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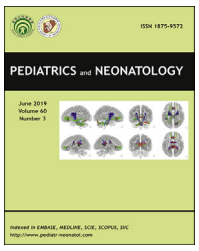

Original Article

Neonatal factors predictive for respiratory and gastro-intestinal morbidity after esophageal atresia repair

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Key Words
children;
esophageal atresia;
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Background: Esophageal atresia is a major congenital foregut anomaly. Affected patients often suffer from respiratory and gastro-intestinal morbidity. The objective of this study is to identify possible neonatal predictive factors contributing to a long-term complicated clinical course in patients after repair of esophageal atresia.
Methods: A total of 93 patients born between 1993 and 2013, with esophageal atresia and surviving the neonatal period were included in this retrospective study. A complicated clinical course was defined as the occurrence of $\geq$1 of these complications: severe gastro-esophageal reflux, esophageal stricture requiring dilatations, need for tube feeding for >100 days, severe tracheomalacia, severe chronic respiratory disease and death. We used linear models with a binomial distribution to determine risk factors for gastro-intestinal or respiratory complicated evolution and a backward stepwise elimination procedure to reduce models

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until only significant variables remained in the model. Multinomial logistic regression was used to assess risk factors for different evolutions of complication. Model parameter estimates were used to calculate odds ratios for significant risk factors.
Results: Fifty-seven patients (61%) had a complicated clinical course in the first year of life and 47 (51%) had a complicated evolution during years 1–6. In the first year, prematurity was a significant factor for complicated gastro-intestinal (OR 2.84) and respiratory evolution (OR 2.93). After 1 year, gastro-intestinal morbidity in childhood was associated with VACTERL association (OR 12.2) and a complicated first year (OR 36.1). Respiratory morbidity was associated with congenital heart disease (OR 12.9) and a complicated first year (OR 86.9). Multinomial logistic regression showed that prematurity ($p = 0.018$) and VACTERL association ($p = 0.003$) were significant factors of complications.
Conclusion: Prematurity is an important predictive factor for a complicated clinical course in early life. A complicated first year often predicts a complicated clinical course in childhood. These risk factors may be helpful in counseling of parents in the neonatal period.

1. Introduction

Esophageal atresia is a congenital foregut anomaly, often associated with a trachea-esophageal fistula and occurring in 1 of 2500 live births. Of the different types of esophageal atresia according to the Gross Classification, type C is the most common, accounting for 86% of patients with this condition.[1] About 48% of patients with esophageal atresia have associated anomalies, most involving the cardiovascular system. VACTERL and CHARGE associations, as well as triploid syndromes, are frequently diagnosed.[2–4] Although a primary anastomosis is feasible in most patients, surgical treatment of long-gap esophageal atresia remains challenging. Different surgical strategies are used, but no technique seems to be superior, and postoperative complication and morbidity rates remain high.[5–9]

Primary anastomosis, first performed successfully in 1941, has improved surgical outcomes and neonatal care. The long-term survival rates of children born with esophageal atresia are about 98% in low-risk populations, and over 80% in very low birthweight infants (<1500 g) and infants born with major cardiac anomalies.[10] Preventing and treating morbidities associated with esophageal atresia have become increasingly important. Patients with esophageal atresia are at risk for respiratory morbidity, including severe tracheobronchomalacia leading to severe blue spells, recurrent pulmonary infections, and asthma-like disease.[11–16] Gastrointestinal complications observed in children with esophageal atresia include dysphagia, esophageal strictures, gastro-esophageal reflux, esophagitis, Barrett's esophagus, and failure to thrive.[17–20] Children born with esophageal atresia are also at risk for neurodevelopmental delays, learning problems, and growth failure.[21] A large national study in the United States showed the multifactorial origin of morbidity after esophageal atresia, as well as possible risk factors for mortality, such as very low birthweight and extreme prematurity.[22] Disease-specific prognostic scoring systems (Spitz, Waterston) for mortality are unable to predict early non-mortality outcomes.[23–25] Patients with long gaps are at greater risk than infants with smaller gaps, especially those with anastomotic tension.[26] A detailed study showed that reflux was predictive of the need for fundoplication and gastrostomy, with fundoplication being predictive of a later aortopexy.[27] A study describing early predictive factors for short and long-term morbidity in children with esophageal atresia found that tracheal intubation prior to surgery, birth weight <2500 g, anastomotic leak and inability to be fed orally during the first month were predictive of complications before age 1 year.[28] After age 1 year, only long-gap esophageal atresia and the inability to feed orally during the first month remained predictive.

To compare our clinical data on risk factors with the data from other centers, and to establish risk models for later morbidity, which are currently lacking, we evaluated previously identified predictive factors.[28] This study focused on neonatal variables predictive of respiratory and/or gastro-intestinal morbidity in children with esophageal atresia during the first year of life and at age 1–6 years.

2. Patients and methods

This retrospective single-center study evaluated neonates diagnosed with esophageal atresia and admitted to the Neonatal Intensive Care Unit of University Hospitals Leuven (Belgium) between 1993 and 2013. The study was approved by the ethics committee of University Hospitals Leuven. The medical and nursing records of all patients were reviewed. Patients were excluded if they died within the first month of life. Neonatal data included *patient variables* (birth weight, gestational age, associated anomalies, respiratory distress syndrome, preoperative pneumonia, preoperative endotracheal intubation, and cardiac resuscitation at birth) as well as *surgical variables* (type of esophageal atresia, excessive tension at the anastomosis as reported by the surgeon, and whether a 1-step or 2-step surgery was performed. *Postoperative variables* were also evaluated, including postoperative intubation >5 days, pneumothorax, anastomotic leak and the need for tube

feeding for >100 days. A long-gap was defined as a gap >3 cm or greater than the height of two vertebral bodies. The first-line surgical treatments for patients with long-gap esophageal atresia in our institution are gastrostomy and esophagostomy, followed, if necessary, by second stage colonic interposition. A complicated clinical course was defined as the occurrence of at least one of the following complications: severe gastro-esophageal reflux (defined as the presence of severe esophagitis on esophago-gastroscopy or biopsy and/or the need for an anti-reflux procedure and/or jejunal feeding), esophageal stricture requiring two or more dilatations, need of tube feeding for more than 100 days, severe tracheomalacia (defined as the occurrence of at least one of the following: cyanotic spells, bronchoscopic findings, or requirement for an aortopexy and/or tracheostomy), severe chronic respiratory disease (defined as severe airway infection requiring hospitalization or an asthma-like disease), or death.

3. Statistical analysis

Bivariate associations between predictive variables and between complicated clinical course and individual predictive variables were analyzed using the phi-coefficient, a chi-square-based measure of association between two categorical variables. Generalized linear models with binomial distribution and the logit link function were used to determine the statistically most significant risk factors for respiratory and gastro-intestinal complications during the first year of life and at age 1–6 years. Controls consisted of patients without either gastro-intestinal nor respiratory complications.

Full models were built initially using potential risk factors as binary factors and birth weight and gestational age as continuous covariates. Birth weight and gestational age were used as continuous, not as categorical, variables because a small number of patients had extremely low birth weight or were extremely preterm, rendering birth weight and gestational age unsuitable for statistical analyses. Indeed, classification of infants by birth weight showed that only one had an extremely low birth weight (<1000 g) and only six had very low birth weight (<1500 g). Similarly, evaluation of gestational age showed that none of these infants was extremely premature (gestational age <28 weeks) and only four were very premature (gestational age <32 weeks).

Main effects and an intercept were included in these models. A threshold of $p < 0.10$ and a backward stepwise elimination procedure were used to build reduced generalized linear models until only significant ($p < 0.05$) factors and/or variables remained in the model. P-values and odds ratios (OR) are presented for these reduced models only, because model parameter estimates, p-values and ORs of full models tend to be unreliable due to overfitting or problems related to multicollinearity. The parameter estimates of the reduced models were used to calculate ORs and their 95% confidence intervals (CI) for factors associated with significant risks of complications. The performance of the models was assessed by calculating their positive and negative predictive values (PPV and NPV). Patients were stratified into four groups, as determined by the clinical course of their complications: 1) patients with complications only during the first year, 2) patients who developed complications after 1 year, 3) patients with complications in both time windows, and 4) patients without complications during either time period (controls). Multinomial logistic regression analyses were used to determine risk factors within strata. Potential risk factors were included in a full regression model and a similar backward stepwise elimination procedure was used to produce reduced models that included only those variables with a significant effect. The goodness of fit of the generalized linear models and the regression models was assessed using the Akaike Information Criterion (AIC) and omnibus chi-square tests. All statistical analyses were performed using IBM SPSS Statistics 24 (IBM Corp., Armonk, NY, USA).

4. Results

4.1. Population

Of the 102 patients with esophageal atresia born between 1993 and 2013 and admitted to NICU Leuven (Fig. 1), 93 were included in our analysis. The other nine patients were excluded, five due to insufficient or no follow-up data in their medical records, and four due to death during the neonatal period. Fifty-seven patients were male (61%). The median birth weight of this cohort was 2635 g (range 830–4450 g) and their median gestational age was 38 weeks (range 28–41 weeks). Gross classification of types of esophageal atresia in these patients showed that 88% had type C, 8% had type A, 3% had type B, and 1% had type E. Of the 79 (85%) patients who underwent primary repair, all underwent open thoracotomy. Because of long-gap esophageal atresia, 14 (15%) patients required gastrostomy placement and cervicostomy during the first surgery. Long hospital stay was associated with prematurity and more severe pathology, including severe cardiorespiratory events and combined severe congenital pathology, such as congenital diaphragmatic hernia.

4.2. Clinical course (Fig. 1)

Patients were stratified into four groups depending on the timing of their complications. Of the 93 patients, 12 (13.2%) presented with complications only during the first year, five (5.5%) only developed complications after the first year, 43 (47.3%) had complications during both time periods, and 31 (34.1%) had no complications. During the first year of life, 57 of the 93 patients (61%) had a complicated clinical course, with 32 (34%), 18 (19%), and 7 (8%) experiencing 1, 2, and ≥3 complications, respectively. After the first year of life, 47 of the 93 patients (51%) had a complicated clinical course, with 17 (36%), 21 (45%), and 9 (19%) experiencing 1, 2, and ≥3 complications, respectively. Fig. 2 shows the number of patients with a complicated clinical course and a detailed description of these complications according to the age of the children. These complications included the need for two or more esophageal dilatations or two or more hospitalizations due to lower respiratory tract infections. Four neonates died, one each due to perinatal

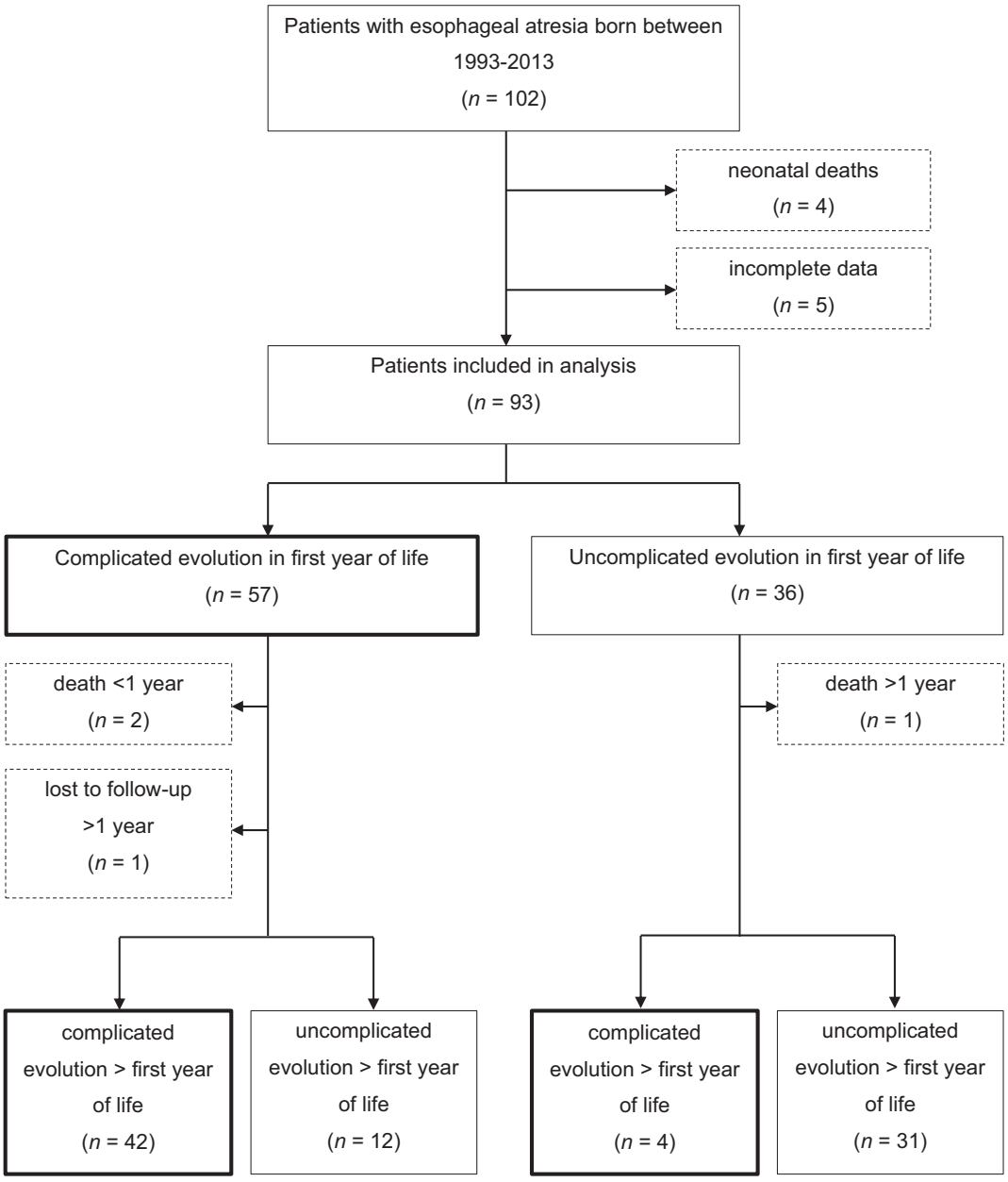
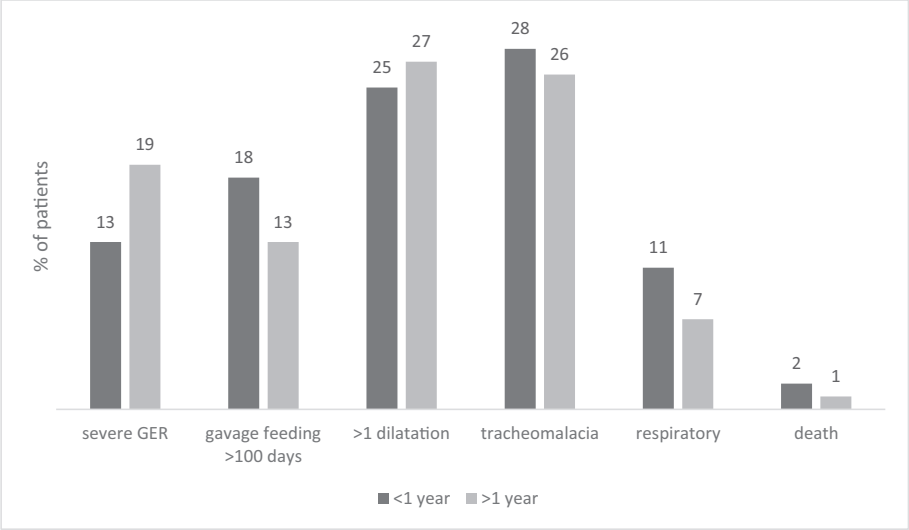


Figure 1 CONSORT flow diagram of 102 children born with esophageal atresia included in the study.

asphyxia associated with multiple organ failure, congenital pulmonary lymphangiectasia, overwhelming sepsis in preterm with severe growth restriction and persistent pulmonary hypertension. Two infants died, one of a severe respiratory infection and the other, with severe neurological impairment, of hemophagocytic lymphohistiocytosis. One child died at age 3 years; the cause of death is unknown.

4.3. Predictors of a complicated clinical course (Tables 1–3)

Bivariate analysis showed that variables predictive of a complicated clinical course during the first year were CPR at birth ($p = 0.044$), prematurity ($p = 0.046$), 2-step surgery ($p = 0.009$), long-gap atresia ($p = 0.009$), and length of stay >30 days ($p = 0.010$) (Table 1). Factors predictive of a complicated clinical course during years 1–6 were CPR at birth ($p = 0.016$), prematurity ($p = 0.017$), VACTERL ($p = 0.014$), congenital heart disease ($p = 0.046$), 2-step surgery ($p < 0.001$), long-gap ($p < 0.001$), intubation >5 days ($p = 0.003$), length of stay >30 days ($p < 0.001$), and a complicated first year of life ($p < 0.001$) (Table 2). An additional analysis to assess correlations between predictive variables (bivariate phi-coefficient test) showed that prematurity was associated with twin pregnancy ($p = 0.007$; phi = 0.280), low birth weight ($p < 0.001$; phi 0.700), respiratory distress syndrome ($p < 0.001$; phi 0.444), preoperative intubation ($p < 0.001$; phi = 0.372), 2-step surgery ($p = 0.031$; phi = 0.226), long-gap esophageal atresia ($p = 0.031$; phi = 0.226), intubation >5 days ($p < 0.001$; phi



GER: gastro-esophageal reflux

Figure 2 Complications in 93 patients with esophageal atresia before and after age of 1 year.

0.532), and length of stay >30 days ($p < 0.001$; phi = 0.578).

For the first year of life, the reduced linear model (AIC full model 119.2, AIC reduced model 12.1, goodness of fit $p = 0.028$) showed that, for patients with gastro-intestinal complications (44/81), only prematurity was a significant risk factor ($p = 0.032$), with an OR = 2.84 (95% CI [1.09—7.39]). The PPV of this model was 21/30 (70%) and the NPV was 28/51 (55%). In the model for respiratory complications (33/70) (AIC full model 115.9, AIC reduced

Table 1 Characteristics and complications identified during the first month of life and complicated or non-complicated development during the first year of life. Total number of patients N = 93.

Neonatal predictor variables	Complicated evolution (N = 57) n (%)	Non-complicated evolution (N = 36) n (%)
Twin birth	5 (9%)	2 (6%)
CPR at birth	6 (11%)*	0
Prematurity (<37 weeks)	26 (46%)*	9 (25%)
Birth weight <2500 g	29 (51%)	14 (39%)
VACTERL	15 (26%)	8 (22%)
Congenital heart disease	16 (28%)	10 (28%)
Pre-operative		
Neonatal RDS	6 (11%)	4 (11%)
Pre-operative intubation	7 (12%)	3 (8%)
Surgery		
2-step surgery	13 (23%)*	1 (3%)
Primary anastomosis tension	13 (23%)	6 (17%)
Type of atresia		
A	6 (11%)	1 (3%)
B	3 (5%)	0
C	47 (83%)	35 (97%)
E	1 (2%)	0
Long gap	13 (23%)*	1 (3%)
Post-operative		
Anastomotic leak	5 (9%)	3 (8%)
Pneumothorax	11 (19%)	5 (14%)
Intubation >5 days	16 (28%)	5 (14%)
Hospital stay >30 days	26 (46%)*	7 (19%)

*$p < 0.05$ versus patients with non-complicated evolution (phi-coefficient test).
CPR cardiopulmonary resuscitation; RDS: respiratory distress syndrome.
VACTERL ≥3 Vertebral, Anorectal, Cardiac, Tracheo-esophageal fistula and Esophageal atresia, Renal or Limbs anomalies.

Table 2 Characteristics identified during the first month of life and complicated or non-complicated development of patients at 1–6 years. Total number of patients N = 89.

Neonatal predictor variables	Complicated evolution (N = 46) n (%)	Non-complicated evolution (N = 43) n (%)
Twin birth	5 (11%)	2 (5%)
CPR at birth	6 (13%)*	0
Prematurity (<37 weeks)	24 (52%)*	11 (26%)
Birth weight <2500 g	26 (57%)	17 (40%)
VACTERL	15 (33%)*	5 (12%)
Congenital heart disease	18 (39%)*	8 (19%)
Pre-operative		
Neonatal RDS	6 (13%)	4 (9%)
Pre-operative intubation	7 (15%)	3 (7%)
Surgery		
2-step surgery	14 (30%)*	0
Primary anastomosis tension	10 (22%)	9 (21%)
Type of atresia		
A	6 (13%)	1 (2%)
B	3 (7%)	0
C	36 (78%)	42 (98%)
E	1 (2%)	0
Long gap	14 (31%)*	0
Post-operative		
Anastomotic leak	3 (7%)	5 (12%)
Pneumothorax	8 (17%)	7 (16%)
Intubation >5 days	17 (37%)*	4 (9%)
Hospital stay >30 days	25 (54%)*	7 (16%)
Complicated first year	42 (91%)*	12 (28%)

*$p < 0.05$ versus patients with non-complicated evolution (phi-coefficient test).
CPR: cardiopulmonary resuscitation; RDS: respiratory distress syndrome; VACTERL: ≥3 Vertebral, Anorectal, Cardiac, Tracheo-esophageal fistula and Esophageal atresia, Renal or Limbs anomalies.

model 11.8, goodness of fit $p = 0.034$) again only prematurity was identified as a significant risk factor ($p = 0.038$), with an OR = 2.93 (95% CI [1.06–8.08]). The PPV was 16/25 (64%) and the NPV was 28/45 (62%).

Of the children aged 1–6 years, 41/84 had gastro-intestinal complications. Factors significantly associated with gastro-intestinal complications included VACTERL ($p = 0.006$, OR 12.2, 95% CI [2.1–71.9]) and complications during the first year of life ($p < 0.001$, OR 36.1, 95% CI [7.6–170.7]) (AIC full model 88.2, AIC reduced model 16.0, goodness of fit $p < 0.001$). The PPV was 36/48 (75%) and the NPV was 31/36 (86%). Factors associated with respiratory complications in this age group (30/73) included congenital heart disease ($p = 0.02$, OR 12.9, 95% CI [1.5–111.3]) and complications during the first year ($p < 0.001$, OR 86.9, 95% CI [9.3–813.9]) (AIC full model 75.9, AIC reduced model 15.9, goodness of fit $p < 0.001$).

Table 3 Significant risk factors identified during the first month of life and their ability to predict a complicated or non-complicated course during the first year of life and during years 1–6 years based on generalized linear models.

Type of complication	Risk factors	n cases (n controls)	p-value	OR (95% CI)
<1 year				
respiratory	prematurity	33 (37)	0.038	2.93 (1.06–8.08)
gastro-intestinal	prematurity	44 (37)	0.032	2.84 (1.09–7.39)
1–6 year				
respiratory	complicated first year	30 (43)	<0.001	86.9 (9.3–813.9)
	congenital heart disease		0.020	12.9 (1.5–111.3)
gastro-intestinal	complicated first year	41 (43)	<0.001	36.1 (7.6–170.7)
	VACTERL		0.006	12.2 (2.1–71.9)

Total number of patients first year n = 93.
Total number of patients 1–6 years n = 89.
Controls are defined as having no respiratory nor gastro-intestinal complications.
Prematurity <37 weeks.
VACTERL ≥3 Vertebral, Anorectal, Cardiac, Tracheo-esophageal fistula and Esophageal atresia, Renal or Limbs anomalies.

Table 4 Early risk factors for short (<1 year) and long-term (1–6 years) complications and their development in children with esophageal atresia.

	Present study		Castilloux et al. (2010)	
Statistical test	ϕ coefficient		two-tailed χ^2 test	
Neonatal predictor variables	First year of life	> first year of life	First year of life	> first year of life
	$n = 93$	$n = 91$	$n = 134$	$n = 116$
Twin birth			•	
CPR at birth	•	•	n/e	n/e
Prematurity (<37 weeks)	•	•	n/e	n/e
Birth weight <2500 g			•	
VACTERL		•	•	
Congenital heart disease		•		
Pre-operative				
Neonatal RDS				
Pre-operative intubation			•	
Surgery				
2-step surgery	•	•	•	•
Primary anastomosis tension				
Long gap	•	•	•	•
Post-operative				
Anastomotic leak			•	
Pneumothorax				
Intubation ≥5 days		•	•	
Hospital stay >30 days	•	•	n/e	n/e
Need of tube feeding	n/e	n/e	•	•
Complex evolution in the first year of life	–	•	–	•

• $P < 0.05$ versus patients with non-complicated evolution.
n/e not evaluated.
– not applicable.
CPR cardiopulmonary resuscitation; RDS: respiratory distress syndrome.
VACTERL ≥3 Vertebral, Anorectal, Cardiac, Tracheo-esophageal fistula and Esophageal atresia, Renal or Limbs anomalies.

Multinomial logistic regression analysis showed that prematurity ($p = 0.018$) and VACTERL ($p = 0.003$) were significant predictors of complications (AIC = 44.3). Within the four strata, prematurity was the only significant factor and only in the patients who had complications during both time periods ($p = 0.008$ OR = 4.2, 95% CI [1.5–12.0]). By contrast, VACTERL tended to be significant in patients who had complications during years 1–6 ($p = 0.05$, OR = 8.1, 95% CI [0.997–65.3]) and in those who had complications during both time periods ($p = 0.06$, OR = 3.3, 95% CI [0.95–11.2]).

5. Discussion

In our cohort, CPR at birth, prematurity, 2-step surgery, long-gap atresia and length of hospital stay >30 days were associated with a complicated clinical course during the first year of life. In the modelling approach, however, prematurity was the only neonatal variable associated with a complicated respiratory and gastro-intestinal clinical course during the first year. After the first year, several risk factors were individually associated with a complicated clinical course, including CPR at birth, prematurity, VACTERL, congenital heart disease, 2-step surgery, long gap, intubation ≥5 days, length of stay >30 days and a complicated first year of life. In the linear models, congenital heart disease (for patients with complicated respiratory evolution), VACTERL (for patients with gastro-intestinal complications) and a complicated clinical course during the first year of life (for all patients) remained significant risk factors for a complicated clinical course after stepwise reduction of the models. Of these children, 61% had a complicated clinical course before age 1 year, and 51% during years 1–6. Most patients with a complicated clinical course during years 1–6 had a complicated clinical course during the first year of life; however, 11% of patients with complications during years 1–6 did not have complications during the first year.

Improvements in neonatal care have increased the survival rate of low-risk infants with esophageal atresia, with this rate being as high as 80% in patients with a birth weight <1500 g.[10] The focus has thus shifted gradually from neonatal survival and evaluation of surgical techniques to multidisciplinary follow-up and prevention and management of early and late morbidity. More than half of our patients with esophageal atresia experienced complications requiring therapeutic interventions, not only during

the first year of life but subsequently. The high neonatal survival rate (98/102, 96%), the causes of death and the rate of serious complications in this population (61/93, 66%) are in good agreement with previous studies.[12,13,22,29] It was not surprising that 72% of children with complications during the first year of life had complications after the first year. More strikingly, 11% of patients without complications during the first year developed new complications after age 1 year. The complication rates in our study were comparable to those in an earlier study, except that we observed a lower complication rate after age 1 year in patients with without complications during the first year (11% vs. 30%).[28]

Table 4 compares the results of bivariate analyses of risk factors in our study with those reported in a previous study.[28] In contrast to these earlier results, bivariate analysis in our study showed that twin birth, preoperative tracheal intubation, low birth weight, anastomotic leakage, and postoperative tracheal intubation for $\geq$5 days were not significantly associated with complications during the first year of life. In both studies, long-gap esophageal atresia and 2-step surgery were significantly associated with complications during both time periods. This was not surprising, inasmuch as long-gap esophageal atresia remains the most difficult type of esophageal atresia to treat, with no consensus reached on optimal treatment.

In contrast to bivariate analysis, our multifactor analysis could assess only a small number of predictive risk factors, although these factors remained significant in a statistical model with a reliable goodness of fit. Correlated risk factors were eliminated and only the strongest, independent risk factors remained significant. In the multivariable analysis, prematurity was the only statistically significant factor influencing respiratory and gastro-intestinal complications. Prematurity is a risk factor associated with many other risk factors, including twin birth, low birth weight, respiratory distress syndrome, preoperative intubation, 2-step surgery, long-gap esophageal atresia, intubation longer than 5 days and a length of stay longer than 30 days ($p < 0.05$ each by bivariate analysis). In addition, a complicated clinical course during the first year is a strong predictor of complications during childhood. Congenital heart disease and VACTERL are significant factors predicting respiratory and gastro-intestinal complications.

To predict the clinical course in these patients, we analyzed neonatal risk factors as predictors of complications in the four patient strata. Prematurity was the only significant factor and only in the group with complications during both time periods. VACTERL was marginally significant in patients who developed complications during the second time period and in patients who experienced complications during both time periods. It remains difficult to predict which children will progress from no complications during the first year of life to complications later in childhood.

The results of our study were in agreement with those of other studies, showing that patients with esophageal atresia experience both gastro-intestinal and respiratory problems.[30–32] Two-thirds of our patients had one or more problems. The prevalence of severe GER was lower in our patients than that in other populations (21% vs. 34–46%).[28,33] This discrepancy may have been due, in part, to underdiagnosis resulting from the absence of systematic gastro-intestinal endoscopic examination and of pH monitoring in young children treated at our center.

This study focused on complicated medical and surgical developments over a limited time period. Morbidities in these patients occur after age 6 years, continuing throughout adolescence and into adulthood.[16] Growth failure, motor delay and delays in mental development have been reported.[21,34] Problems such as learning disabilities and behavioral problems may become evident only at school age. These problems should be addressed in multidisciplinary clinics, in parallel with the medical and surgical problems observed in these patients.

The strength of this study was the ability to test previously published risk factors within this population of patients with esophageal atresia. Despite some limitations of this study, related to the wide CIs of some ORs and to the respective acquisition of data, our findings suggest that recognizing risk factors at an early stage could help identify patients most at risk for complications later in life. Additionally, these findings can be used to more accurately counsel parents of newborn infants born with esophageal atresia. Knowledge of these risk factors and earlier and closer monitoring of the development of these complications are advised. Advanced diagnostic methods, such as high resolution manometry impedance, are needed to assess esophageal motor function.[35,36] Prevention and earlier management of medical and surgical complications could also improve the quality of life and neurocognitive outcomes of patients with esophageal atresia.

In conclusion, several neonatal factors were found to predict complications in children with esophageal atresia of childhood. Prematurity is a major risk factor and is associated with other risk factors, including twin pregnancy, low birth weight, respiratory problems, long-gap esophageal atresia and a longer length of hospital stay. Identifying these risk factors may be helpful in counseling parents during the neonatal period. The early management of these complications could also improve neurological outcomes and the quality of life of these patients.

Conflict of interest

The authors have no conflicts of interest relevant to this article.

Acknowledgments

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.pedneo.2018.07.003