients with Edward's syndrome, two with agenesis of the diaphragm with severe lung hypoplasia, five with severe congenital heart disease, one with severe hyaline membrane disease, one with epidemolysis bullosa, and the two patients who died preoperatively), our postoperative mortality rate was 8.4%. Sepsis was the main cause of death in our series. The overall outcome according to Spitz's classification is shown in Table 4.

Discussion

EA with or without TEFs is a fairly common congenital malformation, with a reported incidence of one in 2500 to one in 4000 live newborns. The treatment of esophageal atresia has advanced markedly over the last 50 years, from a nearly fatal condition to a current overall survival approaching 90–100% [2–5]. Associated severe anomalies, low birth weight, and prematurity continue to affect treatment and outcome. In 1962, Waterston [7] proposed the risk classification of patients with EA/TEF and separated patients into three groups on the basis of birth weight, presence of associated pneumonia, and presence

Fig. 2

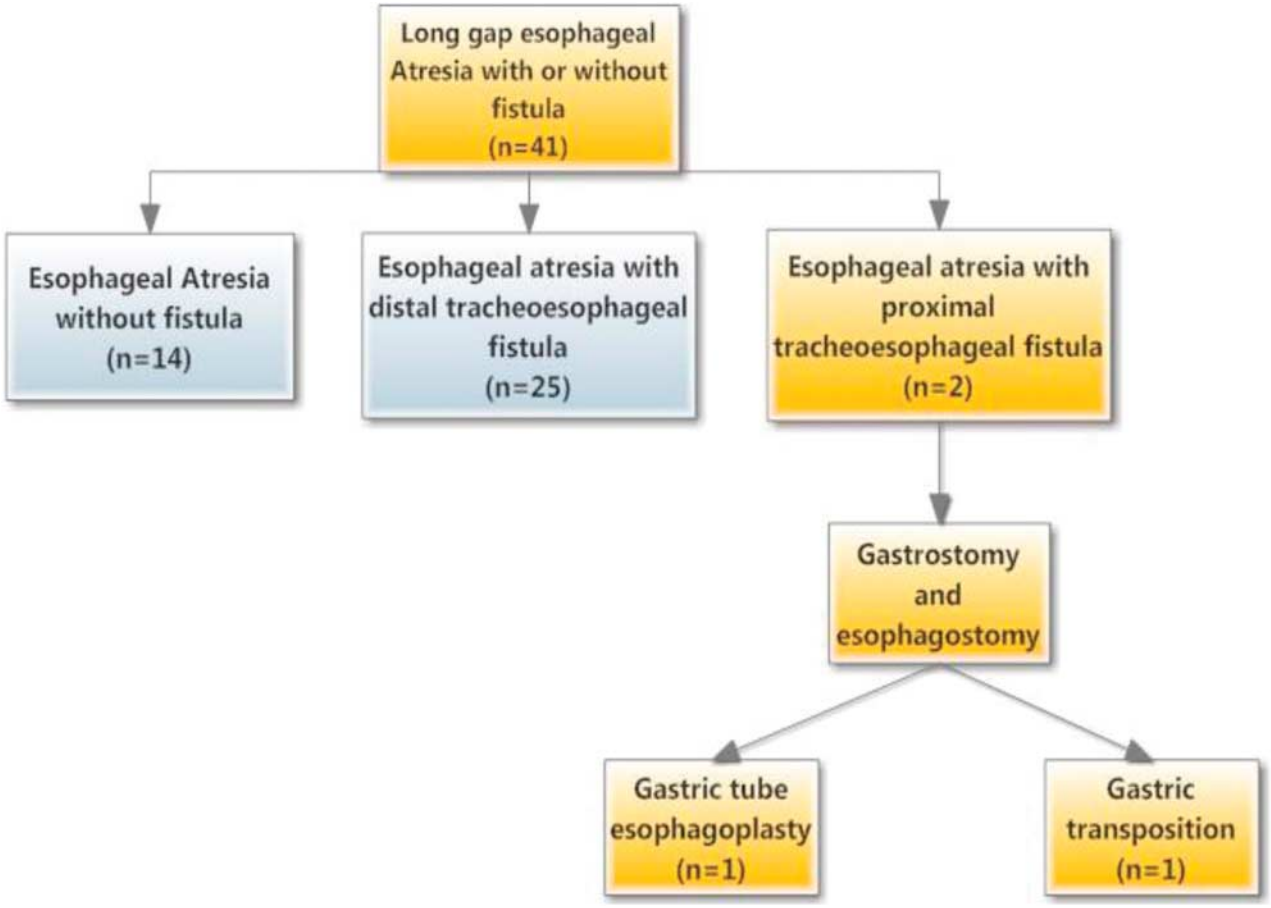


Long-gap esophageal atresia with a distal fistula.

of congenital anomalies. This classification was subsequently modified by Spitz in 1994 [6]. Spitz's classification is the most commonly used classification and divides patients into three groups on the basis of birth weight and the presence or absence of cardiac anomalies. In 1993, Poenaru *et al*. [8] proposed a simpler two-group classification system (Montreal classification) based on ventilator dependency and the presence or absence of major associated anomalies. At present, associated severe congenital anomalies are the main contributing factor for mortality, and aspiration pneumonia is no longer considered a prognostic factor. One reason for this is the early diagnosis and prompt referral of these patients to specialized centers. This, however, was not the case in our setting, wherein 34.8% of our patients had aspiration pneumonia at the time of their referral. One contributing factor for this is that a large number of our patients were referred from other hospitals in the region, some of which are very distantly located. The delayed and improper transfer of such patients contributed to the high incidence of aspiration pneumonia. Another factor is the use of a contrast study in 28.5% of our patients to confirm the diagnosis before their referral. The use of contrast esophagograms is seldom necessary to confirm the diagnosis of EA and should be abandoned, as this will not only delay their transfer but also increases the risk of hypothermia, aspiration pneumonia, and reactive pulmonary edema. At present, the diagnosis of neonates with EA/TEF is made within the first few hours of life, and arrangements are made to transfer them immediately to specialized centers where pediatric surgeons are available. Delay in diagnosis and transfer is reflected in a high incidence of aspiration pneumonia. This was clearly shown in our study, in which there was a marked improvement between the two study periods, not only in terms of mortality but also as a decreased incidence of aspiration pneumonia and reduced postoperative leak and stricture formation. This, we feel, is attributed to a better understanding of the anomaly, early diagnosis, rapid and proper transfer, and improved surgical techniques.

EA with or without TEF is often associated with other congenital anomalies, most commonly cardiac abnormalities. This was the case in our series. Associated anomalies were seen in 82 (51.9%) patients, and congenital heart disease was the most common associated anomaly, which was seen in 52 (33%) patients; because of this, echocardiography should be part of the routine preoperative workup of these patients. Some of the cardiac defects were complex and severe and had a negative impact on the outcome. At present, we routinely perform an echocardiogram and an abdominal ultrasound for all our patients. Chromosomal abnormalities are common with EA and were seen in 13 (8.2%) of our patients [9]. These included Edward's syndrome in eight and Down's syndrome in five patients. In many centers, patients with Edward's syndrome, because of the already known outcome, will not be operated upon and will eventually die. All our patients with Edward's syndrome were operated upon for religious and social reasons and

Fig. 3



Long-gap esophageal atresia with a proximal fistula.

because surgical repair makes it easier for parents to care for these patients until their death. In general, about 5% of infants with EA have a right-sided aortic arch, and if this is detected preoperatively a left thoracotomy is advocated to achieve repair. Of interest was the finding of a right-sided aorta in 11 (7%) of our patients; in six patients, this was diagnosed preoperatively, whereas in the other five it was detected intraoperatively. However, the finding of a right-sided aortic arch did not alter our surgical approach, and similar to another study we found it possible to perform the anastomosis from the right side [10].

Most infants with EA/TEF undergo repair during early infancy, with division of the TEF and primary esophageal anastomosis. Patients with long-gap EA with or without TEF continue to present a major surgical challenge. In the past, these patients were managed with gastrostomy and esophagostomy and subsequent esophageal replacement with stomach, gastric tube, jejunal, or colonic segments. At present, these procedures are rarely used as they are associated with a higher prevalence of long-term respiratory and esophageal complications, and every attempt should be made to preserve the native esophagus. In the first half of our study, we managed our patients with long-gap using a similar approach; however, in the last 12 years, none of our patients has undergone an esophageal replacement procedure. At present, most of our patients with long-gap EA are managed with gastrostomy and delayed primary anastomosis. Despite the higher incidence of esophageal stricture and gastroesophageal reflux, delayed primary anastomosis provides good long-term functional results [11]. Neonatal esophageal stretching has been reported to allow primary anastomosis of the esophagus, even in infants with a very long-gap EA/TEF [12]. One of our patients with a long-gap EA was referred to us with cervical esophagostomy and was managed with extrathoracic esophageal elongation [13]. Late complications of EA/TEF include esophageal stricture, tracheomalacia, recurrence of TEF, and gastroesophageal reflux. The complication rates observed in our study are as follows: anastomotic leak, 12.7%; anastomotic stricture, 13.9%; recurrent TEF, 0.6%; tracheomalacia, 1.2%; and gastroesophageal reflux, 11.4%. These results are comparable to those reported from Western centers [2–5,14]. All leaks were minor and managed conservatively. Patients with strictures were managed with balloon dilatation, except one patient who was not responding and underwent resection of the stricture with end-to-end anastomosis. It is our practice to manage gastroesophageal reflux after repair of EA/TEF medically, and only four of our patients with gastroesophageal reflux underwent Nissen's fundoplication.

The management of newborns with EA with or without TEF has advanced over several decades because of improvements in surgical techniques and neonatal intensive care. With the rapid advancements in minimally invasive surgical techniques and instruments for neonates, many of these patients will be managed thoracoscopically in the future. This is especially evident from encouraging reports, which show that thoracoscopic repair of EA/TEF can be safely performed by experienced endoscopic surgeons [15–17].

Conclusion

This is a relatively a large series from a developing country, and although our postoperative complication rates are similar to those from developed countries the overall mortality was higher. There was, however, a marked improvement in the second period of the study. This is attributed to better understanding of the anomaly, early diagnosis, prompt referral and better surgical techniques. Prematurity, sepsis, and associated severe malformations continue to be the causes of death. Patients with long-gap EA/TEF continue to be a management challenge, and every attempt should be made to preserve the native esophagus. Delayed primary repair and/or esophageal stretching are at present the preferred management techniques with good long-term functional results.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

References

1 Haight C, Towsley HA. Congenital atresia of the esophagus with tracheoesophageal fistula and end-to-end anastomosis of esophageal segments. *Surg Gynecol Obstet* 1943; **76**:672–688.
2 Louhimo I, Lindahl H. Esophageal atresia: primary results of 500 consecutively treated patients. *J Pediatr Surg* 1983; **18**:217–229.
3 Randolph JG, Newman KD, Anderson KD. Current results in repair of esophageal atresia with tracheoesophageal fistula using physiologic status as a guide to therapy. *Ann Surg* 1989; **209**:526–531.
4 Manning PB, Morgan RA, Coran AG, Wesley JR, Polley TZ Jr, Behrendt DM, *et al*. Fifty years' experience with esophageal atresia and tracheoesophageal fistula. *Ann Surg* 1986; **204**:446–451.
5 Spitz L, Kiely E, Brereton RJ. Esophageal atresia: five year experience with 148 cases. *J Pediatr Surg* 1987; **22**:103–108.
6 Spitz L, Kiely EM, Morecroft JA, Drake DP. Oesophageal atresia: at-risk groups for the 1990s. *J Pediatr Surg* 1994; **29**:723–725.
7 Waterston DJ, Carter RE, Aberdeen E. Oesophageal atresia: tracheo-oesophageal fistula. A study of survival in 218 infants. *Lancet* 1962; **1**: 819–822.
8 Poenaru D, Laberge JM, Neilson IR, Guttman FM. A new prognostic classification for esophageal atresia. *Surgery* 1993; **113**:426–432.
9 Torfs CP, Curry CJ, Bateson TF. Population-based study of tracheoesophageal fistula and esophageal atresia. *Teratology* 1995; **52**:220–232.
10 Wood JA, Carachi R. The right-sided aortic arch in children with oesophageal atresia and tracheo-oesophageal fistula. *Eur J Pediatr Surg* 2012; **22**:3–7.
11 Friedmacher F, Puri P. Delayed primary anastomosis for management of long-gap esophageal atresia: a meta-analysis of complications and long-term outcome. *Pediatr Surg Int* 2012; **28**:899–906.
12 Foker JE, Kendall TC, Catton K, Khan KM. A flexible approach to achieve a true primary repair for all infants with esophageal atresia. *Semin Pediatr Surg* 2005; **14**:8–15.
13 Takamizawa S, Nishijima E, Tsugawa C, Muraji T, Satoh S, Tatekawa Y, Kimura K. Multistaged **esophageal** elongation technique for long gap **esophageal** atresia: experience with 7 cases at a single institution. *J Pediatr Surg* 2005; **40**:781–784.
14 Chittmittrapap S, Spitz L, Kiely EM, Brereton RJ. Anastomotic leakage following surgery for esophageal atresia. *J Pediatr Surg* 1992; **27**:29–32.
15 Rothenberg SS. Thoracoscopic repair of esophageal atresia and tracheo-esophageal fistula in neonates: evolution of a technique. *J Laparoendosc Adv Surg Tech A* 2012; **22**:195–199.
16 Holcomb GW 3rd, Rothenberg SS, Bax KM, Martinez-Ferro M, Albanese CT, Ostlie DJ, *et al*. Thoracoscopic repair of esophageal atresia and tracheoesophageal fistula: a multi-institutional analysis. *Ann Surg* 2005; **242**:422–430.
17 Rothenberg SS. Thoracoscopic repair of tracheoesophageal fistula in newborns. *J Pediatr Surg* 2002; **37**:869–872.