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Case control study

Outcome of Long Gap Esophageal Atresia at 6 Years: A Prospective Case Control Cohort Study

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ABSTRACT:

Objective: Our primary aim was to assess the outcome, at age 6 years, of long gap esophageal atresia (EA) compared with non-long gap EA/tracheo-esophageal fistula (TEF). The secondary aim was to assess whether initial treatment (delayed primary anastomosis of native esophagus vs. esophageal replacement) influenced mortality and morbidity at ages 1 and 6 years.

Summary Background Data: EA is the most frequent congenital esophageal malformation. Long gap EA remains a therapeutic challenge for pediatric surgeons.

Methods: A multicentric population-based prospective study was performed and included all patients who underwent EA surgery in France from January 1, 2008 to December 31, 2010. A comparative study was performed with non-long gap EA/TEF patients. Morbidity at birth, 1 year, and 6 years was assessed.

Results: Thirty-one patients with long gap EA were compared with 62 non-long gap EA/TEF patients. At age 1 year, the long gap EA group had longer parenteral nutrition support and longer hospital stay and were significantly more likely to have complications both early post-operatively and before age 1 year compared with the non-long gap EA/TEF group. At 6 years, digestive complications were more frequent in long gap compared to non-long gap EA/TEF patients. Tracheomalacia was the only respiratory complication that differed between the groups. Spine deformation was less frequent in the long gap group.

Conclusions: There were no differences between conservative and replacement groups at ages 1 and 6 years except feeding difficulties that were more common in the native esophagus group. Long gap strongly influenced digestive morbidity at age 6 years.

Level of evidence: Prognosis study, Level II

Esophageal atresia (EA) is the most frequent congenital esophageal malformation with an incidence of 1.8/10000 newborn in France.¹ Although most patients undergo anastomosis soon after birth, a subset of patients (10%, mainly pure EA) present a long gap EA in whom immediate anastomosis is not possible. Long gap EA remains a therapeutic challenge for pediatric surgeons. These children generally undergo a neonatal gastrostomy and, when it exists eso-tracheal fistula (TEF) closure.^{2,3} Insufficient esophageal length requires a delayed repair that postpones oral feeding, increasing the risk of oral disorders and aspiration.⁴

Different surgical techniques may be used for esophageal repair: delayed anastomosis of native esophagus after spontaneous growth or after elongation or, as recently described, by intrathoracic rapid elongation of both esophageal stumps⁵ or esophageal replacement (gastric tube⁶ or transposition⁷, eso-colooplasty⁸, or jejunoplasty⁹). There is no consensus on the ideal surgical management.¹⁰

Since the first successful surgery in 1941, anesthetic, surgical, and neonatal care have improved remarkably. In 2022, the long-term survival rates of these children reach 95% in the absence of associated malformation.^{1,11} Survival rates of children with long gap EA are however lower than children with the classical form.¹² Mortality rate for long gap EA can reach up to 16% during infancy, partly because of associated malformations (58% of cases).¹ In survivors, long-term sequelae are mainly digestive (gastro-esophageal reflux disease (GERD)), anastomotic strictures, dysphagia and dysmotility, delayed growth, nutritional dependency, and respiratory conditions (asthma, tracheomalacia, pulmonary infections) which impact quality of life (schooling, sport practices, etc.).^{12,13} Currently, there are very limited data on the outcome of these patients.

The primary aim of this study was to assess the morbidity in surviving patients, at age 6 years, of a cohort of long gap EA compared to paired non-long gap EA/TEF patients. The secondary aim was to assess if initial treatment (delayed primary anastomosis vs. esophageal replacement) influenced mortality and morbidity at ages 1 and 6 years.

METHODS

After an institutional review board approval by the scientific committee of the CRACMO (Centre de reference des Affections Chroniques et Malformatives de l'Oesophage), a multicentric population-based prospective study was performed including all patients who underwent EA surgery in France. During the 3-year period from January 1, 2008 to December 31, 2010, all patients with long gap EA performed in France were included in the French register. Long gap EA was defined as delayed esophageal repair (after 1 month of life) due to the size of gap length. Patients who had delayed surgery for other reasons than the length of the gap were excluded (i.e., extreme prematurity or severe malformations). Patients lost to follow-up were also excluded (Figure 1). All medical data were collected and centralized in the national register.¹⁴ Data were collected at birth and at ages 1 and 6 years.

In the long gap population at birth, we *a priori* defined two groups of patients depending on the surgical management of long gap EA before loss of follow up (47 patients) : native esophagus conservation and esophagus replacement groups.

At age 6 years, for each long gap EA case, 2 non-long gap EA/TEF patients operated on before 7 days of life in the same hospital were included. For each case, the non-long gap patients had to be born immediately before or after the long gap EA

patient. If the medical records of these patients were missing, then the next patients to be born immediately before or after the long gap EA case were included.

Two sources were used to collect the medical data: the data from the French national register at birth and at age one year as previously described.¹⁴ and the medical records from each center at the planned visit at age 6 years (a multidisciplinary visit that is systematically scheduled in France following the French official patient pathway).¹⁵ Collected data included demographic data, prenatal information, early post-natal events and type of EA, surgical information and postoperative course, clinical characteristics at first discharge, and one-year and 6-year follow-up. Anastomotic tension was subjectively assessed by the surgeon at the time of operation.

At age 6 years, we assessed digestive, respiratory, and orthopedic outcomes. We generally defined a complicated natural history as all situations that required at least one therapeutic intervention and/or impact on the child's wellbeing and quality of life. We defined digestive morbidity by the presence of GERD defined as suggestive clinical symptoms (unexplained chronic cough, chest pain, epigastric pain, ear-nose-throat (ENT) manifestations such as laryngitis/pharyngitis or even burning, and a sensation of a foreign body in the throat), positive pH-metry or peptic esophagitis at endoscopy and biopsy, GERD surgery, anastomotic stricture (defined as a reduction of the diameter of the anastomosis and clinical signs¹⁶), number of dilatations, dysphagia or bolus impaction, and anastomotic leak. Feeding disorders were assessed using the Functional Oral Intake Scale (FOIS).¹⁷

Respiratory morbidity was defined by cough, dyspnea, asthma, tracheomalacia, or the need for respiratory medication. Finally, we defined orthopedic comorbidity at age 6 years by deformation of the spine and orthopedist follow-up.

Data were expressed as count (proportion) for binary variables and mean (\pm standard deviation) for continuous variables. Comparison between long gap EA and non-long gap EA/TEF groups was assessed by t-test (using the odds ratio, its confidence interval, and the *P*-value). Missing values were ignored in statistical tests and reported in corresponding tables. All analyses were processed using R software 'Vienna, Austria' version 4.0.1 with a significance threshold of 0.05.

Within the framework of the French national plan for rare diseases, the French national registry for EA was created as a population-based registry and began collecting prospective data on all infants born with EA in France on the January 1, 2008. The registry was approved by the Advisory Committee on Information and Research in Health (CCTRIS no. 08.297), by the National Commission on Informatics and Liberty (CNIL no. 908362) and was qualified by the National Register Committee (InVS, CNR). All data were used anonymously, and parents were informed about what information was registered and why. In accordance with French laws, no written consent was needed. The register was recorded in ClinicalTrials.gov (NCT02883725).

RESULTS

Over the study period, a total of 466 patients with EA were identified in the French EA registry, of which 55 had an anastomosis after 1 month of life. Six cases were excluded after reviewing the medical charts. Anastomosis in those cases was delayed because of a low birth weight in 2 cases, respiratory failure in 2 cases, a right aortic arch in 1 case, and polymalformative syndrome with care limitation in 1 case. Forty-nine cases from 22 different hospitals were included, accounting for 11% of all EA cases over the study period.

Two patients died after the primary surgery for fistula closure. Forty-seven patients had a corrective intervention: 33 delayed anastomosis and 14 esophageal replacement including gastric transposition (n = 8), gastric tube (n = 3), coloplasty (n = 2), and the Collis–Nissen procedure (n = 1). Four patients died after corrective surgery and 12 patients were lost to follow-up before age 6 years.

Finally, 31 patients with long gap EA were included and 62 EA/TEF with immediate primary anastomosis patients were selected. In the non-long gap EA/TEF group, 2 patients died (1 at age 4 months due to cardiac arrest after hypokalemia, and 1 at age 5 months due to septic shock after digestive perforation, Figure 1).

Characteristics of children at birth are reported in Table 1. Compared to non-long gap EA/TEF infants, those presenting with long gap EA were more likely to have a prenatal diagnosis and had significantly lower gestational age and birth weight.

Postoperative outcome before age 1 year is reported in Table 2. Compared with non-long gap EA/TEF, those presenting with long gap EA were significantly more likely to have complications both early post-operatively and before age 1 year. Early postoperative complications were digestive in 24 cases for long gap EA and 10 cases for non-long gap EA/TEF (2 duodenal stenoses, 18 anastomotic leaks, 23 anastomotic strictures, 1 digestive perforation, 2 bowel obstructions, and 1 eventration). There were 7 respiratory complications in the long gap EA group and 9 in the non-long gap EA/TEF group (2 atelectasis, 10 pneumothorax, 5 pneumopathies, and 2 recurrent eso-tracheal fistulas). We identified 3 long gap EA patients and 4 non-long gap EA/TEF patients who had septic related complications (4 central line infections, 1 pyelonephritis, 1 mother-fetal infection, and 2 mediastinitis). Moreover, there were 6 long gap EA and 8 non-long gap EA/TEF patients that had other types of unfavorable outcome (3 acute renal failures, 4 bradycardias, 3 surgeries for arterial canal, 1

chylothorax, 1 intra-ventricular hemorrhage, 1 Claude Bernard Horner syndrome, and 2 deep vein catheter thrombosis). Complications during the first year of life were mostly digestive (one or more for the same patient): 17 cases for long gap EA group (3 GERD, 12 anastomotic strictures, 9 anastomotic leaks, 1 recurrent eso-tracheal fistula) and 15 cases for non-long gap EA/TEF group (2 dysphagia, 3 GERD, 10 anastomotic strictures, and 3 other digestive problems). Respiratory complications concerned 6 cases in the long gap EA group (6 bronchiolitis and 1 pneumopathy) and 11 cases in non-long gap EA/TEF group (8 bronchiolitis and 3 pneumopathies). Other complications were 1 pulmonary hypertension in the long gap EA group and 1 cardiac failure in the non-long gap EA/TEF group.

When comparing the groups at age 6 years, we found that digestive complications were much more frequent in long gap compared to non-long gap EA patients, resulting in a higher rate of gastroenterologist follow-up in this group (Table 3). Tracheomalacia was the only respiratory symptom that differed between the 2 groups and also resulted in a higher rate of pulmonologist involvement in this group (Table 3). Moreover, spine deformation was less frequent in the long gap group (Table 3). There was no difference in weight between the two groups.

At age 6 years, 90% of long gap EA patients were fully oral fed. Presentation with a feeding disorder, evaluated by abnormal FOIS, was found in 52% of patients.

Within the long gap EA group, children with native esophagus conservation had comparable neonatal characteristics as well as early complications compared to the esophageal replacement group, except for birth weight, which was 2072 grams for native esophagus conservation and 2459 grams for esophageal replacement group ($P = 0.04$, Table 4).

We classified postoperative complications during the few days after surgery in four main groups: related to surgery, iatrogenic, respiratory, and infections. They occurred at a similar rate between the conservative and replacement groups (Table 4).

Two patients died after corrective surgery, 1 due to early necrosis of colic transplant and 1 from septic shock due to mediastinitis.

Survival rate was 92% at age 1 year. There were no significant differences between the conservative and replacement groups. Thirty-eight patients required readmission (84%). Causes of readmission were postoperative complications (59%), gastro-intestinal or nutritional complications (23%), respiratory complications (11%), associated malformations (5%), and other reasons (2%). Three patients were still hospitalized at age 1 year. Revision of the anastomosis due to refractory stricture was performed in 4 cases, all of them being in the conservative group.

The group of long gap EA patients who retained their native esophagus presented significantly more feeding difficulties compared to the group with esophageal replacement (Table 5). We did not find any other difference between these two groups concerning either weight or growth at the age of 1 and 6 years (Table 5). The FOIS score was significantly worse for children with native esophageal conservation compared with esophageal replacement. There was no significant difference between the group with native esophageal conservation and the group with esophageal replacement for undernutrition, GERD, dysphagia, and asthma, and nor was there any significant difference between the two groups concerning the number of dilatations.

DISCUSSION

This is the first longitudinal population-based study addressing midterm morbidity of long gap EA compared with non-long gap EA/TEF. The long gap strongly influenced digestive, respiratory, and orthopedic morbidity at age 6 years.

Morbidity during the first year of life was significantly worse in patients with long gap EA in our study. Indeed, more than 75% of long gap EA patients presented with at least one postoperative complication: 66% during the first year of life, which is much higher than in non-long gap EA/TEF. Although the survival rate of children with EA has increased dramatically since the 1980s, complications requiring therapeutic intervention occur in more than half the patients during the first year of life and later, mainly in long gap EA patients as our study clearly shows.^{18,19} The length of initial hospital stays that we used as a proxy for neonatal disease severity was indeed significantly higher in the long gap EA group. As expected, due to the presence of hydramnios, the incidence of prematurity was higher in the long gap EA group which could in part explain the difference we observed between non-long gap EA/TEF and long gap EA patients.

At age 6 years, we showed that morbidity remains higher in long gap EA children. We observed more anastomotic strictures in the long gap EA group, probably due to inevitable damage to the esophagus during the surgical procedure.²⁰ Dissection and mobilization of the esophageal segments and/or the esophageal lengthening procedures may lead to local ischemia, postoperative scarring of the esophagus, and injury of the vagal nerves. This results in repeated hospitalizations for anastomotic stricture dilatation under general anesthesia, as already reported in long gap EA patients.²¹ Although not assessed in the present study, the quality of life of these children is known to be affected by these comorbidities.¹³

Prevalence of GERD in the long gap EA population is high and more severe than in non-long gap EA/TEF patients.²² Our study did not show a significantly higher rate of GERD in the long gap EA group at age 6 years. Children with long gap EA have more anti-reflux surgery, and there is a higher rate of esophagitis in a greater number of children with long gap EA. Since GERD was in part clinically defined, its prevalence might potentially have been underestimated. As some cases of GERD may be poorly symptomatic but responsible for complications, recent international consensus-based guidelines for the long gap EA population recommend regular monitoring, including esophageal endoscopy during childhood in order to monitor the natural history of GERD.²³ The high prevalence of GERD in our population of long gap EA patients supports the need for long-term follow-up to evaluate risk of Barrett and esophageal cancer in this high-risk population.

Another finding of our study is that feeding disorders are much higher in long gap EA than in controls. Feeding disorder is defined as a broad range of eating problems that may or may not be accompanied by swallowing difficulties for food, liquids, or both. Oral motor and sensorial functions normally develop within the first 12 to 24 months of age. We know that delayed introduction of an oral diet could impair acquisition of feeding and swallowing abilities.^{24,25,26,27} Another explanation is the higher frequency of peptic esophagitis, which may trigger feeding disorders in a nutritionally precarious population.²⁸ As a consequence of late reconstructive surgery, long gap EA patients depend longer on gastrostomy enteral feeding.²⁹ In this population, this seems a good option as it facilitates easy and efficient intake of calories and nutrients and causes less interference with the normal development of oral sensitivity and feeding and swallowing abilities³⁰, thus allowing normal growth and

nutritional status as we observed in our study, given that the weight of long gap EA did not differ from controls.

Children with EA are also subject to respiratory comorbidities in the medium and long term.^{31,32} Our results clearly show that long gap EA patients do not have an increased risk of respiratory complications compared to non-long gap patients and even presented less frequent symptomatic tracheomalacia. Regarding the tracheomalacia, the first human data described a deficiency in cartilage in 75% of examined tracheas.³⁴ These trachea abnormalities not only concern the site of the fistula but may also touch a long tracheal segment and sometimes extend to the bronchus. Persistent or worsening respiratory symptoms associated with persistent tracheomalacia may potentially be aggravated by a tracheal diverticulum at the fistula repair site. The higher rate of symptomatic tracheomalacia in the non-long gap EA/TEF group may be related to the presence of the eso-tracheal fistula but may also be related to anastomotic stenosis (more frequent in non-long gap EA/TEF) and dilatation of the upper pouch. Further studies are necessary but to the best of our knowledge, this is the first time it has been shown that tracheomalacia is less prevalent in long gap EA.

Surprisingly the prevalence of scoliosis was significantly lower in long gap compared to non-long gap EA/TEF patients. The high prevalence of scoliosis reported in patients after EA repair (ranging from 6 to 50%) is explained either by thoracotomy sequela and/or associated spine malformation.³⁵ Indeed, thoracotomy is a risk factor for scoliosis development during puberty.³⁶ Shoulder asymmetry and rib blocks at the site of thoracotomy can explain the occurrence of scoliosis.³⁷ Congenital vertebral malformation is frequent in EA patients, especially in VACTERL syndrome.³⁸ We can hypothesize that early surgery by thoracotomy performed in non-long gap patients

induced more damage in spine static development than delayed surgery in long gap patients. To the best of our knowledge, while there is no evidence in the literature of the impact of early surgery on midterm spinal deformity, our study may be the first to show this result. In our two groups, the rate of vertebral malformations was similar and therefore cannot explain the difference found between our non-long gap and long gap EA. However, it should be borne in mind that the national registry does not describe in detail the thoracotomy technique (e.g., whether or not the muscle was cut) and therefore conclusions are difficult to draw.

In 2020s, thoracoscopic surgery is being developed for EA surgical treatment.³⁹ The majority of our patients, both long gap and non-long gap EA, have undergone thoracotomy. As thoracoscopy is less invasive, it could greatly reduce the rate of orthopedic malformation caused by surgery in the long term.⁴⁰

Our study is one of the first to compare the outcome of long gap EA according to a conservative or replacement surgical approach. Although the conservative group differs from the replacement group in terms of birth weight and weight at surgery, we found, as expected, that anastomotic stenosis and feeding disorders are more frequent in the conservative group. This could be explained by the greater dysmotility in this group in the presence of a scarred esophagus. Substantial variation in the management of infants with EA is reported in the literature. Most authors are of the opinion that native esophagus should be preferred and argue for delayed anastomosis^{41,42}, sometimes requiring elongation techniques.^{43,44,45,46} For others, preserving the native esophagus leads to severe complications⁴⁷ and they advocate esophageal replacement using gastric transposition⁷, coloplasty⁸, gastric tube^{6,48}, jejunoplasty⁹ or a Collis procedure.⁴⁹ Most studies concern short periods of time and few patients.^{41,50-53} There are different studies in the literature that compare these two

groups, but none of them show a significant difference between different surgical techniques.^{41,48,49,54-61}

In our study, at age 6, and despite the consensus among pediatric surgeons that the conservation of native esophagus is associated with the best postoperative results, oral disorder is higher in case of native esophagus conservation compared with replacement surgery.

The strength of our study is the prospective population-based setting compared to retrospective series coming from a single center. Even if the number of subjects is limited, it is one of the largest series reported of patients with long gap EA.^{59,62} Moreover, realization of a case control study between long gap and non-long gap EA based on data collection from a national register allows precise comparison between groups. Due to the relatively low number of patients, we were not able to control our results on prematurity regarding the long-term outcomes.

Furthermore, due to the high number of surgical techniques used in the long gap group we were only able to compare the conservative to the replacement groups but not compare one technique with another.

Our results clearly show differences in the outcome of EA according to the gap length and supports a more intensive follow-up program in long gap EA patients.⁶³

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Author contributions

Agate Bourg, Marie Auger Hunault, Frédéric Gottrand and all participative centers for data collections and management.

Agate Bourg, Julie Thomas and Benoit Parmentier for data analysis.

Agate Bourg, Marie Auger-Hunault and Frédéric Gottrand for manuscript writing.

Frédéric Gottrand and Benoit Parmentier for project development.

Rony Sfeir : scientific coordinator of the national register.

Compliance with ethical standards

All the authors declare that they have no conflict of interest.

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Legends

Figure 1: Flow chart

Table 1: Population characteristics at birth

Table 2: Population characteristics during the first year of life

Table 3: Morbidity at age 6 years for non-long gap EA and long gap EA patients

Table 4: Characteristics and outcomes of “native esophagus conservation” and “esophagus replacement” groups

Table 5: Outcomes at one year of “esophagus replacement” and “native esophagus conservation” groups

Tables and figures:

Figure 1: Flow chart of the study

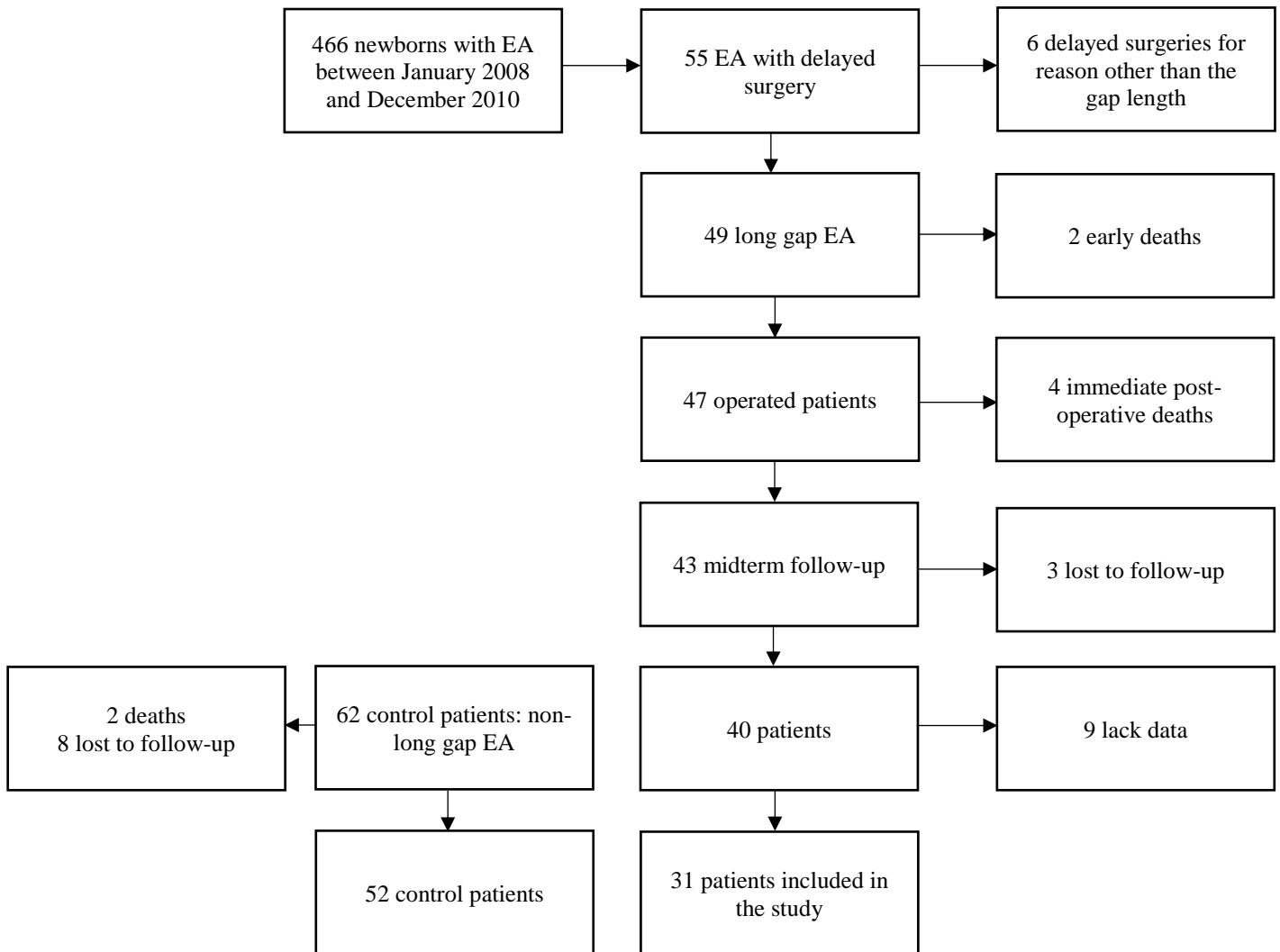


Table 1. Population characteristics at birth

Characteristics	Long gap EA n = 31 ¹	Non-long gap EA n = 62 ¹	Size effect ²	P-value
Sex			OR = 1.7 [0.65; 4.6]	0.3
Male	17 (55%)	42 (68%)		
Prenatal diagnosis	25 (81%)	13 (21%)	OR = 15 [4.8; 55]	<0.001
Associated malformations	16 (52%)	35 (56%)	OR = 0.82 [0.32; 2.1]	0.7
VACTERL	4 (13%)	12 (19%)	OR = 0.62 [0.13; 2.3]	0.6
CHARGE	0 (0%)	2 (3.2%)	OR = 0.00 [0.00; 11]	0.6
Mother age (years) (mean SD)	30.0 (4.5)	30.1 (5.3)	$\mu = -0.08 [-2.3; 2.1]$	>0.9
Gestational age (mean SD)	35.6 (3.2)	37.4 (3.0)	$\mu = -1.8 [-3.1; -0.37]$	0.014
Weight gr. (mean SD)	2,205 (516)	2,533 (714)	$\mu = -327 [-585; -69]$	0.014
Height cm (mean SD)	44.6 (4.4)	46.4 (4.2)	$\mu = -1.8 [-3.9; 0.30]$	0.09

¹Mean (standard deviation), n (%)

²OR, Odds ratio; μ , Mean difference

SD: standard deviation

Table 2. Population characteristics during the first year of life

Characteristics	Long gap EA, n = 31 ¹	Non-long gap EA, n = 62 ¹	Size effect ²	P-value
Surgical procedure				
Thoracotomy	25	57	CI95% [-0.03; 0.25]	0.11
Thoracoscopy	6	5		
Endotracheal ventilation				
(days)	6.5 (12.2)	4.4 (8.3)	$\mu = 2.0 [-2.9; 6.9]$	0.4
Missing value(s)	0	2		
Non-invasive ventilation				
(days)	1.97 (4.38)	1.15 (3.48)	$\mu = 0.82 [-1.1; 2.7]$	0.4
Missing value(s)	2	2		
Parenteral nutrition (days)				
	27 (30)	6 (15)	$\mu = 21 [7.4; 34]$	0.004
Missing value(s)	7	8		
Immediate postoperative complications				
	24 (77%)	30 (48%)	OR = 3.6 [1.3; 11]	0.008
Hospital stay (days)				
	144 (53)	34 (23)	$\mu = 110 [90; 131]$	<0.001
Missing value(s)	1	2		
Complication before age 1 year				
	20 (65%)	19 (31%)	OR = 4.0 [1.5; 11]	0.003

Number of hospitalizations	1.19 (1.14)	0.92 (0.98)	$\mu = 0.28 [-0.21;$ 0.76]	0.3
Missing value(s)	0	2		
Surgery consultation	25 (81%)	50 (83%)	OR = 0.84 [0.24;	0.8
			3.1]	
Missing value(s)	0	2		

¹Mean (standard deviation), n (%)

²OR, Odds ratio; μ , Mean difference

Table 3. Outcome at age 6 years in long gap EA and non-long gap EA patients

Characteristics	Long gap EA, n = 31 ¹	Non-long gap EA, n = 62 ¹	Size effect ²	P-value
DIGESTIVE MORBIDITY				
Weight (mean, kg)	18.2 (15; 24.9)	20.7 (13.3; 30)	CI = 95% [1.1; 4.2]	0.001
Missing value	9	27		
Weight z-score (SD)	-0.84 (-3.52; 2.5)	-0,34 (-5.3; 2.18)	CI = 95% [-1.30; 0.31]	0.23
Missing value	0	27		
Clinical GERD (actual)	17 (55%)	19 (37%)	OR = 2,1 [0.78; 5.8]	0.12
Missing value(s)	0	10		
Actual peptic esophagitis	14 (45%)	8 (15%)	OR = 4.4 [1.4; 15]	0.005
Missing value(s)	0	10		
Anti-reflux surgery before age 6	20 (65%)	10 (19%)	OR = 7.4 [2.5; 24]	<0.001
Missing value(s)	0	10		
History of anastomotic stricture	22 (71%)	20 (38%)	OR = 3.8 [1.4; 12]	0.006
Missing value(s)	0	10		
History of dilatations (mean)	3.03	0.77	μ = 2.3 [1.0; 3.5]	0.001
Missing value(s)	0	10		

Characteristics	Long gap EA, n = 31 ¹	Non-long gap EA, n = 62 ¹	Size effect ²	P-value
Actual dysphagia	21 (68%)	17 (33%)	OR = 4.2 [1.5; 13]	0.003
Missing value(s)	0	10		
Previous gastrostomy	31 (100%)	6 (12%)	OR = -	<0.001
Missing value(s)	0	10		
Gastrostomy still in place	5 (16%)	1 (1.9%)	OR = 9.5 [1,0; 471]	0.025
Missing value(s)	0	10		
Gastroenterologist follow-up	29 (94%)	25 (48%)	OR = 15 [3.3; 145]	<0.001
Missing value(s)	0	10		
RESPIRATORY MORBIDITY				
Respiratory symptoms	10 (32%)	25 (48%)	OR = 0.52 [0.18; 1.4]	0.2
Missing value(s)	0	10		
Symptomatic tracheomalacia	2 (6.5%)	17 (33%)	OR = 0.14 [0.02; 0.69]	0.006
Missing value(s)	0	10		
Cough	19 (61%)	31 (60%)	OR = 1.1 [0.39; 3.0]	0.9
Missing value(s)	0	10		
Dyspnea	22 (71%)	42 (81%)	OR = 0.59 [0.18; 1.9]	0.4

Characteristics	Long gap EA, n = 31 ¹	Non-long gap EA, n = 62 ¹	Size effect ²	P-value
Missing value(s)	0	10		
Asthma	13 (43%)	14 (27%)	OR = 2.1 [0.72; 5.9]	0.15
Missing value(s)	1	10		
Need for respiratory medication	24 (77%)	27 (52%)	OR = 3.1 [1.1; 10]	0.035
Missing value(s)	0	10		
ORTHOPEDIC MORBIDITY				
Spine deformation	1 (3.2%)	12 (23%)	OR = 0.11 [0.00; 0.84]	0.026
Missing value(s)	0	10		
Orthopedist follow-up	2 (6.5%)	17 (33%)	OR = 0.14 [0.02; 0.69]	0.006
Missing value(s)	0	10		

¹n (%), Mean (standard deviation)

²OR, Odds ratio; μ , Mean difference

The OR for gastrostomy is not calculable as all subjects in the long gap esophageal atresia group had one.

Table 4. Characteristics and outcomes of “native esophagus conservation” and “esophagus replacement” groups

Characteristics	Native esophagus N = 33	Esophagus replacement N = 14	P-value
Median term in gestational age (range)	36 (26.8; 39.8)	37 (31; 41)	0.23
Median birth weight in grams (range)	2072 (1040; 3740)	2459 (550; 3025)	0.04 *
Associated anomalies (%)	15 (45)	9 (64)	0.34
Cardiac malformations (%)	7 (21)	4 (28)	0.46
VACTERL (%)	7(21)	4 (28)	0.46
Ladd classification (%)	type I 25 (76) type II 3 (9) type III 4 (12) type IV 1 (3)	type I 10 (71) type II 2 (14) type III 2 (14) type IV 0 (0)	0.46

Characteristics	Native esophagus N = 33	Esophagus replacement N = 14	P-value
Median age at primary intervention in days (range)	2 (1; 20)	2 (1; 19)	0.37
Esophagostomy (%)	1 (3)	3 (21)	0.07
Fistula closure (%)	5 (15) 4 type III 1 type IV	3 (21) 2 type III 1 type II	0.68
Postoperative complications (%)	42	43	1
Median age at corrective surgery in days (range)	79 (19; 165)	98,5 (38; 454)	0.27
Median weight at corrective surgery in grams (range)	4105 (2400; 6750)	5587 (2950; 8300)	0.04*
Presence of anastomotic tension (%)	22 (67)	6 (43)	0.19

Characteristics	Native esophagus N = 33	Esophagus replacement N = 14	<i>P</i> -value
Elongation artificie (%)	3 (9)	0	0.54
Invasive ventilation in days (median)	0.5 (0; 53)	3 (0.5; 43)	0.48
Non-invasive ventilation in days (median)	5 (0; 21)	0 (0; 15)	0.61
Inotropes (%)	2/28 (7)	4/11 (36)	0.02
Parenteral nutrition (%)	24/27 (89)	11/11 (100)	0.26
Parenteral nutrition withdrawal in days after surgery (range)	21 (10; 123)	32 (6; 164)	0.97
Complications during first year of life (%)	26 (79)	12 (86)	0.59
Anastomotic fistula (%)	16 (48)	6 (43)	0.73
Anastomotic stricture (%)	20 (60)	8 (57)	0.83
Mortality (%)	1 (3)	1 (7)	0.53
Days of hospitalization before discharge (range)	151 (68; 317)	138 (59; 393)	0.59

CI 95%, Confidence interval 95%

** Statistically significant data*

Table 5. Outcomes at one year and 6 years of “esophagus replacement” and “native esophagus conservation” groups

Characteristics	Esophagus conservation n = 32	Esophagus replacement n = 13	P-value
<u>1 YEAR</u>			
Weight (grams)	8128	8106	0.99
Readmission (%)	25 (78%)	13 (100%)	0.06
Number of readmission median (ranges)	2.5 (0; 6)	3 (1; 7)	0.96
Median readmission duration in days (extreme)	9 (0; 148)	13 (0; 114)	0.51
Total length of stay in days during the first year (extreme)	152 (86; 365)	160 (70; 365)	0.43
Anti-reflux surgery	17 (53%)	6 (46%)	0.67
GERD	25/32 (78%)	5/12 (42%)	0.009
Dysphagia	9/31 (29%)	3/12 (25%)	0.73
Exclusive oral feeding	16 (50%)	4 (31%)	0.25
Intercurrent respiratory event	9 (28%)	5 (38%)	0.74
Respiratory treatment	9/28 (32%)	6/13 (46%)	0.25
<u>6 YEARS</u>			
Lost to follow-up since age one year	n = 22 10	n = 9 4	
Weight (grams) mean	24.6 (SD)	24.4	0.9

FOIS (mean)	6	6	0.33
GERD	6	4	0.36
Undernutrition	16	8	0.34
Dysphagia	14	3	0.13
Asthma	8	2	0.46