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Review Article

Esophageal atresia and tracheoesophageal fistula: A review

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Abstract

Esophageal atresia is one of the most common congenital malformations requiring surgical management in the newborn period. The first successful primary repair was done in 1941. Since then, with the advances in medical and surgical aspects of management, the survival rates have shown drastic improvement even in resource challenged areas. Early diagnosis, appropriate peri-operative management, and regular follow-up are key to reducing disease-related morbidity and improving the quality of life in these children. This review is an attempt to highlight the etiopathogenesis of the anomaly and to sensitize the readers about the association of various other congenital malformations with EA/TEF in addition to the surgical management of the disease.

Key words: Esophageal atresia, Tracheoesophageal fistula, VACTERL, foregut, anastomotic leak.

Introduction

Esophageal atresias (EA) with or without Tracheo-esophageal fistula (TEF) is one of the most common congenital malformations seen by paediatric surgeons. This is the most common anomaly of the gastrointestinal tract. Early diagnosis and careful surgical correction are the key determinants in managing these children. Patients of TEF are commonly associated with various other congenital anomalies, which has an impact on the treatment outcome of these children.

The reporting of newborns with EA dates back to the 17th century. The first successful attempt of fistula ligation and end-to-end anastomosis was credited to Cameron Haight[1]. Since then, the right extra-pleural approach via a thoracotomy has been the basis of operative care in EA/TEF. The outcomes in these patients have improved significantly over time.

Epidemiology

The estimated incidence of EA ranges from 1 in 2500-4500 live births, varying geographically[2]. The exact incidence of EA in the Indian subcontinent and southeast Asia is not known due to a lack of registries for congenital malformations. Several classifications exist and various types of TEFs are reported in literature[3]. However, the most commonly used classification: Gross Classification is based on the anatomical patterns (Figure 3). Esophageal atresia with distal tracheoesophageal fistula (type C) accounts for about 86% of the cases whereas EA with fistula opening at both pouches accounts for just 1% of cases showing huge variability in incidence as per the type of defect[3].

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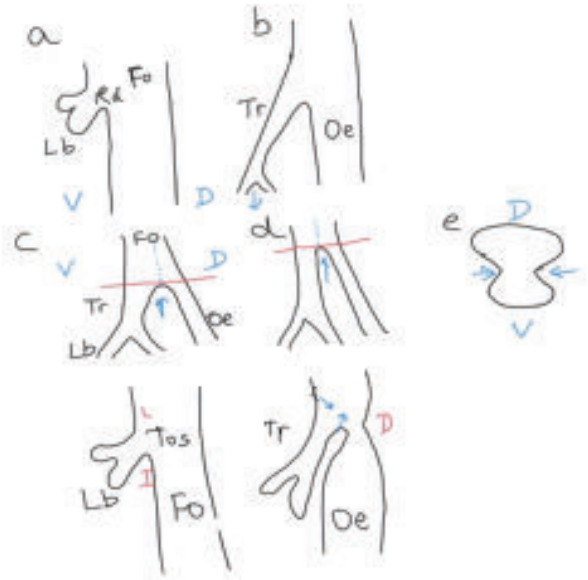


Figure 1(a-g): *Models of trachea-esophageal separation.*

The Sagittal foregut (Fo) section in a,b,c,d,f,g. and transverse section in e. Rd- respiratory diverticulum, Tr-trachea, Oe – esophagus, Lb – Lung buds, arrows in c and d shows rostral progression, in f and g, paired laryngeal (L) and single Inferior (I) folds determines the tracheoesophageal space (Tos). Dorsal (D) folds mark the boundary between the pharynx and esophagus.

Etiology

The exact etiology of EA is yet to be unfolded. More than 50% of newborns with EA/TEF are associated with other anomalies, the commonest being cardiac defects. Data from genetic studies has suggested that recurrence rate of EA/TEF in a family is as low as less than 1% with twin concordance rate of only 2.5%. If more than one sibling is affected in the family, the risk increases to 20%. The risk in children of EA/TEF parents is about 3-4%[4].

Most cases are sporadic with environmental risk factors playing an important role during the fetal development of esophagus and trachea. The Adriamycin rat model for EA/TEF indicates that environmental teratogens may be responsible in the etiopathogenesis of EA. Prolonged intrauterine exposure to contraceptive pills have long been implicated as an etiological factor for EA in neonates[5].Till date three separate genes have been associated with EA/TEF: those with CHARGE syndrome (CHD7), anophthalmia-esophageal-genital (AEG) syndrome (SOX2) and Feingold syndrome (N-MYC)[6].

Syndromic EA/TEF

More than 50% of patients with EA/TEF have an associated anomaly due to early disturbances in the organogenesis. About half of them are associated with recognizable malformation syndromes like VACTERL (vertebral defects, anal atresia, cardiac defects, TEF, renal anomalies, and limb anomalies) or CHARGE (coloboma, heart defects, atresia choanae, growth retardation, genital abnormalities, and ear abnormalities) syndrome[2]. It generally requires a minimum of three components to qualify as a VACTERL patient'. Down's syndrome (Trisomy 21) and Edward syndrome (Trisomy 18) are a significant risk factor for EA/TEF. Esophageal atresia is a well-known anomaly in the spectrum of various syndromes like Feingold syndrome, Fanconi anemia, Townes-Brocks syndrome, Pallister-Hall syndrome, etc[6].

Feingold syndrome – also known as the oculo-digito-esophago-duodenal syndrome, is characterized by digital anomalies, microcephaly, and atresias of the alimentary tract, such as the esophagus and duodenum. Microcephaly with learning disabilities occurs in the majority of cases. Digital anomalies include hypoplastic thumb and clinodactyly of second and fifth fingers. This syndrome shows autosomal dominant inheritance with the affected gene mapped on chromosome 2p23[7]. Approximately one in three patients have associated esophageal or duodenal atresias. Recently, loss of function mutations in the N-MYC gene have impacted embryonic organogenesis in these patients[8].

CHARGE syndrome:

EA/TEF occurs in about 10% of patients with this syndrome[9].This shows an autosomal dominant inheritance, with the majority of them being diagnosed in the neonatal period, with an incidence of 1 in 10,000 births. CHD (chromodomain helicase DNA binding protein) gene on chromosome 8q12 is the most commonly mutated gene in these children. This is a pleiotropic disorder with many life-threatening abnormalities like coloboma, choanal atresia, cranial nerve abnormalities, and typical vestibular areflexia as a major criterion of diagnosis. The minor criteria include the presence of heart defects, cleft lips/palate anomalies, genital abnormalities, renal defects, esophageal atresia, growth retardation, etc. Esophageal atresia, if present, has a deep influence on increasing morbidity and mortality in these children[10].

Anophthalmia-esophageal -genital (AEG) syndrome

Esophageal atresia is a rare complication of this syndrome, with less than 20 cases reported in the literature. Loss-of-function mutations in the SOX2 gene have been implicated in various foregut and lung anomalies[6].

VACTERL association

Esophageal atresia is a part of this association of vertebral defects, anal atresia, cardiac defects, tracheo-esophageal fistula, renal malformations, and limb defects. The estimated incidence is 1 in 10000 to 1 in 40000 live births[11]. The association is diagnosed by confirming the presence of three of the above-mentioned anomalies with no clinical and laboratory evidence of another differential diagnosis. The differential diagnoses include Alagille syndrome, CHARGE syndrome, Currarino syndrome, Fanconi anemia, Feingold syndrome, Pallister Hall syndrome, VACTERL-H association, etc. Patients with VACTERL association do not have facial dysmorphic features, learning disabilities, and abnormal growth, including head circumference[11].

VACTERL-H (Hydrocephalous) is genetically distinct from VACTERL's association with de-novo mutations in the PTEN gene. Hydrocephalus in these children is due to aqueductal stenosis or Arnold-Chiari malformation. Fanconi anemia is considered one of the major associated anomalies with VACTERL-H. These children require multiple surgical interventions in the neonatal period and have poor prognosis as compared to VACTERL association[12].

The incidence of associated anomalies is highest in children with isolated EA and is lowest in children with H-type fistula. Various other associated anomalies with frequency are shown in Table 1[13].

Table -I : *Abnormalities associated with Esophageal atresia/TEF[13]*

Anomaly	Frequency
Cardiac	27%
Urogenital	18%
Skeletal	12%
Vertebral	11%
Anorectal	12%
Gastrointestinal	9%
Palate/laryngotracheal	8%
VACTERL	19%

Embryology

Multiple hypotheses exist; however, these theories explain not all anatomical variations. To understand the embryogenesis of the EA/TEF, it is critical to understand the normal embryological development of the trachea and esophagus from the primitive foregut.

Separation of respiratory foregut from the esophageal foregut.

The **Tap and Water theory** suggests that the respiratory system buds out from the foregut and shows rapid longitudinal outgrowth, as shown in Figure 1(a,b)[14].

The **mesenchymal ridge theory suggests that initially, the foregut** elongates as a whole without any division. The foregut then separates into the ventral trachea and dorsal esophagus by the growth of lateral mesenchymal ridges as a septum, which grows in a cauda-cranial direction as shown in Fig 1(c,d,e).

The **caudo-rostral separation theory** proposes that caudo-rostral separation occurs due to the collapse and fusion of lateral walls, as shown in Figure 1(f,g)[15]. This has been demonstrated using scanned electron microscopic images of chick embryos.

Tracheoesophageal fistulous tract develops due to the faulty epithelial-mesenchymal interactions[16]. In the Adriamycin rodent model for EA/TEF, the findings like an increased number of tracheal rings, longer tracheal tube and association of 13 pairs of ribs in long gap TEF has strengthened the arguments of hyper somatization with preferential tracheal development at the expense of esophagus[17].

Theories of disturbed trachea-esophageal morphogenesis

Studies on the rat model have helped in understanding the embryogenesis of EA/TEF.

a) The respiratory diverticulum fails to elongate, resulting in progressive elongation of the foregut with bronchial structures originating directly from the foregut. The foregut cranial to the bronchial origin has tracheal histology, and the foregut distal to the bronchial origin connects to the stomach, forming a TEF, as shown in Figure 2a,b.

b) Arrest of the tracheo-esophageal division. The undivided foregut develops the histology of the trachea, and the initially separated esophagus acts as a fistula connecting it with the stomach, as shown in Figure 2 c,d.

c) A vascular accident is proposed to cause tissue ischemia, leading to the loss of part of the esophagus, forming an upper atretic pouch. The remaining esophagus acts as a fistula connecting the stomach, as shown in Figure 2 e,f).

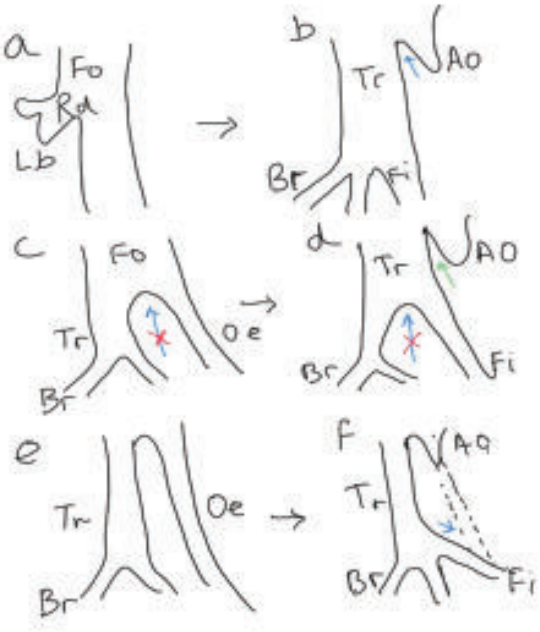


Figure 2 (a-f): *Theories on the development of EA/TEF. Ao – atretic esophagus, Br – bronchial structure*

There are molecular mechanisms, as detailed by the Adriamycin rat model, which lead to disturbed morphogenesis. Understanding molecular and embryogenic theories will help in the future development of targeted therapy to prevent these anomalies[15].

Classification

Based on radiology and post-mortem reports, Vogt proposed the first anatomical classification for EA/TEF in 1929. Several classification systems are in use; however, the most commonly used is the system proposed by Gross. (figure3)[3]. Kluth described the most detailed classification system incorporating almost all available anatomical variants described to date[18].

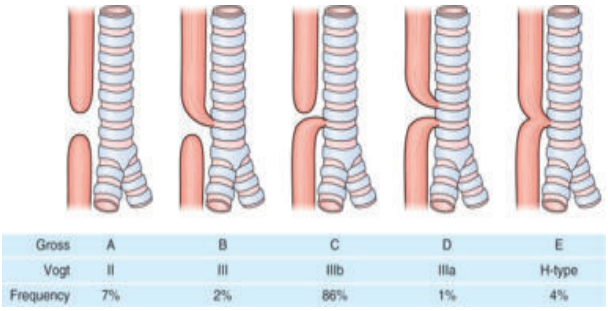


Figure 3: *Classification of EA/TEF*

Risk stratification

Risk stratification allows the comparison of outcomes among different centers. In 1962, Waterston stratified infants with EA based on birth weight, pulmonary disease, and associated congenital anomalies[19]. This classification guided the surgical care of these neonates, which was considered outdated due to the advances in neonatal intensive care facilities. In 1993, Montreal Children's Hospital proposed risk stratification based on two characteristics affecting survival: pre-operative ventilator dependence and associated major anomalies. Compared to Teich S et al.[20], the Montreal system stratifies more accurately than Waterston's. In 1994, Spitz et al.[21] proposed a classification system based on birth weight and associated congenital anomalies, which, after the Okamoto modification proposed in 2009, improved the stratification system and is the most commonly used system, as shown in Table 2.[22]. Children with pure esophageal atresia or long gap EA experience higher morbidity and mortality due to peri-operative complications[23].

Table II Okamoto modification of Spitz classification.

Table -II : *Okamoto modification of Spitz classification – Predictors of survival in EA*

Class	Description	Risk	Survival
Class I	No major cardiac anomaly, BW > 2 kg	Low	100%
Class 2	No major cardiac anomaly, BW < 2 kg	Moderate	81%
Class 3	Major cardiac anomaly, BW > 2 kg	Relatively high	72%
Class 4	Major cardiac anomaly, BW < 2 kg	High	27%

Diagnosis and clinical findings

Antenatal diagnosis

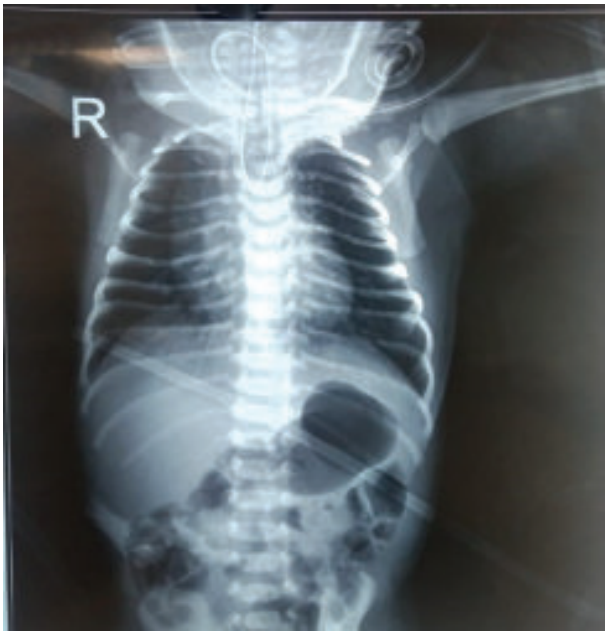
The antenatal detection rate of EA/TEF ranges from 10%-40%.[24,25]. The classic ultrasound features of EA/TEF are the absence of stomach bubble, dilated blind-ending upper esophageal pouch ('pouch sign'), distended fetal hypopharynx (DHP), and polyhydramnios. The sensitivity of antenatal ultrasonography is about 30%, with a high chance of false positive scans (50%). Antenatal detection can help us in planning the delivery at a specialized center. The identification of associated chromosomal anomalies may help in the timely termination of pregnancy counseling if required. Magnetic Resonance Imaging (MRI) and amniotic fluid analysis of gamma-glutamyl transpeptidase (GGTP) and Alpha-fetoprotein (AFP) increase the sensitivity and specificity of early diagnosis of EA/TEF in case of suspicious ultrasound[26].

Clinical presentation and diagnosis

Esophageal atresia is typically suspected in a neonate with excessive salivary secretions. Neonates may have a history of respiratory distress or cyanosis due to choking after inadvertent feeding trials. Diagnosis can be ascertained greatly by observing a characteristic resistance at the blind-ending esophageal pouch on passing an infant feeding tube orally.

The child with EA on the plain chest and abdomen x-ray shows an infant feeding tube coiling in the upper esophageal pouch, as shown in Figure 4. Further, TEF can be confirmed by observing gas-filled intestinal loops on the plain X-ray films. In children with pure EA, featureless and gasless abdominal X-rays are seen. Controlled fluorography with water-soluble contrast can detect proximal fistula in suspected cases. The incidence of detecting proximal fistula is increasing in the literature. Pre-operative bronchoscopy can rule out proximal fistulas and diagnose the degree of tracheobronchomalacia [27]. The diagnosis of TEF without EA (H-type) is difficult, often delayed, ranging from 26 days to 4 years, requiring a high index of suspicion. Sometimes, diagnosis can be delayed even up to adulthood. H-type TEF is usually suspected in a child with a repeated history of coughing and choking during feeds with pulmonary infiltrates in a chest radiograph. The diagnosis can be facilitated by doing a contrast study in the back technique by filling the distal esophagus first. Then the catheter is pulled out in a cephalad direction gradually[28]. In suspected missed out cases, bronchoscopy and esophagoscopy will help establish the diagnosis.

Figure 4 – shows a plain X-ray film of a neonate with EA shown by a coiled tube in the upper pouch and air in all bowel loops.



Evaluation of a child with EA/TEF

- Esophageal atresia is associated with other congenital malformations in more than 50% of children. The co-occurrence of these complex deformities significantly increases the morbidity and mortality in these children. A detailed history of various factors like exposure to teratogens (methimazole) in pregnancy and maternal diabetes is essential. The history of feeding is to be ascertained to prognosticate.
- Family history – history of previous births with EA/TEF, cardiac defects, renal anomalies, microcephaly, learning disabilities, etc., should be noted as these can be commonly noted with Feingold syndrome
- It is essential to examine the patient to look for other associated anomalies thoroughly
- Clinical examination – carefully and diligently examining the to rule out syndromes is a must. Head circumference, fingers, and toes (indicate Feingold syndrome), eyes (coloboma in CHARGE syndrome), café au lait patches and growth retardation (suggestive of Fanconi anemia), anal

and vertebral defects (suggestive of VACTERL anomaly).

- Investigations – echocardiography to rule out major cardiac defects. Karyotyping in suspected Edward and Down's syndrome child. All children with EA should undergo limb and spine x-rays and an ultrasound of the kidneys to see the existing picture of the VACTERL anomaly.

Pre-operative treatment: The main purpose of the stay is to prevent continuous aspiration of salivary and gastric secretions. This can be aided by humidified oxygen support, the use of double lumen Replogle catheters in the upper pouch, and nursing the patient in a head-up, prone position.

- Neonates with EA/TEF usually have dehydration with hyponatremia due to excessive losses in the form of salivary secretions and inability to start feeds. Isotonic fluids can be started as a maintenance in these neonates. Post-operatively, it is known that these neonates are at increased risk of developing SIADH (syndrome of inappropriate antidiuretic hormone secretion). The main stimuli for SIADH are post-operative stress, prolonged ventilation, and pain[29]. The authors prefer to give restricted fluid at about 100 ml/kg/day in post-operative neonates. This practice helps to prevent post-operative severe hyponatremia in these neonates as it is known to be associated with poor neurological outcomes in them[30].
- Antibiotics, as per the institutional antibiogram, should be initiated in the immediate preoperative period, along with vitamin K analogues.
- In resource-challenged settings, routine endobronchial intubations should be avoided. Intubation in TEF, if required, should be done by an expert paediatric surgeon or anesthesiologist to try and place the tube beyond the fistula to prevent unwanted respiratory distress due to a distended stomach and, subsequently, gastric perforation.
- Role of pre-operative bronchoscopy (POB) – done in the operating room before surgical repair. After induction with inhalational agents, the neonate is maintained on spontaneous ventilation with 100% oxygenation by face mask. One can use local anesthetic sprays (0.5-2% Lidocaine)31 to avoid laryngospasm during the procedure. The scope is slowly passed across the vocal cords till the carina and then gradually withdrawn out to visualize the entire anatomy. This helps to rule out associated tracheobronchial anomalies like ectopic right upper bronchus, laryngotracheal esophageal clefts, vascular compressions, tracheomalacia, congenital vocal cord paralysis, etc. These anomalies can be the reason for multiple extubation failures, making it critical to be aware of preoperatively[32].
- The use of pre-operative bronchoscopy is debated due to the very low incidence (<1%) of proximal pouch fistula. With more and more use of POB, an increased prevalence of double TEF has been reported, showing that proximal pouch TEF is always underdiagnosed[27].
- So, various advantages of doing POB are as follows:

1. It helps accurately diagnose EA with upper pouch TEF.
2. This gives an estimate of the position of the aortic arch by noticing the side of major pulsation, which can influence the side of the thoracotomy needed[33].
3. This helps facilitate mechanical ventilation by occluding the TEF using a Fogarty catheter. If a guide wire is placed across the fistula, it helps to detect the fistula easily during surgery.
4. Helps in correct placement of endotracheal tube beyond the fistula, but proximal to the carina[34].
5. A pre-operatively placed Fogarty catheter in the right bronchus can help selectively ventilate the left lung intermittently to facilitate thoracoscopic repair.
6. Bronchoscopy helps estimate the approximate gap length between the two esophageal pouches by measuring the distance of the fistula from the carina. Gap length can also be assessed by seeing the chest X-ray with a nasogastric tube in the upper pouch and tip of the bronchoscope at the lower pouch fistula site[27].
7. In H-type TEF, guide wire can be passed across the fistula, passing retrogradely in the esophagus to the oral cavity, which can be used to give outward traction to the fistula site, facilitating the cervical approach of repair[35].

Operative repair

Open thoracotomy or thoracoscopic division of fistula with end-to-end anastomosis is the procedure of choice.

With proper planning and improved operative technique, outcomes have improved even in very low birth weight (< 1500 g) neonates throughout time[36].

Right posterolateral thoracotomy is the standard approach. Muscle-sparing thoracotomy is preferred by some. The chest is entered via the 4th intercostal space. The most commonly used approach is an extra-pleural approach to minimize the chances of empyema after an anastomotic leak. In case of an inadvertent pleural breech, the entire pleura should be completely opened to prevent the formation of air pockets later on. If the patient is sick, it may be prudent to take the transpleural route as it has a significantly shorter operative time. The post-operative complications in both groups are similar[37].

Azygos vein acts as a beacon to identify the fistula in EA patients. The azygous vein may be occluded before ligating so as to look for a fall in cardiac output. It may have an important role in select individuals' venous return to the heart. Dividing the azygous vein helps in further identification of the fistula. Few authors advocate that dividing the azygos vein increases postoperative edema at the anastomotic ends of the esophagus, causing a significant increase in anastomotic leak[38].

The Azygous vein and the vagus nerve pass close to the lower pouch and TEF. The fistula can be seen inflating with every breath, and to avoid inadvertent injury to the right lung bronchus, we temporarily occlude the fistulous communication with slings to check for adequate conduction of ventilatory breaths to the right lung. Pre-operative bronchoscopy-guided placement of guidewire may aid in identifying the fistula; however, the authors do not practice this. To avoid slipping of ligature knots and to save time, it is prudent to transfix the fistula with an absorbable suture (Polydioxanone/Polyglactin). The site of trans fixation should be chosen wisely enough to prevent future tracheal stenosis and unwanted tracheal diverticulum.

The distal esophageal pouch should be cannulated with a small infant feeding tube to rule out congenital distal esophageal stricture and decompress the already distended stomach. The lower pouch is usually poorly developed and has a segmental blood supply, so mobilization should be attempted carefully to avoid damage to vagal branches and their blood supply. The proximal esophageal pouch is usually well-developed and has a robust cervical blood supply. This is closely associated with the membranous trachea, necessitating sharp dissection to mobilize the upper pouch till the thoracic inlet is complete. End-to-end full-thickness anastomosis is done using 5-0 Polyglactin or Polydioxanone suture with a small-sized infant feeding tube passed as a nasogastric tube for early feeding and stomach decompression. When the gap length is wide, an upper pouch myotomy or upper pouch flap can be created to bridge the defect.

In tension-free anastomosis, no RCT recommends prophylactic intra-operative chest tube (IOCT) placement. The routine use of prophylactic IOCT is debatable and is often used as a one-way valve to drain excess fluid and air after surgery. At the European Reference Network for Rare Inherited and Congenital Anomalies (ERNICA) consensus conference, no consensus was found, with only 21.4% of members voting for the use of IOC[39]. A systematic review and meta-analysis by Ladefoged MR et al. shows that there is no randomized trial to support or discontinue the prophylactic IOCT, and it needs further trials[40]. Few authors believe IOCT acts as a foreign body, the source of infection, and the site of increased exudative focus. Placement of IOCT does not prevent early postoperative complications, and despite the adequate placement of IOCT, most of the time, we require the reinsertion of a new chest tube to drain air or secretions effectively[41].

The routine use of trans anastomotic feeding tube (TAFT) is very commonly used in EA repairs. This has been the standard of care in many institutes with a belief that TAFT is a neutral tactic to cover up for lack of confidence and surgical skills in the learning curve. This is one such practice being followed blindly without understanding the related negative consequences of it. The view on the use of TAFT is conflicting, with proponents believing that it helps in the early start of feeding and helps in supporting the anastomosis as a stent[42]. On the other hand, there are many studies, such as a systematic review and metanalysis by Wang C et al.[43]. suggesting that routine use of TAFT is associated with a significant increase in risk of esophageal stricture with no significant increased risk of anastomotic leak, gastroesophageal reflux(GER), pneumonia,

tracheomalacia, etc. The multicenter study published as 'The Quebec experience' by La Russo K et al. [44] and the Mid-west paediatric surgery consortium stated by Lal DR et al.[45] proposed that TAFT is associated with an increased risk of anastomotic stricture. An ongoing randomized controlled trial registered with The Clinical Trials Registry -India (CTRI/2023/05/052527) has demonstrated a significant increase in the incidence of anastomotic leaks in the TAFT group of patients. This study proposed that avoiding TAFT leads to reduced requirements of parenteral nutrition and reduced rates of GER.

After surgery, Nasogastric tube feeds can be initiated after 24 hours, and the contrast study may be done on postoperative days 6-7. If there is no anastomotic leak, then oral feeds can be started and built up ad-lib.

As per a multi-institutional observational study by Shimizu T et al.[46] and another study by Ritz LA, 47 complication rates are higher in low-birth-weight neonates, and staged repair can be considered for a better outcome in these neonates.

Thoracoscopic repair

Thoracoscopy in selected children offers a better operative view and fewer incision-related complications. Thoracoscopic repair of EA with TEF (TREAT) is a well-known procedure and should be acknowledged wherever feasible.

The elaborative technique is described by Kanojia RP et al.[48]. For better identification of esophageal pouches and good operative view, few surgeons prefer to use Fogarty balloon occlusion for lung isolation during the surgery. Three ports are placed following the basic principle of triangulation in laparoscopy with a target to align the scope with the horizontal fissure to avoid lung lobes occluding the vision. After identifying the major landmarks like the azygous vein and vagus nerve, the lower pouch fistula is located. We prefer to hitch the fistula with a 4/0 polypropylene suture to the chest wall. This allows for well-controlled transfixation and division of fistula. Thereafter, adequate mobilization of both pouches allows for end-to-end primary anastomosis. As per the recent meta-analysis, it was postulated that thoracoscopic surgery has better outcomes than open procedures in terms of leakage, stricture formation, stricture dilatation, and mortality. The only drawback postulated was the increased requirement of antireflux surgery in the follow-up period[49]. Multicenter analysis of TREAT in comparison to open repair by Holcomb et al.[50] has concluded that both techniques have similar outcomes with respect to the requirement of esophageal dilatation and fundoplication. They have also proposed that TREAT is safe and efficacious in these neonates, with better musculoskeletal outcomes in later life. Similar results were proposed by another multi-institutional study by Okuyama et al[51]

Right-sided aortic arch

Right-sided aortic arch is often rarely seen, with an incidence of 1.8-3.6% in the literature. This is often undetected preoperatively, with the positive predictive value of pre-op echo being just 20%. The site of thoracotomy is usually based on the surgeon's preference. The repair is feasible from either side, but right-side thoracotomy is more challenging, as evidenced by the significantly high anastomotic leak rate. So, if known pre-operatively, a left-sided approach may be carried out depending on the surgeon's comfort[52,53].

Long gap EA (LGEA)

If the distance between two pouches is long enough not to allow end-to-end anastomosis, it is presumed to be an LGEA. There is no postulated objective definition for the same. Pure EA can also be considered a part of this group. A gap measurement is based on the number of vertebral bodies or intra-operative measurement in centimeters, but no method is the standard of care.

There is a belief that every attempt should be made to use the native esophagus to fill the gap as no other available tissue is better than the native esophagus.

Delayed primary repair is the best option. It was seen that with time, due to repeated swallows in the upper pouch and gastric reflux into the lower pouch naturally increases the length of two pouches. As the growth is maximally noted by three months of age, this is the best time to undergo primary repair. Other methods available in the literature to increase the length of pouches such as Foker's technique, where external traction sutures were applied on both the pouches to shorten the gap. The long wait period of about three months predisposes these children to recurrent aspiration pneumonitis and hospital-acquired sepsis. To keep these neonates free from aspirating upper esophageal pouch secretions, the requirement for dedicated, well-trained nursing personnel is difficult

to provide at resource-challenged centers. So, some centers, especially in developing nations, prefer to do diversion esophagostomy and feeding gastrostomy followed by esophageal replacement later on when the child has gained adequate weight.

As per the meta-analysis, the most common early complication was an anastomotic leak, which could be managed successfully in a conservative manner. Up to 30% of patients require fundoplication to treat gastroesophageal reflux, and very few suffer from dysphagia. Usually, these children have normal long-term growth and development, requiring regular endoscopic surveillance to rule out esophagitis and Barrett's esophagus[54].

The other techniques used to bridge the long gap in LGEA are Livaditis circular myotomy and upper pouch full-thickness flap. In contrast to the common notion of poor blood supply to the lower pouch, the authors usually do complete mobilization of the lower pouch till the hiatus of the diaphragm. Based on a similar concept, Scharli described a Scharli's isoperistaltic tube creation from the superior aspect of greater fundus[55].

Some centers prefer post-operative sedation on ventilator support with prevention of neck extension as a measure to avoid anastomotic disruption in LGEA.

Isolated (H type) TEF

These fistulas can be missed on routine contrast studies in more than 50% of patients. Operating room bronchoscopy and esophagoscopy help in diagnosis and accurate localization. Most of them can be successfully repaired via a cervical approach. The right-sided low cervical approach is preferred. The recurrent laryngeal nerve should be identified and preserved. This type of TEF can be managed by endoscopic ablation and histoacryl glue injection[56]

Prognosis

The overall prognosis for neonates with isolated EA/TEF is good. Overall survival is 85-90%, and survival is 72% among syndromic EA. Prognosis mainly depends upon the associated cardiac and chromosomal anomalies, as shown in Table 1 above. The risk of mortality is three times higher in those with VACTERL association and six times higher in those with CHARGE syndrome and Down's syndrome[57]. The gap length between two esophageal pouches also determines the outcome, as shown in table 3[58].

TableIII shows anastomotic leak rates and mortality rates per gap length.

Groups (gap length measured)	Leak rates	Mortality
Group A (>3.5 cm)	80%	80%
Group B (2.1-3.5 cm)	50%	50%
Group C (1-2 cm)	28%	22%
Group D (<1 cm)	10.5%	15.6%

Early Complications

Gastrointestinal complications

- Anastomotic leak- This occurs in approximately 15% of patients. Most of them are minor leaks that close spontaneously on conservative management[59].
- Esophageal stricture- Occurs in 35% of patients. This can be successfully managed by endoscopic dilatation. More than 50% respond to one or three dilatations, but Recalcitrant strictures need steroid (triamcinolone) or mitomycin C application. The remaining may need resection and reanastomosis[60].
- Recurrent fistulae- occurs in approximately 3% of patients[61].

Late complications

Gastrointestinal motility disorders

As per a systematic review[62], the following complications are reported in Table IV.

Table IV: showing complications with prevalence

Complications	Pooled estimated prevalence
Dysphagia	50%
Gastroesophageal reflux disease (GERD) with esophagitis.	40%
GERD without esophagitis	57%
Barrett's esophagus	6%
Esophageal cancer(squamous cell)	1%

Respiratory complications

Infections and respiratory functional abnormalities are common in children with EA. Children with a post-operative persistent cough, wheeze, and recurrent respiratory infections require long-term follow-up as long-term bronchiectasis develops in 15-25% of patients[62].

Long term management

Both respiratory and gastrointestinal complications may persist throughout the life of a child. An expert panel[63] made specific recommendations

- All children and adults should be monitored for symptoms of GERD, dysphagia, aspiration, and nutritional status.
- All patients should undergo at least three surveillance endoscopies in childhood to detect early esophagitis. It should be repeated every 5-10 years in adulthood.
- Patients with symptoms of GERD or dysphagia should be evaluated with contrast study and endoscopy. Treat esophagitis with proton pump inhibitors (PPI) and strictures with dilatation. Asymptomatic patients do not require routine screening.
- Patients with respiratory symptoms should be evaluated for various respiratory tract abnormalities like laryngeal clefts, etc.
- Acid suppression does not improve respiratory symptoms but rather predisposes to infections.
- Fundoplication has a limited role in patients with TEF because underlying dysmotility predisposes to post-fundoplication complications. This is indicated only when GERD is poorly controlled on maximal PPI therapy. Eosinophilic esophagitis must be ruled out before fundoplication.

Tracheomalacia

This is the dynamic collapse of the trachea during breathing, resulting in airway obstruction. 30-40% of children develop tracheomalacia after surgical repair of EA/TEF. Dynamic airway endoscopy is the investigation of choice. The long-term prognosis is usually good. Most affected children improve spontaneously by 6-12 months of age. Few children with severe tracheomalacia may need aortopexy, the surgical suspension of aorta from the sternum[64]

All patients and family members should be educated about the health risks and the importance of long-term surveillance.

Conclusions:

In the current practice, the mortality and morbidity of EA/TEF have significantly improved, due to the advances in neonatal care, including surgical, anesthesia, and neonatal intensive care. The long-term outcomes in syndromic patients and those with specific conditions like long-gap TEFs are still suboptimal. Advances in aerodigestive tract management and management of babies with multiple anomalies are areas in need of future research.

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