Multidisciplinary Care of Children With Repaired Esophageal Atresia and Tracheoesophageal Fistula

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Summary. Objectives: Children with congenital esophageal atresia with tracheoesophageal fistula (TEF) require complex medical and surgical care, but few guidelines exist to guide the long term care of this population. The purpose of this study is to describe the findings and initial management of a comprehensive aerodigestive team in order to understand the ongoing needs of children with repaired TEF. Methods: A retrospective chart review was performed on children with TEF who were seen in the multidisciplinary Aerodigestive Clinic at Children's Hospital Colorado. Diagnostic studies were ordered based on physician discretion. Results: Twenty-nine children with TEF were evaluated (mean age 3.8 years) between 2010 and 2014. All children had symptoms attributed to breathing, swallowing, and digestive difficulties. Less than half of the children had seen a pulmonary or gastrointestinal specialist in the past year. Tracheomalacia was diagnosed in all children who had a bronchoscopy (23/23), and the presence of dysphagia was correlated with severe tracheomalacia. 7/25 children who had a swallow study had aspiration. 7/25 children had a diagnosis of active reflux despite current management. Four patients were diagnosed with bronchiectasis as a result of the multidisciplinary evaluation. Conclusion: Although all children had persistent aerodigestive symptoms, over 50% had not been seen by an appropriate subspecialist in the year prior to the clinic visit. The multidisciplinary evaluation resulted in new diagnoses of bronchiectasis and active reflux, which can both lead to long-term morbidity and mortality. Children with TEF require evaluation by multiple subspecialists to manage not only current symptoms but also long term risks. Ongoing care should be guided by protocols based on known risks. **Pediatr Pulmonol.**

Key words: bronchiectasis; pediatric; aerodigestive.

INTRODUCTION

Children with congenital esophageal atresia with tracheoesophageal fisula (TEF) have chronic respiratory and digestive symptoms due to the abnormal development of the trachea and the esophagus in utero. Symptoms of patients after TEF repair commonly include cough, pneumonia, dyspnea on exertion, dysphagia, and gastrointestinal reflux disease (GERD).[1–4] Respiratory symptoms are as common in children with repaired TEF as in children with congenital diaphragmatic hernia and severe pulmonary hypoplasia.[5] Feeding difficulties are also widespread and can be associated with GERD, recurrent stricture, esophageal dysmotility, respiratory complications, and the need for repeated procedures requiring general anesthesia.[6] These difficulties cause not only repeated health care utilization but also result in significant family stress.[1,4,7]

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After initial surgical management and prolonged intensive care, children are discharged to the care of their parents and general pediatrician. Management is often continued by a pediatric surgeon, however consultation by other pediatric subspecialties including pulmonology, gastroenterology (GI), and otolaryngology is less consistent and likely based on the referring preferences of the surgeon and the pediatrician.[3,4] Multidisciplinary aerodigestive programs serve as an ideal clinical setting for management of TEF patients[6,8]; however, these programs are not uniformly available in all referral centers. Research and input from these programs is needed to understand the care of children with complex health care needs, such as repaired TEF, and to develop, test, and validate management guidelines.[6]

The purpose of this study is to describe the findings and initial management of a comprehensive aerodigestive clinic in order to understand ongoing needs for children with repaired TEF. To do this we describe the diagnoses in this population based on history, physical exam, and diagnostic testing performed by a team of pediatric subspecialists (pulmonary, otolaryngology, and GI). We describe the medical and surgical management changes recommended by the team after their initial clinic visit, diagnostic testing, and procedures. Based on this information we propose a plan for ongoing management of children with TEF.

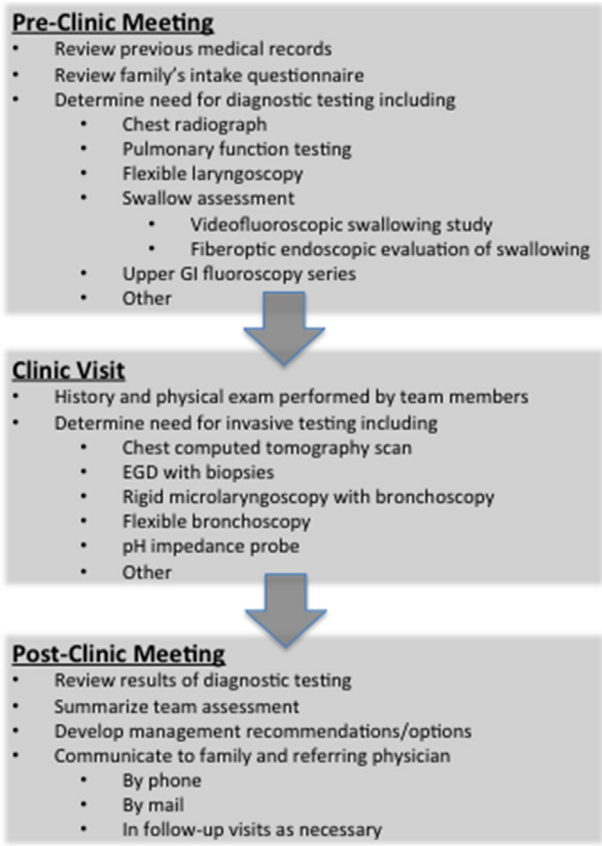

Fig. 1. Aerodigestive Clinical Process.

MATERIALS AND METHODS

This is a retrospective cross-sectional study of children with repaired TEF who were referred to the Aerodigestive Program at Children's Hospital Colorado by pediatricians, general surgeons, or pediatric subspecialists. Patients of the Aerodigestive Program are evaluated by a multidisciplinary team composed of pediatric otolaryngology, pediatric pulmonology, pediatric GI, feeding therapy, clinical nutrition, respiratory therapy, pediatric anesthesia, and social work. The Aerodigestive Clinical process at our institution is briefly summarized in Figure 1.

All patients with a diagnosis of TEF who were treated by the Aerodigestive Program at Children's Hospital Colorado between 2010 and 2014 were identified. Colorado institutional review board approval was obtained. Methods were in compliance with the Health Insurance Portability & Accountability Act of 1996 (HIPAA). Medical history was reviewed via the electronic medical record. Age at presentation to the program, demographics, medical history, medical treatment, and surgical treatment were recorded. Results of diagnostic testing were collected including video fluoroscopic swallow study, upper GI fluoroscopy series, chest computed tomography (CT) scan, esophgogastroduodenoscopy (EGD) with biopsies, rigid microlaryngoscopy with bronchoscopy, flexible bronchoscopy with bronchoalveolar lavage (BAL), and pH impedance probe. GERD was defined as a positive esophageal biopsy or a positive pH impedance study. Definition of a positive pH impedance study was adapted from NASPGHAN/ESPGHAN standard protocol to suit our clinical practice.[9,10] A pH impedance study was considered positive if bolus reflux events were greater than 100 in 24 hr for children less than one year of age or greater than 70 in 24 hr for children older than one year of age, the pH < 4 for more than 11.7% of the study for infants and 5.4% of the study for children, or symptom correlation was greater than 50%.[9,10] Regarding BAL microbiology, "normal respiratory flora" was considered positive for an organism on culture but not a pathogenic organism. Children treated with antibiotics for their abnormal BAL microbiology were considered to have a pathogenic organism. A normal lipid index on BAL was defined as $<10\%$ lipids seen within alveolar macrophages. Tracheomalacia was assessed during flexible bronchoscopy under light sedation. Mild/moderate tracheomalacia was defined as 50–90% dynamic collapse of the airway with quiet breathing or coughing and severe tracheomalacia was considered $>90\%$ dynamic collapse of the trachea. A sub-analysis was done to compare children with mild/moderate

tracheomalacia and those with severe tracheomalacia. A Student's two-sided *t*-test was used to compare continuous variables and a Chi-square test was used to compare proportions.

RESULTS

Twenty-nine children with a diagnosis of TEF were included in the study. The mean age at time of referral was 3.8 years and 15/29 (52%) had an associated syndrome (Table 1). The most common symptoms at referral were cough 21/29 (72%), dysphagia 16/29 (55%), and recurrent pneumonia 10/29 (34%). Less than half were followed by each subspecialty in the year prior to referral (Table 1).

Diagnostic Results

All patients were seen by the entire Aerodigestive team including the three pediatric subspecialty physicians.

20 of the 29 patients had an upper GI series performed as part of their clinical evaluation for dysphagia, the majority of which demonstrated abnormalities (Table 2). In addition, 24 patients had a video fluoroscopic swallow study with thin and thickened liquids to assess for aspiration based on clinical concern for aspiration, and nearly 30% (7/24) of those studies demonstrated aspiration (Table 2). In the cohort, 9 children had a pH impedance study. Of four positive pH impedance studies, all were positive based on number of episodes of nonacid reflux per day, and two were also positively correlated with respiratory symptoms of cough and wheeze.

TABLE 1— Demographics

Total	29
Age at evaluation, mean (range)	3.8 years (0.2–17.2)
Gestational age, mean (range)	36.6 weeks (30–41)
Male Sex, No. (%)	19 (65.5)
Syndromes/chromosomal, No. (%)	15 (51.7)
Down syndrome	5 (17.2)
Craniofacial anomalies (cleft lip/palate, etc.)	2 (6.9)
VACTERL association	7 (24.1)
CHARGE syndrome	1 (3.4)
Neuromuscular disease, No. (%)	2 (6.9)
Epilepsy	1 (3.4)
Cerebral palsy	1 (3.4)
Cardiovascular disease, No. (%)	11 (37.9)
Pulmonary hypertension	1 (3.4)
Congenital anomalies of the heart	10 (34.5)
Presenting symptoms, No. (%)	
Cough	21 (72.4)
Dysphagia	16 (55.2)
Recurrent pneumonia	10 (34.5)
Services 1 year prior to aero evaluation, No. (%)	
Pulmonary	13 (44.8)
Otolaryngology	15 (51.7)
GI	10 (34.5)
General surgery	18 (62.1)

Of children who had procedures under general anesthesia, 18/26 (69%) had them the day following the multidisciplinary clinic visit. For various clinical reasons, procedures were delayed in seven patients from 29 to 442 days following the multidisciplinary clinic visit. 15/25 patients had a visually abnormal EGD revealing mucosal or structural esophageal abnormalities (Table 2). All patients who underwent flexible bronchoscopy (23/23) had dynamic tracheomalacia, 16/23 had erythema, edema, or abnormal secretions visualized in the airway, 15/22 had inflammation on the BAL as defined by abnormally high segmented neutrophils and lymphocytes, and 13/22 had a pathogenic organism found on BAL microbiology. Only the presence of dysphagia was significantly correlated with the presence of mild/moderate versus severe tracheomalacia ($P = 0.02$) (Table 3). Five children had abnormal lipid index on their BAL stain. Of the seven children who had documented aspiration, only one had abnormal lipid index on their BAL.

Some patients had a chest CT scan based on clinical concern for recurrent pneumonia or bronchiectasis. Of 15 children who had a chest CT during the aerodigestive evaluation, 4 (27%) had visual evidence of bronchiectasis (Table 2). Of four children who had a chest CT before enrolling in the aerodigestive program, one had bronchiectasis, resulting in a diagnosis of bronchiectasis in 5/29 (17%) of the entire cohort. The five children with bronchiectasis were more likely to be older than the rest of the group: median age 5.5 years versus 2.7 years ($P = 0.02$). Due to the young age of our cohort, only four children successfully completed pulmonary function testing. None of the children had recurrent tracheoesophageal fistula.

Treatment Changes

19/29 (66%) of patients were on reflux medication, specifically a proton pump inhibitor (PPI) or histamine 2 (H2) blocker, at the time of their evaluation. After the evaluation, 14/29 (51.7%) were on a PPI or H2 blocker. This included 10 patients who had their reflux medication stopped and five patients who had reflux medication started as a result of the evaluation. Antireflux surgery was not recommended as part of the aerodigestive evaluation in this cohort. ENT procedures were recommended on an individual basis for the patients with subglottic stenosis and laryngeal clefts (Table 2).[11]

18/29 (69%) of patients were receiving pulmonary medical therapy, defined as inhaled or oral corticosteroids or other inhaled medications, at the time of their evaluation. After the evaluation, 5 of these had their medications stopped and eight patients had new medications started as a result of the evaluation. 7% of patients had Airway clearance techniques (manual chest physiotherapy, acapella, or vest) as part of their daily routine at

TABLE 2—High Incidence of Multisystem Findings/ Diagnoses

EGD, No. (%)	25 (86.2)
Normal endoscopy results	10 (40.0)
Anatomical defect	15 (60.0)
Stricture	8 (53.3)
Visual esophagitis	3 (20.0)
Dilated proximal esophagus	3 (20.0)
Anatomic ridge/shelf	1 (6.7)
Normal histological results	17 (68.0)
Esophagitis	8 (32.0)
GERD	6 (75.0)
Eosinophilic Esophagitis	2 (25.0)
Upper GI series, No. (%)	20 (69.0)
Expected post-surgical changes	7 (35.0)
Abnormal findings	13 (65.0)
Stricture	7 (35.0)
Dysmotility/dilation	8 (61.5)
pH Impedance study, No. (%)	9 (31.0)
GERD	4 (44.4)
Microlaryngoscopy bronchocopy, No. (%)	24 (82.7)
Laryngeal cleft	3 (12.5)
Subglottic stenosis	6 (25.0)
Chest CT Scan, No. (%)	15 (51.7)
Airspace/airway disease	5 (33.3)
Pneumonia	2 (13.3)
Bronchiectasis	4 (26.7)
Atelectasis	9 (60.0)
Flexible Bronchoscopy, No. (%)	23 (79.3)
Mild/moderate tracheomalacia	10 (43.5)
Severe tracheomalacia	13 (56.5)
Erythema,edema and/or secretions	16 (69.6)
BAL microbiology, No. (%)	22 (75.9)
Normal	3 (13.6)
Organism identified	19 (86.4)
Treated with antibiotics	13 (59.0)
BAL cell count, No. (%)[1]	23 (79.3)
Nucleated cells, mean (range)	868 (4–13080)
Abnormal segmented neutrophils	15 (65.2)
Abnormal lymphocytes	11 (47.8)
Abnormal lipid index	5 (21.7)
Video fluoroscopic swallow study, No. (%)	24 (82.7)
Aspiration, No. (%)	7 (29.2)

[1]Normal segmented neutrophils $< 5\%$; Normal lymphocytes $< 12\%$; Normal lipid index ≤ 10

the time of their evaluation. Following our evaluation, 55.2% of patients had airway clearance recommended as part of their daily routine.

DISCUSSION

In children with a repaired TEF referred to an aerodigestive program, not only are symptoms common, but also many multi-systemic diagnoses are present. We have found that tracheomalacia is universally present (100% of the children studied by bronchoscopy), and diagnoses requiring specific treatment recommendations including bronchiectasis, bacterial bronchitis, and aspiration were under-recognized. The incidence of these significant diagnoses has not been shown in previous cohorts.[1,4,5] Dysphagia, reflux, gastritis, and anatomic abnormalities of the esophagus and the airway were found in many of these symptomatic children (Table 2).

Data in the adult population with repaired TEF have shown that multi-system problems continue into adulthood in many patients.[1,4,12,13] To determine what symptoms and diagnoses are most important, longitudinal studies including studies on lifespan are needed. Jayasekera et al. has shown that the risk of esophageal carcinoma, presumably related to chronic gastritis and Barrett's esophagus, is increased by 50 fold in this population.[14] The incidence of chronic pulmonary symptoms and low lung function in adults is very high, exceeding 70%,[1,15,16] and one could postulate that the incidence of bronchiectasis might be higher in older patients with TEF. The impact of the medical management of children with TEF on these outcomes as adults is not clear, but we propose that better management of reflux, aspiration, feeding regimens, growth, work of breathing, and infection early in life can lead to better outcomes regarding cancer and lung function. The impact of the medical care of these children on developmental outcomes is not known, however this is an increasing topic of interest,[7] especially considering 52% of the population in our clinic had an associated syndrome.

The composition of our cohort has referral bias because it consists of children referred to our aerodigestive program and may reflect children with more severe symptoms related to repaired TEF. Because of the number of patients studied, we believe our cohort to be representative of a large subset of symptomatic children with repaired congenital TEF. In this cohort we saw widespread respiratory symptoms—72% had a chief complaint of cough. In the 23 flexible bronchoscopies performed, 100% had tracheomalacia, 65% had microscopic evidence of inflammation on BAL, and 59% had significant pathogenic organism requiring antibiotics, consistent with chronic bacterial bronchitis. This is much greater than the level of significant tracheomalacia previously described,[17] as well as the amount of bacterial infections described in this age group.[1,13] Lipid index, as previously reported,[18] had very low sensitivity and specificity for aspiration in this group. Although we did not study a control group, the incidence of tracheomalacia using the same flexible bronchoscopy and anesthesia techniques has not been seen in other populations in our clinic. We believe that cough is multifactorial in these patients (associated with reflux, aspiration, atopy and hyperreactivity, infection, and tracheomalacia) and the role of chronic protracted bronchitis may be under acknowledged.[19] Complaints of dysphagia were more common in children with severe tracheomalacia, emphasizing the interdependent relationship between GI and pulmonary symptoms in this population.

TABLE 3— Characteristics of Patients With Tracheomalacia

	Mild/moderate tracheomalacia	Severe tracheomalacia	*P* value
Total with flexible bronchoscopy	10	13	
Male Sex, No. (%)	6 (60.0)	7 (53.8)	0.76
Age at bronchoscopy, mean (range)	3.77 (0.71–14.01)	4.60 (0.17–17.20)	0.68
Syndromes/chromosomal, No. (%)			
Down syndrome	3 (30.0)	1 (7.7)	0.16
Craniofacial anomalies (cleft lip/palate, etc.)	0	2 (15.4)	0.19
VACTERL association	3 (30.0)	3 (23.1)	0.71
CHARGE syndrome	0	1 (7.7)	0.37
Presenting symptoms, No. (%)			
Cough	7 (70.0)	9 (69.2)	0.97
Dysphagia	3 (30.0)	10 (76.9)	0.02
Recurrent pneumonia	3 (30.0)	6 (46.2)	0.43
BAL microbiology results, No. (%)	10 (100)	12 (92.3)	
Normal	4 (40.0)	2 (16.7)	0.22
Organism identified	6 (60.0)	10 (83.3)	0.22
Treated with antibiotics	5 (83.3)	8 (80.0)	0.43
BAL cell count, No. (%)[1]	10 (100)	13 (100)	
Abnormal segmented neutrophils	6 (60.0)	9 (69.2)	0.64
Abnormal lymphocytes	6 (60.0)	5 (38.5)	0.30
Abnormal lipid index	3 (30.0)	2 (15.4)	0.40
Swallow study, No. (%)	9 (90.0)	10 (76.9)	
Aspiration	1 (11.1)	5 (50.0)	0.07
GERD, No. (%)	5 (50.0)	2 (15.4)	0.09

[1]Normal neutrophils $< 5\%$; Normal lymphocytes $< 12\%$; Normal lipid ≤ 10

Our data suggest that all children should be seen by pediatric subspecialties including pulmonary, otolaryngology, and GI because treatable abnormalities will be found. Longitudinal data is needed to better understand the most important outcomes (cancer, limited pulmonary function, decreased lifespan) and which interventions are most important in preventing them. The utility of the multidisciplinary Aerodigestive team in this population should be highlighted to limit the impact that multiple individual clinic visits can have on families.[20] Studies in this specific population have not yet been done to understand if the team approach limits health care costs while enhancing patient health and family satisfaction.

As stated, there are limitations to this study. In addition to referral bias, data were collected retrospectively and all the children in the cohort did not have all the studies. Only 18/29 of these children had ever had a chest CT scan. It is possible that we have underdiagnosed bronchiectasis in this group. Although many children had both esophageal biopsies and pH impedance studies to rule in or rule out reflux, many children were maintained on their current reflux management at time of evaluation without further diagnostics. This limits our ability to make inferences about the percentage of children with reflux in this study. The high percentage of syndromes in this population likely affected the providers' clinical decision making regarding GERD management.

The high incidence of tracheomalacia, bacterial bronchitis, and bronchiectasis in this cohort supports the need for aggressive pulmonary and airway evaluation. The significant risk of GERD, aspiration, and structural esophageal abnormalities supports the need for GI and feeding therapy evaluations. We propose that children with TEF should be seen by a multidisciplinary team between six months and one year of age to establish care and help in the critical developmental period with swallowing and feeding. The entire team should see the children at intervals to evaluate progress, but if the child is doing fairly well these intervals could be extended. It is appropriate for individual subspecialists to follow the child on an as needed basis in between large team evaluations. Our dataset is too small to make inferences regarding the effects of the Aerodigestive team interventions on long-term outcomes. Collaboration between other aerodigestive programs to maximize knowledge is needed to understand if this schedule is appropriate and to determine the factors and symptoms that put patients at highest risk. Ideally, future multicenter efforts could help establish care guidelines applicable to neonatologists, surgeons, general pediatricians, and specialists who manage these children from initial presentation and subsequently across the continuum.

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