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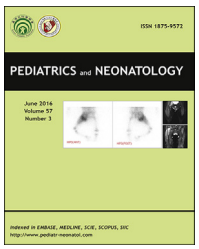

REVIEW ARTICLE

Longitudinal Follow-up of Chronic Pulmonary Manifestations in Esophageal Atresia: A Clinical Algorithm and Review of the Literature

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In the past decades improved surgical techniques and better neonatal supportive care have resulted in reduced mortality of patients with esophageal atresia (EA), with or without tracheoesophageal fistula, and in increased prevalence of long-term complications, especially respiratory manifestations. This integrative review describes the techniques currently used in the pediatric clinical practice for assessing EA-related respiratory disease. We also present a novel algorithm for the evaluation and surveillance of lung disease in EA. A total of 2813 articles were identified, of which 1451 duplicates were removed, and 1330 were excluded based on review of titles and abstracts. A total of 32 articles were assessed for eligibility. Six reviews were excluded, and 26 original studies were assessed. Lower respiratory tract infection seems frequent, especially in the first years of life. Chronic asthma, productive cough, and recurrent bronchitis are the most common respiratory complaints. Restrictive lung disease is generally reported to prevail over the obstructive or mixed patterns, and, overall, bronchial hyperresponsiveness can affect up to 78% of patients. At lung imaging, few studies detected bronchiectasis and irregular cross-sectional shape of the trachea, whereas diffuse bronchial thickening, consolidations, and pleural abnormalities were the main chest X-ray findings. Airway endoscopy is seldom included in the available studies, with tracheomalacia and tracheobronchial inflammation being described in a variable proportion of cases. A complete diagnostic approach to long-term respiratory complications after EA is mandatory. In the presence of moderate-to-severe airway disease, patients should undergo regular tertiary care follow-up with functional assessment and advanced chest imaging.

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1. Introduction

Esophageal atresia (EA) with or without tracheoesophageal fistula (TEF) occurs in one per 3000 live births.[1–3] In recent decades, improved surgical techniques and better neonatal supportive care have resulted in reduced mortality and increased prevalence of long-term disease-related complications, the most frequent of which include respiratory manifestations.[4]

Recurrent-to-chronic respiratory symptoms may upset daily life of EA survivors,[5] and this is the reason why the assessment of pulmonary disease is recommended in these patients. This integrative review describes the various techniques currently used in pediatric clinical practice for assessing EA-related respiratory disease. Moreover, we present a novel algorithm for the evaluation and surveillance of lung disease in EA survivors. We carried out an electronic keyword literature search for English articles published on this topic up to September 22, 2015, in the Scopus, Web of Science, PubMed, and MEDLINE databases. We excluded the studies conducted exclusively on adults, but included those with a study population comprising children (or adolescents) and adults. The terms "esophageal atresia" AND (lung OR respiratory OR pulmonary OR airway or spirometry or complications or diagnostic tools) were used as keywords in combination, and the studies found were evaluated for selecting relevant literature. In addition, a manual search was conducted to evaluate review articles' references. Literature reviews on diagnostic procedures for EA-related pulmonary disease prompted us to develop a novel algorithm for the evaluation and surveillance of lung disease in EA survivors.

2. Etiology

The etiology of pulmonary manifestations following EA repair is multifaceted. Because newborns with EA have an increased risk of premature birth that may initiate the clinical scenario,[6] the association with anomalies such as tracheomalacia and lung hypoplasia may significantly contribute to respiratory morbidity since birth.[2] Gastrointestinal symptoms (i.e., regurgitation and/or feeding difficulties with repetitive cough during swallowing, and/or dysphagia and heartburn likely due to peptic esophagitis and Barrett's esophagus) represent the major complaints at any age, and an association of gastrointestinal and respiratory symptoms has been hypothesized to imply a correlation between esophageal and lung dysfunction.[1,5,7] Indeed, esophageal dysmotility and gastroesophageal reflux (GER) may cause and/or worsen wheezing, bronchial asthma, and pneumonia.[8] Although the underlying mechanisms are still being debated, literature suggests that chronic asthma is likely elicited by a reflex mechanism and that recurrent pneumonia may be explained by repetitive acid aspiration.[9,10] Chronic airway inflammation with bouts of infection can eventually result in segmental or even lobar damage leading to the development of severe, life-threatening lung disease in a proportion of patients.[11–14] Finally, recurrent TEF may further complicate the clinical course.[15] Following EA-TEF repair, structural anomalies persist in both the trachea and the esophagus, and chest wall deformities, exacerbated by thoracotomy, may further contribute to alter pulmonary function.[2]

3. Respiratory complications

Patients with EA with or without TEF experience respiratory complaints more often and more persistently than other individuals, and recurrent bronchitis, chronic cough, repeated pneumonia, and asthma-like wheezing represent the major clinical manifestations.[11,16]

Lower respiratory tract infection is abnormally common especially in the first years of life, with more than five annual respiratory tract infections and a rate of more than three attacks of bronchitis per year of up to 78%.[17,18] In a study from Finland, aspiration pneumonia likely related to impaired esophageal peristalsis and esophageal stricture was reported in approximately 50% of affected children, although they did not experience more current respiratory or esophageal symptoms than those without.[12]

Coughs with sputum production and recurrent bronchitis are significantly more common among patients with repaired EA than among healthy individuals,[19] and although respiratory morbidity tends to improve with age, chronic cough, associated with bronchial constriction and hyperresponsiveness, can persist or even become more frequent in adulthood.[20] As a consequence of repeated bouts of lower airways infection, bronchiectasis may also develop.[21]

Although some respiratory complications may be accounted for by documented tracheomalacia, esophageal dysmotility, GER disease (GERD), or surgical complications, a high proportion of EA survivors have abnormal pulmonary function that is apparently unrelated to these conditions.[2] A restrictive pattern generally prevailing over obstructive or restrictive-obstructive airway disease has been described in up to 96% of children, adolescents, and adults previously treated for EA with or without TEF.[1,12,22–24] Interestingly, approximately one-third of a Finnish pediatric population had restrictive or obstructive defects that were apparently unrelated to current respiratory or esophageal symptoms.[12] In the same study, bronchial hyperresponsiveness was found to be severe/moderate or mild in 26% or 52% of the cases, respectively. Airflow obstruction may be explained by several mechanisms including small airway disease or proximal obstruction due to airway malacia or epithelial damage caused by GERD and recurrent episodes of bronchitis or aspiration pneumonia worsened by poor tracheal clearance, or decreased lung growth during infancy.[25] Multiple potential predisposing factors to restrictive lung disease are also congenital or acquired vertebral or chest wall abnormalities (i.e., scoliosis or postoperative rib fusions), surgical trauma, aspiration, and/or recurrent chest infections.[1]

Chronic asthma is considered to be common in EA survivors, with significant bronchial inflammation also occurring in patients with nonallergic asthma.[13,26] Whatever the initial trigger is, asthma significantly contributes to respiratory morbidity in EA, and it might even worsen pre-existing GERD.[13]

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