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Functional residual capacity and lung clearance index in infants treated for esophageal atresia and tracheoesophageal fistula☆

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ABSTRACT

Background: Newborn babies with esophageal atresia/tracheoesophageal fistula (EA/TEF) are prone to respiratory tract disorders. Functional residual capacity (FRC) and lung clearance index (LCI) are commonly considered useful and sensitive tools to investigate lung function and early detecting airways diseases. The aim of the present study is to report the first series of EA/TEF infants prospectively evaluated for FRC and LCI.

Methods: Prospective observational cohort study of all patients treated for EA/TEF. Lung volume and ventilation inhomogeneity were measured by helium gas dilution technique using an ultrasonic flow meter. Babies were studied both in assisted controlled ventilation (sedated) and in spontaneous breathing (quiet sleep). Three consecutive FRC and LCI measurements were collected for each test at three different time points: before surgery (T0), 24 hours after surgery (T1) and after extubation (T2).

Results: 16 EA newborns were eligible for the study between December 2011 and July 2013. Three were excluded because of technical problems. At T0 FRC values were in the normal range regardless the presence of TEF but worsened afterwards at T1, with a subsequent recovering after extubation; a significant improvement after surgery was observed concerning LCI while no differences were found in tidal volume.

Conclusion: Helium gas dilution technique is a suitable method to measure the effect of surgery on lung physiology, even in ventilated infants with EA. The changes observed could be related to the ventilatory management and lung compression during surgical procedure.

Esophageal atresia (EA) with or without tracheoesophageal fistula (TEF) is a rare congenital anomaly that occurs in 1:4500 live births. The expected survival rate after surgical correction is approaching 100%, although this may vary depending on different factors such as birth weight, gestational age, presence of pulmonary complications and associated congenital cardiac anomalies [1,2].

Newborns with EA/TEF are prone to respiratory tract disorders, either congenital (e.g. tracheomalacia), or acquired (e.g. aspiration pneumonia). Functional residual capacity (FRC) and lung clearance index (LCI) are commonly considered useful and sensitive tools to investigate lung function for an early detection of airway disease [3,4]. Determination of FRC and LCI is relevant when assessing lung development in health and disease and for interpretation of volume-dependent lung function parameters (respiratory compliance, resistance, forced expiratory flows, indices of gas mixing efficiency, and ventilation inhomogeneity) [5].

The FRC is the volume of gas contained in the lungs at the end of a normal expiration during tidal breathing. It is determined by the compliance of the lung and chest wall [3].

The LCI is a physiological test that measures ventilation distribution in the lungs and it is defined as the number of times the lung volume has to be "turned over" to clear the lungs from an inert tracer gas. Changes in the small airways lead to inhomogeneous ventilation of different parallel airways, thus resulting in inhomogeneous emptying of peripheral lung units, with concomitant changes in ventilation distribution [4].

Although several techniques to measure lungs volume in spontaneous breathing newborns have been reported, only few data are available on mechanically ventilated patients operated for esophageal atresia [6].

The aim of the present study is to report our series of infants with EA prospectively evaluated for FRC and LCI before and after surgery with a non-invasive technique.

1. Materials and methods

This is a prospective observational cohort study, as approved by Bambino Gesù Pediatric Research Hospital Institutional Review Board. The study was proposed to parents of all patients admitted to our department for EA/TEF, between December 2011 and July 2013. Informed written consent was obtained. All patients were screened for major associated abnormalities.

The helium multibreath gas dilution technique was used to measure FRC and LCI. An ultrasonic flow meter (Spiroson, ndd Medical Technologies, Zurich, Switzerland) was connected to an Exhalyzer D (Eco

☆ None of the authors presented conflict of interest and the study was conducted ethically after the institutional review board approval of the study.

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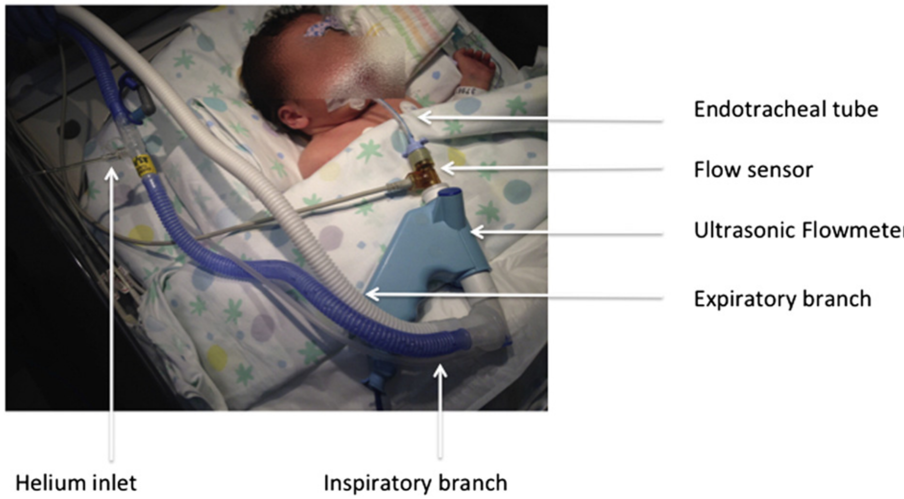

Fig. 1. Ultrasonic flow meter connected to a patient during mechanical ventilation The flow meter was placed between the endotracheal tube and the inspiratory branch of the ventilator circuit.

Medics, Sensormedics, Bern, Switzerland). The software used to extrapolate results was the Spiroware WBreath version 2.0 (ndd Medical Technologies, Zurich, Switzerland).

When infants were on spontaneous breathing, measurements were performed during using a tank filled with 17% helium, 21% oxygen and 62% nitrogen, while in cases of mechanical ventilation, using a tank with 79% helium and 21% oxygen.

Spontaneously breathing infants were studied during quiet sleep without any sedation. Infants mechanically ventilated were instead sedated with fentanyl at the dose of 1 mcg/kg/h.

During mechanical ventilation (Leoni Plus, Heinen-Lowenstein GmbH & Co.) the constant flow of the ventilator was maintained between 7 and 8.5 L/min and the mix of gases (79% helium and 21% oxygen) was administered through a connection in the inspiratory branch of the circuit. The flow meter was placed between the endotracheal tube and the inspiratory branch of the ventilator circuit (Fig. 1). In babies breathing spontaneously, the flow meter was connected to a facemask held snugly over the nose and mouth in order to avoid leaks.

The multi breath washout (MBWO) test was started switching the device to tracer gas at end expiration (wash-in phase). The patient breathed the gas mixture until the helium concentration reached the equilibrium, then the helium was automatically switched to the washout phase that ended when the helium concentration fell below 1/40th of the starting level over several breaths.

FRC calculated with initial and equilibration helium concentration was then adjusted for oxygen consumption, body temperature, pressure and water vapor saturated conditions.

Lung clearance index (LCI) was calculated as the number of turnovers needed to lower the end-tidal tracer gas concentration to 1/40th of the starting concentration [6–8].

The flow sensor was calibrated before starting each test using a 100 ml precision calibration syringe.

Tests were performed before surgery (T_0), 24 hours after surgery (T_1) and after extubation in spontaneous breathing, at least 48 hours after fentanyl discontinuation (T_2). The average of three consecutive FRC and LCI measurements was calculated and related to body weight at each time point.

Fraction of inspired oxygen (FiO_2) delivered was adjusted in order to keep saturation between 90% and 95% (median FiO_2 used was 0.23) and mechanical ventilation parameters were set to maintain blood gases analysis within standardized ranges (pH 7.30–7.35, $paCO_2$ 45–55 mmHg).

1.1. Surgery

Esophageal surgery was performed in all cases as an elective procedure, according to our published protocol [9]. Preoperative flexible laryngotracheoscopy was always performed to evaluate vocal cord motility, to study the level and the number of esophageal fistulas, to rule out laryngotracheal malformation and to preoperatively assess the esophageal gap [10].

Thoracotomy was decided depending on the side of aortic arch. Usually right thoracotomy was performed when faced to a left aortic arch/descending aorta. Esophageal surgery was performed either through an axillary incision (according to Bianchi procedure) or through a classic posterolateral thoracic incision, accessing the posterior mediastinum extrapleurally with azygos sparing technique. Tracheoesophageal fistula was transfixed and ligated with absorbable 4/0 suture and the esophageal anastomosis was performed with 6–8 interrupted long-lasting absorbable monofilament stitches (5/0 PDS II – Ethicon, INC.2012). AC and PB performed all surgical procedures.

1.2. Statistical analysis

Results were expressed as medians and range. The repeated measure ANOVA and Bonferroni post test were used to evaluate possible differences among T_0, T_1 and T_2. The statistical package used was SPSS v.17.0 for Windows.

2. Results

Sixteen newborns diagnosed with EA, were admitted in our NICU, during the study period. All infants were eligible, and after written informed consent was obtained from their parents, all were included in this study. Major malformation was present in about 46% (7/15) of all patients treated.

Table 1 summarizes main clinical and surgical characteristics. Prenatal diagnosis rate was 27% (4/15 infants).

Median gestational age and median birth weight were 37 weeks (range 29–40) and 2435 grams (range 1170–3480) respectively. Females/males ratio was 6/9. Fourteen out of 15 had type C defect and 1 type A. Two patients were excluded from further analysis because of technical problems. Therefore 13 patients completed the study protocol (Fig. 2).

Surgery was performed at a median postnatal age of 3 days and primary anastomosis was executed through a right axillary thoracotomy approach in 12 patients, while a left thoracotomic approach was required in 1, owing to a right aortic arch. Postoperative muscle paralysis was used in 10 patients and maintained for a median duration of 2 days (range 0–6). Median duration of mechanical ventilation was 10 days (range 4–81).

FRC values were in the normal range at T_0 for all babies, while a slight worsening of lung volume was recorded 12–24 hours after surgery (with no statistical significance, $p = 0.15$), followed by a complete