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Pulmonary outcome of esophageal atresia patients and its potential causes in early childhood

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ABSTRACT

Introduction: The aim of this study was to illustrate the pulmonary long term outcome of patients with repaired esophageal atresia and to further examine causes and correlations that might have led to this outcome.
Methods: Twenty-seven of 62 possible patients (43%) aged 5–20 years, with repaired esophageal atresia were recruited. Body plethysmography and spirometry were performed to evaluate lung function, and the Bruce protocol treadmill exercise test to assess physical fitness. Results were correlated to conditions such as interpouch distance, gastroesophageal reflux or duration of post-operative mechanical ventilation.
Results: Seventeen participants (63%) showed abnormal lung function at rest or after exercise. Restrictive ventilatory defects (solely restrictive or combined) were found in 11 participants (41%), and obstructive ventilatory defects (solely obstructive or combined) in 13 subjects (48%). Twenty-two participants (81%) performed the Bruce protocol treadmill exercise test to standard. The treadmill exercise results were expressed in z-score and revealed to be significantly below the standard population mean (z-score = −1.40). Moreover, significant correlations between restrictive ventilatory defects and the interpouch distance; duration of post-operative ventilation; gastroesophageal reflux disease; plus recurrent aspiration pneumonia during infancy; were described.
Conclusion: It was shown that esophageal atresia and associated early complications have significant impact on pulmonary long term outcomes such as abnormal lung function and, in particular restrictive ventilatory defects. Long-running and regular follow-ups of patients with congenital esophageal atresia are necessary in order to detect and react to the development and progression of associated complications such as ventilation disorders or gastroesophageal reflux disease.
Level of evidence: Prognosis study, Level II.

Esophageal atresia is a rare but severe congenital anomaly that, due to its anatomical constitution, frequently leads to gastroesophageal as well as respiratory short- and long term complications. In literature a main focus has been put on the gastroesophageal outcome of patients with repaired esophageal atresia. To our knowledge the first lung function testing of children with tracheoesophageal fistula was performed in the late seventies, but only in recent years the impact of esophageal atresia and tracheoesophageal fistula has been recognized and further investigated [1–3].

Studies have shown that patients with repaired esophageal atresia develop significantly more often symptoms of the respiratory system compared to the standard population. Newborns with esophageal atresia frequently show signs of respiratory insufficiency or symptoms of tracheomalacia such as the typical stridor. Recurrent bronchitis and aspiration pneumonia are commonly occurring in early childhood [4–6].

Over the course of body development acute respiratory infections tend to decline in frequency and severity, whereas asthmatic symptoms and chronic bronchitis come to the fore. Moreover, it has been reported that pulmonary function testing in children and adolescence after repaired esophageal atresia revealed values significantly lower than age-matched control subjects in up to 50% of the patients. Both, restrictive as well as obstructive ventilatory abnormalities have commonly been described [2].

However, only little research has been done on the exercise capacity of those children and adolescence as well as looking for correlations between the reduced pulmonary function and its potential causes in the neonatal period and early childhood.

Abbreviations: FEV 1, volume exhaled at the end of the first second of forced expiration; FVC, forced vital capacity; MEF 25, maximal expiratory flow at 25% of FVC; PEF, peak expiratory flow; RV, residual volume; TEF, tracheoesophageal fistula; TLC, total lung capacity; VC, vital capacity.

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Down to the present day the pathomechanisms that lead to reduced lung capacities as well as to recurrent respiratory symptoms remain uncertain.

The aim of this prospective study was to illustrate the short and long term pulmonary outcomes as well as to examine their potential correlations in early childhood of patients with repaired esophageal atresia.

1. Material and methods

Patients who had surgical treatment of esophageal atresia at our department between January 1991 and December 2010 and were at least 5 years old at the beginning of our investigation were identified. Twenty-seven patients who represent 43% of 62 possible patients decided to take part in the study.

The Charité ethical review board approved the study (EA2/159/11), and written parental informed consent was obtained.

Patient charts and questionnaires were used to acquire data concerning gestation and perinatal period; operative and perioperative outcome; respiratory as well as gastroesophageal complications. Furthermore subjects were investigated for congenital anomalies, potentially influencing the pulmonary function or exercise testing.

Pulmonary function testing was performed at a *JAEGER MasterScope Body* in cooperation with the Department of Pediatric Pneumology and Immunology.

Height and weight were measured and a clinical examination of the respiratory system was completed prior to the testing.

The procedures for measuring infant lung mechanics have been previously described. Briefly, after a period of quiet breathing in and out from the sensor, followed by taking a deep breath to measure the inspiratory vital capacity, the patient had to exhale into the sensor as hard as possible and for as long as possible to measure expiratory flow rates.

Animated images, like a candle that had to be blown out, were used to maximize the participants' motivation.

It was aimed to perform a whole-body plethysmography (inside a sealed glass chamber) allowing the measurement of the residual volume (RV), total lung capacity (TLC) and resistance values.

Since some of the subjects, in particular the younger ones, would not have shown their maximum capacities in a sealed glass chamber, a simple spirometry (body plethysmograph with open door) was also performed. The better results were recorded and analyzed.

Following the pulmonary function testing the subjects completed a treadmill exercise test using a motor-driven treadmill (Viasys LE200CE) according to the Bruce protocol to assess physical fitness in comparison to age matched reference groups. [7] The Bruce protocol was developed in the 1970s and is one of the most frequently used protocols in treadmill cardiac stress tests. It is characterized by a graded increase in angle of inclination and speed over constant periods of three minutes. Pulse, oxygen saturation and ECG was monitored continuously, the blood pressure was recorded before and after the exercise testing [7,8].

The exercise testing was stopped with voluntary exhaustion. Heart rate of at least 180 beats per minute or loss of coordination was considered to indicate maximal performance and the endurance time in minutes was recorded [3]. According to the reference values for pre-school children, subjects up to the age of 5 were allowed to hold the guardrail to maintain body position near the center of the moving belt [9]. The achieved endurance time of subjects up to the age of 13 was compared to reference values published by a Dutch group in 2010 [9,10]. The recorded results of participants from 13.5 years onwards were matched against reverence values by Binkhorst [11].

Data analysis was carried out using IBM SPSS Statistics 19. Results of the treadmill exercise testing were standardized by z-scores and compared to reference values by one-sample t-test. Items with non-normal distributions were compared by Mann–Whitney *U* test (ordinal scale) or chi-square test (nominal scale) respectively. Linear trends were illustrated using the coefficient of determination R^2. The limit for statistical significance was set at $p = 0.05$.

2. Results

2.1. Participating patients

Fifteen boys between the age of 5.6 and 20.6 years as well as 12 girls between 5.1 and 18.6 years took part in the study. The median age was 9.6 years.

Table 1 shows the distribution of types of esophageal atresia within the study group.

In 25 subjects (including two long gap esophageal atresia) primary end-to-end anastomosis was performed. Two other subjects with long gap esophageal atresia underwent gastrostomy initially after birth and secondary end-to-end anastomosis at 2 and 3 months of age. Esophageal replacement or reconstruction was not performed in our study cohort.

2.2. Non-participating patients

Twenty boys between the age of 6.2 and 18.3 and 15 girls between 6.0 and 19.6 years that were treated in the same period did not participate because their address was unknown or they were not interested. The median age of the non-participating group was 10.8 years.

Regarding esophageal atresia types there were 4 Type II (11.4%), 2 Type IIIa (5.7%), 27 Type IIIb (77.1%) and 2 Type IIIc (5.7%) patients in the non-participating group.

2.2.1. Associated anomalies

In total 22 subjects (81%) had at least one associated anomaly. Cardiac defects represented the most frequent associated anomalies in 17 subjects (63%). These included atrial septal defects (n = 7), ventricular septal defects (n = 3), patent ductus arteriosus (n = 8), Tetralogy of Fallot (n = 1) and aortic narrowing (n = 1). Three subjects underwent surgical repair in early childhood, the remaining defects were treated conservatively since they either closed on their own or were haemodynamically insignificant.

Further anomalies at birth included tracheomalacia (n = 6), orofacial cleft (n = 2), choanal atresia (n = 1), duodenal stenosis (n = 2), anal atresia (n = 5) and minor forms of vertebral defects such as slightly wedged vertebrae (n = 2). Chest wall deformities were not found in our cohort.

2.2.2. Pulmonary function testing

Pulmonary function testing was completed in all 27 subjects. In nine of the subjects we decided on performing a simple spirometry instead of a whole-body plethysmography due to the young age and insecurity of those patients. Subsequently, we were unable to record TLC, RV and resistance values in these patients.

Ten subjects (37%), including one patient with a Type II esophageal atresia, did not show any signs for ventilation disorders. Hence, this group of subjects served as internal scientific control group for further investigations.

In contrast, we found abnormal lung function at rest or after treadmill exercise testing in 17 subjects (63%).

Table 1
Frequency distribution of subjects with regard to esophageal atresia types and gender.

Vogt	Description	Boys participating		Girls participating		
		N	%	N	%	∑ (%)
Type II	Long gap, isolated	3	11.1	1	3.7	4 (14.8)
Type IIIa	Proximal TEF	0	0.0	1	3.7	1 (3.7)
Type IIIb	Distal TEF	12	44.4	8	29.6	20 (74.0)
Type IIIc	Proximal and distal TEF	0	0.0	1	3.7	1 (3.7)
Type IV	TEF only, H-Type	0	0.0	1	3.7	1 (3.7)
∑		15	55.6	12	44.4	27 (100)