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Assessment of early pulmonary function abnormalities in giant omphalocele survivors

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Abstract

Purpose: Infants with giant omphalocele (GO) are at increased risk for persistent respiratory insufficiency, yet information regarding the systematic assessment of their lung function is limited. We performed a group of pulmonary function tests (PFTs) including spirometry, fractional lung volume measurements, assessment of bronchodilator responsiveness, and passive respiratory mechanics in GO survivors during infancy and early childhood to evaluate the nature and degree of pulmonary dysfunction.

Material and Methods: Between July 2004 and June 2008, 30 consecutive GO survivors were enrolled in our interdisciplinary follow-up program. Forty-seven percent (14/30) underwent PFT during follow-up evaluation using the raised volume rapid thoracic compression technique to measure forced expiratory flows and bronchodilator responsiveness, body plethysmography to calculate lung volumes, and the single breath occlusion technique to measure passive mechanics of the respiratory system.

Results: The mean age at PFT assessment was 19.3 ± 19.7 months (range, 1.0-58). Mean forced vital capacity and mean forced expiratory volume in the first 0.5 second were significantly reduced compared with published normative values ($P = .03$ and $P < .01$, respectively). Total lung capacity was significantly reduced ($P < .001$), whereas functional residual capacity, residual volume, and residual volume to total lung capacity ratio were within the normative range ($P = .21$, $P = .34$, and $P = .48$, respectively). Among the 46% who demonstrated significant bronchodilator responsiveness, there were greater increases in the mean percentage changes in flow at 25% to 75% ($P = .01$), flow at 75% ($P < .001$), and flow at 85% ($P < .001$) compared with those participants that did not respond. Specific compliance was reduced, whereas specific conductance increased, compared with published normal results.

Conclusions: Abnormalities of pulmonary function in GO survivors include lung volume restriction without airway obstruction, an increased likelihood of airway hyperresponsivness, and reduced

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respiratory system specific compliance. Early recognition of pulmonary functional impairment in GO survivors could help to develop targeted treatment strategies to reduce the risk of subsequent pulmonary morbidity.

Omphalocele is a midline defect in the ventral abdominal wall that results in herniation of abdominal contents into a membrane-covered sac that is composed of an inner layer of peritoneum and an outer layer of amnion. It occurs with an estimated incidence of approximately 1 in 6000 live births [1,2]. The contents of the sac can include solely intestine or can also contain liver and stomach. Omphalocele is usually classified into 3 groups (small, giant, and ruptured omphaloceles) [3,4].

Giant omphalocele (GO) is defined as a large central covered defect containing most of the liver. Improvements in neonatal intensive care, nutritional support, and surgical techniques have reduced the overall mortality for GO [3,5,6]. Despite these improvements in survival, children with GO have been reported to experience ongoing medical and surgical morbidities including nutritional problems, impaired musculoskeletal development, gastroesophageal reflux disease, failure to thrive, and adverse neurodevelopmental outcome [3,5-9]. In addition, GO is associated with a high incidence of pulmonary insufficiency and respiratory failure requiring prolonged intensive support with oxygen, assisted ventilation, and tracheostomy to facilitate assisted ventilation [3,5,10-13]. Pulmonary hypoplasia, increased intraabdominal pressure after repair, narrow chest deformity, diaphragmatic dysfunction, and collapse of the lung attributable to bronchial deformation have been suggested as causes of respiratory insufficiency in infants with GO [12-17]. However, there are limited data regarding lung function in infants and toddlers with GO. Recent advances in infant pulmonary function techniques and equipment have made it possible to measure flows over most of the range of lung volumes, as well as fractional lung volumes in infants and toddlers without the need for airway intubation or paralysis [18,19]. The raised volume rapid thoracic compression (RV-RTC) technique yields results similar to those in older children and adults when they undergo standard spirometry [18]. When combined with measurements of thoracic gas volume, fractional lung volumes (eg, total lung capacity [TLC], functional residual capacity [FRC], residual volume [RV]) can also be derived.

In July 2004, we established an interdisciplinary program for all infants seen at our institution with a diagnosis of pulmonary hypoplasia including children with GO. As part of this prospective program, infants undergo comprehensive and coordinated evaluation by pediatric medical and surgical specialists as well as pulmonary function testing as part of their follow-up care. We sought to describe the nature and degree of respiratory mechanical dysfunction in GO survivors who underwent standardized pre- and postnatal care at our institution and who were subsequently enrolled in our follow-up program.

1. Material and methods

This study was approved by The Children's Hospital of Philadelphia Institutional Review Board, Committee for Protection of Human Subjects (IRB 2004-5-3779). Informed consent was obtained from the parents or legal guardians.

1.1. Patient population

We reviewed the prenatal and postnatal medical records of all GO infants that were enrolled in our interdisciplinary follow-up program between July 2004 and June 2008. Demographic data, including pregnancy and delivery information, neonatal care, surgical intervention, and respiratory support requirements, were recorded for each infant. *Giant omphalocele* was defined as a large abdominal evisceration with a covering membrane containing most (>75%) of the liver. This definition was established by consensus of our pediatric surgeons, as definitions dependent on measurement of the defect were not considered useful [3,5] because a large amount of abdominal viscera and liver may be eviscerated even through a narrow defect in the abdominal wall.

1.2. Postnatal clinical management

When mechanical ventilation was necessary, lung preservation ventilation strategies were used as previously described [20,21]. The mode of ventilation was aimed at administering only enough pressure to maintain preductal oxygen saturations greater then 85% or postductal PaO_2 greater than 30 mm Hg. High-frequency ventilation was reserved for neonates that continued to have hypercapnia refractory to conventional ventilation. Nitric oxide and sildenafil were used to treat pulmonary hypertension using established protocols [20,21]. Echocardiography was performed early to establish the presence and severity of pulmonary hypertension. The operating surgeon determined the type of repair (eg, staged reduction and closure, or "paint and wait") based upon comorbidities and whether the newborn was stable enough for any surgical intervention [5].

1.3. Pulmonary function testing

All families were offered to have their child undergo pulmonary function testing as soon as clinically stable after