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Modern outcomes of oesophageal atresia: Single centre experience over the last twenty years

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Abstract

Aim of the Study: The aim of this study was assessment of the contemporary outcomes of oesophageal atresia (OA) in a national paediatric surgical centre.

Patients and Methods: A review of the hospital records of all patients who underwent repair of oesophageal atresia (OA) in our institute between 1991 and 2011 was performed.

Results: The study included 130 consecutive infants with OA: types A (n=4, 3%), B (n=2, 2%), C (n=110, 85%), D (n=5, 4%), and E (n=9, 7%). Median follow-up was 8.8 (range 0.1–21) years. Twenty-nine (22%) infants had cardiac and 76 (58%) other anomalies, and seventeen (13%) had a long-gap OA. The final repair was primary (n =113, 87%) or delayed (n=3) end-to-end anastomosis, oesophageal replacement (n=8) (6%) with gastric tube (n=4) or with jejunum interposition (n=4), and closure of the trachea-oesophageal fistula (Type E, n=9). Oesophageal continuity was achieved in all patients. Overall mortality was 3/130 (2%) and caused by gastric perforation (n=1), prolonged apnoeic spell (n =1), and food asphyxiation (n=1). Oral feeds were achieved in 121 (94%) children. Eight (6%) children remain dependent on feeding ostomy. Long-gap OA was a major predictor of post-repair complications.

Conclusion: The modern outcome for infants with OA is characterized by an extremely low hospital mortality and satisfactory oesophageal function, enabling full oral feeds in the vast majority of children.

Success in the repair of oesophageal atresia (OA) and trachea-oesophageal fistula (TOF) has been and remains a main index of quality of paediatric surgical service. Centres must be proficient with primary and secondary repairs, oesophageal replacement, treatment of surgical complications and related disorders such as tracheomalacia and gastro-oesophageal reflux. A successful outcome for an infant with OA also requires expertise in cardiac, respiratory, neurological and nasopharyngeal disorders [1,2].

We assessed the early outcomes of infants born with OA and treated in a single tertiary centre over the last twenty years.

1. Patients and methods

Institutional ethical approval for the study was obtained.

The study included 130 successive children who had had repair of OA or TOF between 1991 and 2011 at the Children's Hospital in Helsinki. All significant associated

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anomalies including cardiac surgery and surgery for the anomalies of airway, gastrointestinal tract and anorectal malformations were also performed here.

The medical records were reviewed including details of the operative repair and surgical treatment of other associated conditions and follow-up including radiological imaging, endoscopy and growth. The Gross classification [3] was used, i.e. Type A (OA without TOF), Type B (proximal TOF only), Type C (OA and distal TOF), Type D (OA and both proximal and distal TOF) and Type E (isolated TOF) depending on the surgical anatomy. Long-gap OA was defined by location of the distal TOF and the anastomotic tension experienced during the repair. The present study focused on the early outcome up to two years after definitive repair.

1.1. Primary repair, delayed primary repair and oesophageal replacement

Surgery was usually scheduled within 48 h after birth. Preoperative treatment included intravenous fluid resuscitation and suction drainage in the upper pouch. Preoperative assessment for associated anomalies included clinical examination for anorectal, limb and genital malformations, plain chest, abdominal and vertebral x-rays, an abdominal ultrasound scan and echo cardiography. Urgent surgery required for gastrointestinal or anorectal malformations was scheduled for the same session with oesophageal repair whereas cardiac surgery was usually scheduled after repair.

The operating surgeon performed tracheobronchoscopy before repair to ascertain the existence and the exact location of the TOF, presence of trachea-oesophageal cleft or a compressing vascular ring. Open repair through right thoracotomy (extrapleural or transpleural approach) was preferred, thoracoscopic approach was used in three infants only. Primary anastomosis was attempted In Types C and D OA. Surgical techniques followed the standard methods both in open repair [4] and in thoracoscopic repair [5]. A transanastomotic 6 Fr silicone nasogastric tube was used. Livaditis myotomy was used according to the choice of the operating surgeon. In transpleural operations a strip of parietal pleura was used to seal the anastomosis. Chest drain was used routinely after transpleural or thoracoscopic approach. Feeding by nasogastric tube was started at the first postoperative day and oral feeding 2–5 days after the operation in uncomplicated cases. Nasogastric tube was removed when the oral intake was sufficient for weight gain. Pureed feeds up to the age of two years were recommended.

Feeding gastrostomy and upper pouch insertion of a Replogle® suction drain were used in those with long gap OA (Types A and B). Cervical oesophagostomy was used in infants who remained unmanageable with upper pouch suction. Delayed primary repair was scheduled after two months preceded by assessment of the gap under fluoroscopy with flexible gastroscopes passed into both pouches. Options for repair were end-to-end anastomosis or oesophageal replacement with pedicled jejunal interposition [6] or with reversed gastric tube [7].

An isolated TOF without atresia (Gross Type E) was first located by tracheoscopy and then cannulated with a thin guidewire. Division and suture closure of the fistula with a strip of interposed cervical muscle were performed through a right cervical incision.

1.2. Treatment of postoperative complications

Primary treatment of an anastomotic leakage included chest drainage, antibiotics and nutrition via nasogastric tube with parenteral nutrition support. If leakage could not be controlled with these measures re-thoracotomy with re-suture was performed. Healing was confirmed with contrast oesophagogram.

Anastomotic stenosis was confirmed endoscopically and treated with hydrostatic balloon dilatations starting three weeks after the primary repair. Up to 2002, all infants underwent dilatations until a diameter of 10 mm was reached. After 2002, dilatations were performed selectively in symptomatic infants with dysphagia or respiratory distress during oral feeding. Recurrent stenosis was treated by serial dilatations with 1–3 week intervals with additional endoscopic topical application of mitomycin-C (cotton pledget soaked in 0.1-mg/mL mitomycin-C solution held by endoscopic forceps) [8]. Recalcitrant strictures were treated with resection with or without oesophageal replacement.

The majority of the patients were given anti-reflux medication (omeprazole 1–2 mg/kg or ranitidine 5 mg/kg) for at least 1–3 months after repair. Patients with early postoperative signs of complicated gastro-oesophageal reflux (GOR) (apnoeic episodes, recalcitrant stenosis of the anastomosis, aspiration) were considered candidates for anti-reflux surgery. Respiratory disorders caused by tracheomalacia were primarily treated by respiratory mask or nasal catheters providing positive end-expiratory pressure. Infants with recalcitrant symptoms from tracheomalacia and with tracheobronchoscopic evidence of significant tracheal collapse under anaesthesia with spontaneous breathing were considered candidates for aortopexy. Infants with respiratory problems and apnoeic spells with both tracheomalacia and GER as likely etiological factors usually underwent synchronous anti-reflux procedure and aortopexy. Anti-reflux surgery was also indicated if an infant developed moderate or severe oesophagitis or other symptoms of GOR recalcitrant to medical therapy.

Recurrent TOF was diagnosed endoscopically or with the help of a lateral prone oesophageal contrast radiograph and closed at open operation by preference.

1.3. Follow-up

Routine follow-up included at least bronchoscopy, upper gastrointestinal endoscopy and oesophageal pH-monitoring

at 10 months and upper gastrointestinal endoscopy at the age of 3 and 15 years. Those with significant postoperative complications, GER or other special conditions underwent these investigations repeatedly as often as required. GER was considered significant if the symptoms required anti-reflux surgery, pH-monitoring revealed pathologic GER, or if moderate or severe esophagitis developed [9]. Surveillance by a paediatric pulmonologist started at the age of 10 months. Additional treatment and surveillance of associated anomalies were arranged by the appropriate specialty.

1.4. Statistical calculations

Statistical calculations were made with StatView® 512 computer programme (Brain Power, Calabasas CA, USA). Risk ratios for different outcome variables were estimated using univariate and multivariate logistic regression analysis. Those independent factors which showed statistical significance in a univariate analysis were entered into multivariate analysis. P values of <0.05 were considered statistically significant.

2. Results

Our series (n=130) could be classified anatomically as Types A (n=4, 3%), B (n=2, 2%), C (n=110, 85%), D (n=5, 4%) and E (n=9, 7%). Median follow-up was 8.8 (range 0.1–21) years. Table 1 illustrates the series using the Spitz prognostic classification [10]. Other anomalies were identified in 76 (58%) infants and are illustrated in Tables 2 and 3. These included cardiac (22%), anorectal (11%), gastrointestinal, (11%), syndromic or chromosomal (9%), airway and palate (13%), urogenital (10%), neurological (7%) and skeletal (22%) anomalies.

Table 4 illustrates the type of oesophageal repair (n=130). Nine (7%) patients with type E underwent surgical closure of the TOF, and 113 (87%) underwent primary (n=110) or delayed (n=3) end-to-end oesophageal anastomosis. Long-gap OA was diagnosed in 18 (14%) infants (Type A, n=4), Types B or D (n=5) and Type C with the distal fistula opening into the tracheal carina and considerable anastomotic tension (n=9). Of the 17 patients with long gap OA 11 had primary (n=8) or delayed (n=3) end-to-end repair, five (45%) of 11 had a Livaditis myotomy. The remaining eight (6%) patients underwent oesophageal reconstruction either

Table 1 Classification of 130 patients with oesophageal atresia into risk groups by Spitz et al. (1994).

Group	Definition	No. of patients	Mortality
I	no major cardiac anomalies and birth weight ≥1500 g	99	1 (1%)
II	major cardiac disease or birth weight <1500	31	2 (6%)
III	major cardiac disease and birth weight <1500	0	–
total		130	3 (2%)

Infants with oesophageal atresia (n=130) by Spitz classification [10].

Table 2 Associated cardiac anomalies in 130 patients with oesophageal atresia (n=29).

Anomaly or disease	n=29
Tetralogy of Fallot	3
Double outlet right ventricle+VSD	3
Coarctation of the aorta	5
Atrioventricular septal defect (AVSD)	2
Atrial septal defect (ASD)	2
Ventricular septal defect (VSD)	3
VSD+ASD	5
Interrupted aortic arch+aortopulmonary window	2
Transposition of great arteries	1
Cardiomyopathy	1
Double aortic arch	1
Dextrocardia	1

Table 3 Non-cardiac associated anomalies or disorders (in 76 (58%) of 130 patients with oesophageal atresia, one patient may have several disorders).

Anomaly or disorder	n
Airway	17
-choanal atresia or stenosis	6
-cleft palate	3
-subglottic stenosis	3
-unilateral vocal cord paresis	1
-laryngeal atresia	1
-proximal tracheo-oesophageal cleft (Type I)	3
Gastrointestinal	14
-hypertrophic pyloric stenosis	5
-duodenal atresia or stenosis	7
-ileal duplication	1
- Meckel's diverticulum	2
-extrahepatic portal vein occlusion	1
Omphalocele	1
Anorectal malformations	14
-low	5
-high	9
Genitourinary malformations	13
Upper limb malformation	16
-radial aplasia	9
-malformations of thumb	6
-supernumerary digits	1
Vertebral column malformations	24
Neurological disorder	7
Trisomy 21	2
CHARGE* association	3
Moebius syndrome	1
Klippel–Feil syndrome	1
Feingold syndrome	1

CHARGE=Coloboma, Heart defect, Atresia of choana, Retarded growth and development, Genital abnormality, Ear abnormality.

Table 4 The final mode of oesophageal repair in 130 patients with oesophageal atresia (OA), TEF = tracheo-oesophageal fistula.

	Gross type of OA				
	A	B	C	D	E
Primary anastomosis (n = 110)	–	–	106	4	–
Closure of TEF (n = 9)	–	–	–	–	9
Delayed primary anastomosis (n = 3)	2	1	–	–	–
Oesophageal reconstruction (n = 8)					
-jejunal interposition (n = 4)	1	1	1	1	
-gastric tube (n = 4)	1		3		

with gastric tube (n = 4) or with jejunum interposition (n = 4). Three repairs (OA type C) were performed thoracoscopically.

The indications for oesophageal reconstruction were long-gap OA of type A (n = 2), type B (n = 1), type C (n = 2) and type D (n = 1), recurrent fistula and anastomotic dehiscence in type C (n = 1), recalcitrant anastomotic stricture after primary anastomosis in type C with long-gap (n = 1) (Table 4).

2.1. Postoperative complications

Anastomotic leakage was diagnosed in a total of nine (7%) infants. Two anastomotic leakages occurred after oesophageal reconstruction and seven after primary anastomosis. Five who developed pneumothorax underwent re-thoracotomy, with the remaining children including the two with esophageal replacement treated conservatively.

Recurrent TOF occurred in three (2%) patients, all with type C OA. One occurred after thoracoscopic repair where a metal clip used to close the TOF had slipped. All three underwent thoracotomy with successful closure of the fistula in two. The third developed an abscess, recurrent fistula and dehiscence of the esophageal anastomosis. Closure of the fistula, cervical esophagostomy and subsequent esophageal replacement with gastric tube were required.

Respiratory problems associated with tracheomalacia required aortopexy in 16 (12%) (Type A n = 1, Type D n = 1, Type C, n = 14). Complicated GOR was treated with antireflux surgery in 37 (29%) children. The main indications for early antireflux surgery before eight months of age (n = 33) were recurrent anastomotic stenosis with respiratory complications (n = 23) and respiratory complications (n = 10). Thirteen (39%) patients with early antireflux surgery underwent also synchronous or metachronous aortopexy. Four children underwent anti-reflux surgery between 8 months and 10 years having developed moderate or severe esophagitis on endoscopic surveillance. Overall, by the age of one year 62 (48%) patients had developed significant GOR requiring antireflux surgery (n = 33) or medical treatment (n = 29).

Postoperative anastomotic dilatations were performed to in 102 (78%) children. Fifty-three (52%) underwent < 5 dilatations and 49 required > 5 dilatations. After 2003, only 20/68 children (29%) underwent > five dilatations. Mitomycin application was used in three children for stricture after primary anastomosis (n = 1) and stricture of the proximal anastomosis after esophageal replacement with jejunum graft interposition (n = 2).

Six of the 102 children who underwent anastomotic dilatations had an associated anastomotic leakage and four of these had undergone rethoracotomy and re-suture. Perforation at the gastric cardia with peritonitis and significant late sequelae occurred in one child. In eight (6%) (Type A n = 2, Type C n = 6), six of whom were long gap OA, anastomotic stricture was recalcitrant to dilatations and mitomycin treatment, and they underwent resection of the stricture with end-to-end anastomosis (n = 7), or with esophageal replacement with a pedicled jejunal graft (n = 1).

Other complications after esophageal repair occurred in seven (5%) including anastomotic leakage after repair of duodenal atresia (n = 1), pneumothorax caused by pulmonary tear (n = 1), tearing and perforation of the gastric wall at the site of a gastrostomy (n = 2), gastric perforation by a nasogastric tube (n = 1), and Meckel´s diverticulum with perforation (n = 1) and hemorrhage.

2.2. Outcome

There was one in-hospital death in the series with an overall mortality of 3/130 (2%). One premature baby with OA type C and birth weight of 1000 g (Spitz group 2) died of peritonitis and multi-organ failure caused by gastric perforation on the first postoperative day. In addition, two children (Spitz group I n = 1 and group 2 n = 1) with OA type C died three and four months after a successful repair, one of food bolus asphyxiation and one of a prolonged apnoeic spell. Mortality by prognostic Spitz groups is presented in Table 1.

2.3. Esophageal function

121/129 (94%) children are thriving with oral intake of food. 108 (89%) started full oral feeds without feeding ostomy or nasogastric tube within two months of the repair. The remaining thirteen (11%) patients have achieved full oral feeds within 18 months. Prolonged dependence on nasogastric tube or feeding ostomy was associated with different postoperative sequelae: anastomotic stricture (n = 5), anastomotic rupture at dilatation (n = 3) or associated anomalies including laryngotracheal cleft (n = 1), neurological disorder (n = 1) and heart disease (n = 2).

Currently eight children remain dependent on gastrostomy (n = 6) or jejunostomy feedings (n = 2). Of these two, one with a complex cardiac defect and another with anastomotic stenosis and a laryngotracheal cleft, are expected to gain full oral intake before the age of 18 months. Two patients, one with laryngeal atresia and tracheostomy

and another with mild cerebral palsy have improved but are not expected to gain full oral intake within 18 months. Four patients, three with CHARGE association and a severe swallowing disorder, and one with Feingold syndrome and mental retardation will most likely remain permanently dependent on tube feedings.

2.4. Prognostic value of associated anomalies and complications

The relationships between prognostic risk group, long-gap OA, associated syndromes, complications etc. were assessed in univariate and multivariate logistic regression analyses (Table 5). Long-gap OA was the major and significant risk factor for anastomotic complications, GOR and poor oral intake. In addition, associated syndrome or neurologic disorder and Spitz Class 2 were associated with prolonged insufficient oral intake (Table 5).

Logistic regression analysis showed no significant risk association between cardiac defects and postoperative course and complications.

Table 5 The association between Spitz classification group, long gap oesophageal atresia, heart disease, and CHARGE syndrome/Down's syndrome/neurological disorder and postoperative course after repair of oesophageal atresia.

	Long Gap	CHARGE/ Down/ Neurological disorder	Spitz class
survival/death			
-univariate analysis	0.0, p=0.98 (NS)	0.0, p=0.98	1.6 (95% CI 0.1–18), p=0.70 NS
anastomotic leakage			
-univariate analysis	10 (95% CI 2.4–44) p=0.001	2.1 (95% CI 0.5–9.2), p=0.30 NS	1.7 (95% CI 0.4–7.1), p=0.49 NS
anastomotic stricture			
-univariate analysis	28 (95% CI 5.0–152), p=0,0001	1.4 (0.3–7.2) p=0.71 NS	0–4.3 (95% CI 0.1–26), p=0.11–0.97 NS
-multivariate analysis	13 (95% CI 1.0–151), p<0.05	–	–
insufficient oral intake			
-univariate analysis	14 (95% CI 2.9–64), p=0.001	7.9 (95% CI 1.8–36), p=0.01	4.6 (95% CI 1.1–18), p=0.03
-multivariate analysis	7.0 (95% CI 1.3–38), p=0.02	–	–
recurrent TEF			
-univariate analysis	0.0, p=0.98	0.0, p=0.98 NS	1.7 (95% CI 0.1–19), p=0.70 NS
aortopexy			
-univariate analysis	0.9 (95% CI 0.2–4,2), p=0.87 NS	0.9 (95% CI 0.2–3.5), p=0.89 NS	0.7 (95% CI 0.2–2.7), p=0.61 NS
early ARS			
-univariate analysis	6.4 (95% CI 2.2–18), p=0.001	1.1 (95% CI 0.4–2.9), p=0.84 NS	0.8 (95% CI 0.3–1.9), p=0.59 NS
GER at 1 year			
-univariate analysis	23 (95% CI 3–183), p=0.003	1.8 (95% CI 0.8–4.5), p=0.16 NS	0.5 (95% CI 0.2–1.1), p=0.07 NS

NS=not significant.

3. Discussion

Survival is the most important outcome measure following repair of an OA and several prognostic classifications based on birth weight and an existing heart disease have been developed [10–12]. A simple and widely used prognostic model by Spitz et al. [10] was chosen in the present study as a representative of these. However, long-term outcome is largely determined by oesophageal function and associated morbidity, which still have significant association with the course of the primary repair. Although not considered here it should also be noted that repair complicated by a long gap, anastomotic stricture or recurrent TOF increases the risk of long-term epithelial metaplasia [13].

Our study concentrated on the early outcome after repair of esophageal atresia. Mortality in our series was very low (2%) and was not directly associated with the Spitz prognostic risk classification (1994), partly because none of our patients fell in the Spitz group III with highest risk of mortality. Long-gap OA was the most important factor associated with early complications and functional outcome. In addition, neurological disorder, chromosomal anomaly and congenital disorders of swallowing predicted poor functional outcome.

Our series had a typical distribution of the various anatomical types and spectrum of associated anomalies [11,14,15]. Thoracotomy, rather than thoracoscopy, has remained our preferred approach for the primary repair. In our opinion, the advantages of thoracoscopic repair are questionable compared with its disadvantages such as a higher complication rate and the need for a substantial learning curve [16–18].

Our techniques for esophageal replacement have included reversed gastric tube and more recently pedicled jejunal graft. A two-stage gastric tube replacement has the disadvantage of a temporary cervical esophagostomy. The small number of patients and short follow-up after jejunal graft repair preclude the definite comparison of the two methods.

All children who required surgical or medical treatment for cardiac anomalies survived. The mortality rate in cardiac surgical patients is low in our centre (<4%) [19] and clearly benefitted infants with OA and an associated congenital heart defect. Coexisting heart anomalies may initially cause temporary problems such as poor food intake because of exhaustion during feeding and they must be taken into account in the differential diagnosis of infants with apnoeic episodes or respiratory disorders. In our series heart disorders were, however, not associated with postoperative complications, significant functional disorders or mortality.

Duodenal atresia and hypertrophic pyloric stenosis increase GOR and disturb gastroduodenal motility and may potentially complicate the postoperative course after oesophageal repair, but in our series these disorders were not associated with increased postoperative complications.

The 7% incidence of postoperative anastomotic leakage in our series was comparable with the incidence figures ranging from 3% to 25% in recent studies [14,15,20,21]. The incidence of dilatation related perforations also appears similar to other series [22,23]. Recently the trend of treatment of anastomotic leakage has shifted in our centre from operative to active conservative treatment whenever possible. Compared with contemporary reports [14,24,25] the incidence of recurrent TOF in our series was also relatively low (2%).

Half of our patients developed significant GOR by the age of one year and the majority of the anti-reflux surgery has been performed by that time. After the age of one year, the incidence of OA associated significant GOR rose only moderately and few additional patients needed anti-reflux surgery [8]. Recurring anastomotic stenosis and apnoeic spells were the main indications for early anti-reflux surgery and were perhaps performed more often than other centres [14,15]. Post-repair apnoeic spells may suggest both GOR and severe tracheomalacia, but in an infant with critical condition differentiation and invasive verification of these disorders are often difficult if not impossible [26], and surgical treatment including aortopexy and anti-reflux surgery is performed mainly on clinical grounds.

The reported incidence of anastomotic stricture varies from 17% to 52% and in most reports all cases requiring any number of postoperative anastomotic dilatations are included [14,15,20,25]. From 2003 on we have dilated only symptomatic patients of whom five or more dilatations were performed to 29% which probably reflects the approximate incidence of significant anastomotic stenosis or stricture in our series. This figure includes a relatively high percentage (6%) of patients in whom, after failure of endoscopic dilatations, operative revision of the strictured anastomosis was required.

The 2% overall mortality figure in our series was low and allows no meaningful comparison by the risk groups in Spitz classification. Prior studies have reported mortality rates from 5% to 24% during a comparable time period than our study [14,15,20,27]. The importance of comprehensive pre-discharge counselling on the potential dangers of food-related asphyxia during the post-repair period cannot be overemphasized. Two of the deaths in our series may have been preventable. In the present series 94% of patients enjoyed full oral intake. Prolonged dependence on ostomy feedings was mainly related to long-gap OA, syndromes and neurological disorders associated with impaired swallowing such as the CHARGE syndrome.

The outcome of OA in our series was characterized by low mortality and successful treatment of numerous complications and associated anomalies. However, more than 90% of children ended-up with satisfactory esophageal function with full oral intake. Of all patient and disease related factors, long-gap OA remains the major predictor of complications.

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