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ORIGINAL ARTICLE: DIAGNOSTIC TESTING

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Evaluating the yield of gastrointestinal testing in pediatric patients in aerodigestive clinic

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Abstract

Objective: To improve understanding of the interrelatedness of airway and esophageal diagnoses by evaluating the yield of procedural and radiographic testing of the gastrointestinal tract in children with airway conditions by their referring diagnoses in a pediatric aerodigestive clinic.

Methods: A retrospective chart review of all 325 patients seen in the aerodigestive program from 2010 to 2013 was performed in a single academic medical center. Demographics and results from esophagogastroduodenoscopies with biopsies (EGD), upper gastrointestinal fluoroscopy studies (UGI), and pH multichannel intraluminal impedance probe (pH-MII) performed within 30 days of the clinic visit were evaluated according to presenting diagnoses.

Results: Mean patient age was 3.15 years (range 0.15-24 years) and 41.2% were born premature. 189/325 (58.1%) were on acid suppression. A total of 295 EGD, 193 pH-MII, and 54 UGI were performed. The most common diagnosis with an abnormal pH-MII was asthma. The most common diagnoses with an abnormal EGD were feeding difficulty and tracheal esophageal fistula/ esophageal atresia (TEF/EA). EGDs were normal in 188/295 (63.7%), while 39/295 (13.2%) demonstrated esophagitis, and 22/295 (7.5%) had >15 esophageal eosinophils per high power field. The majority of pH-MII (144/193 [74.6%]) and UGI (47/54 [87%]) were normal.

Conclusions: Children with feeding difficulty, TEF/EA, and asthma were the mostly likely to have a histologic abnormality on EGD or an abnormal pH-MII. The majority of children were previously prescribed acid suppression medication and had a referring diagnosis of gastroesophageal reflux disease but were subsequently found to have normal evaluation. Prospective studies are needed to optimize care of this population.

KEYWORDS
asthma, cough, gastroesophageal reflux, imaging, tracheoesophageal fistula

Emily M. DeBoer and Sarah Kinder share Co-first Authorship.

1 | INTRODUCTION

The care of children with complex airway and digestive disorders has been rapidly changing since the inception of the first multidisciplinary aerodigestive program in the late 1990s. Multidisciplinary pediatric aerodigestive programs are increasing to help provide diagnosis and management of medically complex children with combined gastrointestinal (GI) and airway disorders. Most programs include a pulmonologist, gastroenterologist, otolaryngologist, speech language pathologist, and a dietician.[1] Some programs may also include other service lines such as occupational therapy, general pediatrics, genetics, surgery, anesthesiology, and/or radiology.[1] Historically, these specialties have functioned separately "in siloes" versus integrated within a single clinic due to their expense necessitating extensive investment by the hospital.[2,3]

There has been limited research regarding the most effective algorithm of diagnostic testing in the aerodigestive clinic and its subsequent impact on clinical outcomes.[2–5] The global care models commonly coordinate radiographic studies such as upper gastrointestinal fluoroscopic studies (UGI) and video fluoroscopic swallowing study (VFSS) with consultation from the subspecialists. Most programs have a single procedural day aimed to consolidate diagnostic procedural studies such as flexible bronchoscopy, rigid laryngoscopy/bronchoscopy, esophagogastroduodenoscopy (EGD), and may also include pH multichannel intraluminal impedance probe (pH-MII) under a single anesthesia event.[6,7] The studies are done simultaneously to minimize the risks of multiple sedation events and costs of care.[6] To meet the general goal of aerodigestive programs, this model also attempts to improve the quality and efficiency of care in a single visit, by preventing the need for multiple hospital visits and further sedated tests. There have been few studies that assess the yield of performing diagnostic testing in this manner.[4,5,8–10]

Another purpose of the aerodigestive clinic is to help understand the multifactorial associations between the airway and reflux. For example, studies evaluating the effect of reflux disease and acid suppressive medication on asymptomatic poorly controlled asthma found little effect.[11,12] Because of the concern that reflux and various forms of esophagitis can cause significant airway symptoms, children with cough are often and appropriately referred to aerodigestive programs.[1,8] Based on this conflicting background data, we hypothesized that the GI procedural and radiographic aerodigestive clinic evaluation aimed at elucidating a possible etiology of a patient's feeding difficulties or airway symptoms would find minimal abnormalities. The objective of this study was to evaluate the yield of testing that evaluated GI anomalies and disease in the pediatric aerodigestive clinic. We explored associations between referring diagnoses, prescription for antacid medication, and test results.

2 | PATIENTS AND METHODS

A retrospective chart review of all 325 patients seen in the aerodigestive program at Children's Hospital Colorado from 2010 to 2013 was performed. Children are referred for evaluation in the multidisciplinary aerodigestive clinic for airway and upper gastrointestinal symptoms that are unexplained by their current diagnoses or inadequately controlled by their current plan. The aerodigestive program also manages children with diagnoses that are highly likely to cause airway and esophageal interactions including complicated dysphagia, tracheoesophageal fistula/esophageal atresia (TEF/EA), and airway stenoses. Indications for diagnostic work-up in this population includes unexplained cough, hypoxemia, dysphagia, regurgitation/vomiting, or other concerns of the airway and esophagus, Demographics were collected. The number of EGD, UGI, and pH-MII studies was collected. All studies were completed within the same institution and UGI data was collected only if done within 30 days of the other studies to ensure temporal correlation related to the aerodigestive clinic visit.

EGDs were read as abnormal, independent of need for clinical therapy, if there was any finding of mucosal abnormality on histologic analysis as read by a board-certified pediatric pathologist. pH-MII were read per standard protocol at the center noting the number of events in a 24-h period and symptom correlation to acid or non-acid events. Age appropriate reflux index for abnormal acid exposure in the esophagus, reflux events >50 events in a 24-h period for children >1 year of age and >100 events per 24-h period in children <1 year, or >50% symptom correlation to any reflux event (acid or non-acid) was read as an abnormal pH-MII.[9,13] An UGI was read as abnormal based on a pediatric radiologist review and report of any anatomic abnormalities (excluding reflux reported by radiology). The radiologists mention of reflux on the study was recorded.

A notation of demographics and associated aerodigestive conditions, medications, and timing of procedures relative to each other was also recorded. All data was recorded in a RedCap Database. Proportion of abnormal studies is presented, and sensitivity, specificity, positive predictive value, and negative predictive value were calculated. The odds ratio and 95% confidence interval was calculated to determine the odds of having an abnormal study result in children prescribed antacid medication. This study was approved by the Colorado Multiple Institutional Review Board (COMIRB #13-1956).

3 | RESULTS

A total of 325 charts were reviewed from clinic visits from 2010 to 2013. This represented the entirety of patient visits in the aerodigestive program during the period. The average age of the cohort was 3.15 years (range 0.15-24.8 years). 64.3% were Caucasian, 22.7% Hispanic, 4.6% African American, 4% Mixed Ethnicity, 1.5% not reported,1.2% American Indian/Alaskan Native, 0.9% Asian, 0.3% Pacific Islander, and 0.5% other. 41.2% (134) were reported as premature in their chart per standard medical definition. The average age at the time of the visit for the children born premature was 3.4 years of age. At the time of the aerodigestive visit, 189/325 (58.1%) were on acid suppressive medication with either proton pump inhibitor (PPI) or histamine two receptor antagonist (H2). Pulmonary, GI, and

TABLE 1 Aerodigestive clinic most common presenting diagnoses (n = 325)

Gastroenterology	Otolaryngology	Pulmonary
GERD = 266	Noisy breathing = 113	Cough = 184
Feeding difficulty-174	Stridor = 55	Aspiration = 112
Failure to thrive = 77	Oxygen need = 55	Asthma = 54
Eosinophilic esophagitis = 8	Subglottic stenosis = 45	Recurrent pneumonia = 48
	Tracheostomy = 21	Suspected aspiration = 47
	Laryngomalacia = 19	Airway disease = 16
		Bronchopulmonary dysplasia = 15

ENT diagnoses at patient's presentation to aerodigestive clinic (not exclusive) are in Table 1. Two-hundred ninety-five EGD, 188 pH-MII, and 54 UGI were performed within 30 days of the initial aerodigestive clinic visit.

Of the 295 EGD, 188 (63.7%) were histologically normal and 107 (36.3%) were abnormal, regardless of need for therapy (Figure 1). Out of 295, 39 (13.2%) biopsies demonstrated reflux esophagitis (<15 eosinophils per high power field or other changes diagnostic of reflux esophagitis), 27/295 (9.2%) biopsies demonstrated gastritis, 22/295 (7.5%) biopsies demonstrated >15 esophageal eosinophils per high power field (future diagnosed Eosinophilic Esophagitis or PPI Responsive Eosinophilia), 20/295 (6.8%) reactive changes of the esophagus (not diagnostic of esophagitis) and 19/295 (6.4%) demonstrated duodenitis. The odds of having an abnormal EGD are not statistically different between those on or off antacid (Odds ratio = 0.66 (95% confidence interval 0.41-1.06). (Tables 2 and 3). Of 134 EGDs in premature children, 37 (27.6%) were abnormal.

When divided by referring diagnosis (not exclusive), the number of histologically abnormal EGD (# abnormal/total # condition in EGD cohort, Figure 2) were as follows: feeding difficulty 54/106 (50.9%), TEF/EA 8/16 (50%), recurrent pneumonia 19/45 (42.2%), stridor 19/49 (38.7%), cough 65/170 (38.2%), laryngomalacia 6/17 (35.2%), aspiration 35/100 (35%), asthma 17/49 (34.7%), previously labeled as gastroesophageal reflux disease (GERD) 82/242 (33.8%), laryngeal cleft 6/18 (33.3%), hypoxemia 13/43 (30.2%), subglottic stenosis 11/38 (28.9%), failure to thrive 18/70 (25.7%), and bronchopulmonary dysplasia 3/13 (23.1%).

Of the subset of children who were previously labeled as GERD and underwent EGD, 63/82 had an esophageal abnormality not attributable to infection. OF those 63, 42 (67%) were on acid suppression at time of endoscopy. Of these 32 children had esophagitis, 16 children had >15 eosinophils per high power field on biopsy, and 15 children had other changes of the esophagus not diagnostic of esophagitis.

Of the 193 pH-MII completed in the cohort, 144 (74.6%) were normal and 49 (25.4%) were abnormal. 80/193 pH-MII were done on premature infants. Of the 80 completed on premature infants, 63 (78.5%) were normal. 105 children at the time pH-MII were on PPI or H2. 26/49 (53%) subjects who had an abnormal pH-MII were on PPI or H2 at time of study. The odds of having an abnormal pH-MII are not statistically different between those on or off antacid (Odds ratio = 0.93 (95% confidence interval 0.49-1.78) (Tables 2 and 3).

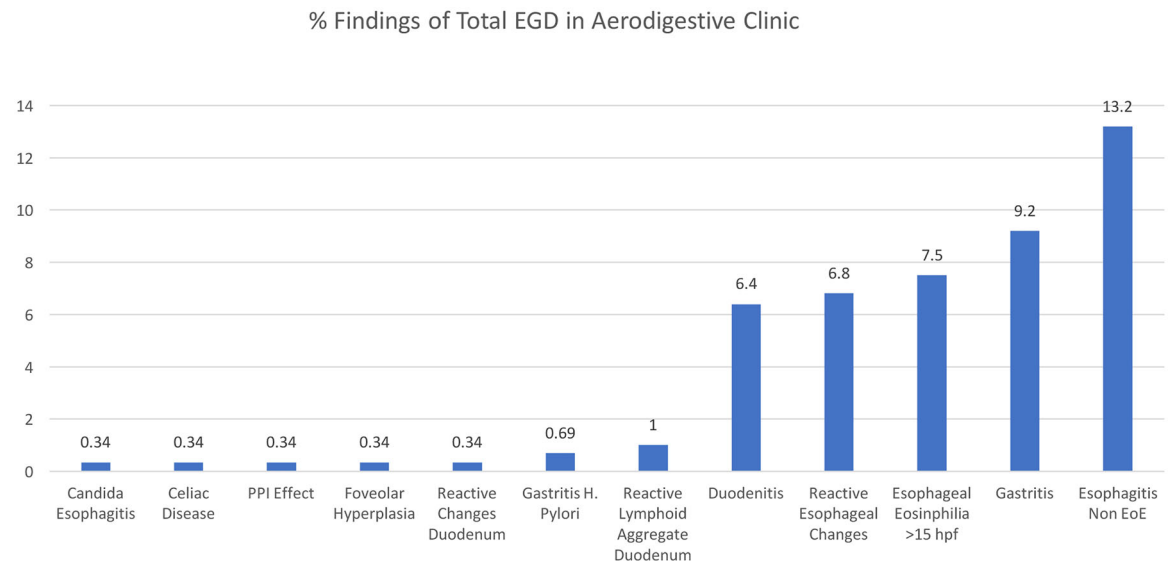

FIGURE 1 EGD biopsy results from aerodigestive clinic

TABLE 2 No difference in testing results in children on or off antacid medication

	Abnormal EGD	Normal EGD	
On antacid	55	116	171
No antacid	52	72	124
	107	188	295

Of the subjects that were on acid suppression therapy, 55/171(32.1%) had an abnormal EGD. The odds of having an abnormal EGD are not statistically different between those on or off antacid (Odds ratio = 0.66 (95% confidence interval 0.41-1.06).

TABLE 3 No difference in testing results in children on or off antacid medication

	Abnormal pH-MII	Normal pH-MII	
On antacid	26	79	105
No antacid	23	65	88
	49	144	193

Of the subjects that were on acid suppression therapy, 26/105 (24.8%) had an abnormal pH-MII. The odds of having an abnormal pH-MII are not statistically different between those on or off antacid (Odds ratio = 0.93 (95% confidence interval 0.49-1.78).

When divided by a specific referred diagnosis (not exclusive), the number of abnormal pH-MII (# abnormal/total # condition in pH-MII cohort, Figure 2) were as follows: asthma 18/45 (40%), TEF/EA 2/5 (40%), laryngeal cleft 5/15 (33.3%), hypoxemia 15/48 (31.3%), cough 32/112 (28.5%), previously labeled as GERD 40/159 (25.2%), stridor 8/34 (23.5%), laryngomalacia 3/13 (23.1 %), feeding difficulty 25/109 (22.9%-7 with aspiration, 4 suspected aspiration, 3 subglottic stenosis, 2 laryngomalacia, 1 TEF/EA), recurrent pneumonia 8/35 (22.8%), failure to thrive 9/46 (19.5%), aspiration 13/78 (16.6%), subglottic stenosis 5/38 (13.1%), bronchopulmonary dysplasia 0/10 (0%).

Regarding consistency between pH-MII and EGD (Table 4), 108 subjects with pH-MII and EGD performed had no abnormalities on esophageal biopsy. Of these, 87/108 (80.5%) had a normal pH-MII and 21/108 (19.4%) had an abnormal pH-MII consistent with GERD, although 13/21 (61.9%) were taking an H2 or PPI.

Of the 54 UGI done within 30 days of the initial aerodigestive visit, 47 (87%) were anatomically normal. Many other UGI were done on subjects for anatomic evaluation but were not within 30 days of the clinic visit and specifically for the clinic. Findings on UGI included: two aberrant subclavian arteries, one esophageal spasm vs cricopharyngeus discoordination, one hiatal hernia, one narrowed esophagus at an anastomosis site, one duodenal diverticulum, and one patulous esophagus. UGI was found to have poor sensitivity (47.3%) in predicting actual GERD based on the test of either abnormal EGDs or abnormal pH-MII and had a specificity of 74.2%. Positive predictive value for GERD of the UGI was 50% and negative predictive value was 72.2%.

4 | DISCUSSION

Aerodigestive programs have been proliferating since their advent in the late 1990s with a goal of improving quality and efficiency of aerodigestive care.[2,3,8–10] The extensive testing proposed by

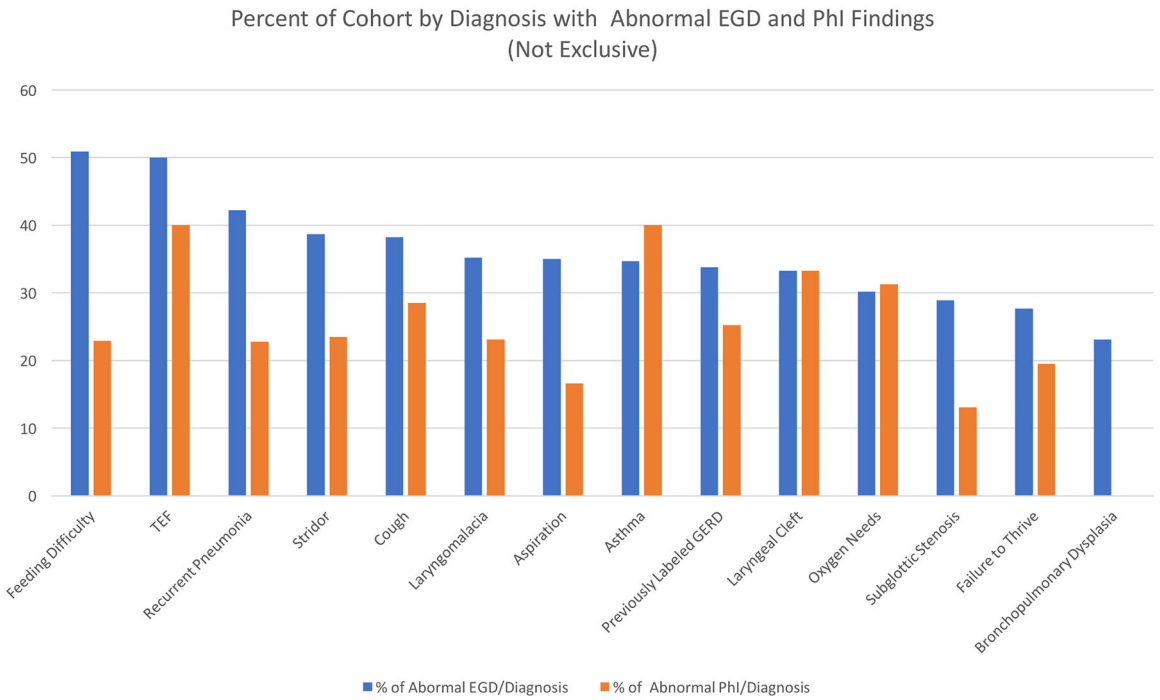

FIGURE 2 Percent of cohort by diagnosis with abnormal EGD and Ph-MII findings (not exclusive)

TABLE 4 2 × 2 Table of ph-MII results versus esophageal biopsy results

	Abnormal pH-MII	Normal pH-MII	
Abnormal esophageal biopsy	7	33	40
Normal esophageal biopsy	21	87	108
	28	120	148

aerodigestive programs is aimed at assessing the possible correlation of esophageal and GI diagnoses on airway symptoms.[1,14] This study evaluated the yield, regardless of needing eventual therapy, of radiographic and procedural GI testing in children referred to an aerodigestive clinic.

Consistent with our hypothesis, three usual GI tests used in aerodigestive medicine (EGD, pH-MII, and UGI) were positive in less than 50% of children. The general EGD yield found histological abnormalities similar to airway populations reported by Thakkar et al,[15,16] Sheiko et al,[17] and Rosen et al[4] in which approximately one in three or greater were abnormal. The highest percent finding of any abnormality on EGD, 40-50%, were found in children with previously diagnosed feeding difficulty, TEF/EA, or recurrent pneumonia.

The diagnosis of any histological esophageal abnormality on EGD in the aerodigestive cohort, though not all needed therapy, was still low at 27.5%, though this may have been skewed by the significant use of PPI at time of EGD. pH-MII probe noted pathologic reflux disease or acid exposure in 25.4% which is similar or higher than the 8.8-25.9% reported in North America, but lower than previously published data of a similar cohort.[4,18] pH-MII results are important to allow for possible medical changes in the aerodigestive population. Data regarding prevalence in specific populations in pediatrics is sparse.[19] In our cohort the pH-MII's highest yield was in TEF/EA and asthma populations (40%), which is higher than the general population. Follow-up evaluation is needed to understand the population of children with a referring diagnosis of asthma, and the effect of antacid changes on health outcomes.

The goal of collecting and reporting diagnostic test results is to develop ways to decrease cost of care and improve quality. Each GI test evaluates the alimentary tract anatomy or presence of excessive esophageal reflux or acid exposure to understand its potential risk on the airway or feeding issues. The number of subjects with abnormal findings, though higher than normal, was low. The number of children on PPI or H2 blocker at the time of referral was very high, especially considering only 25% of subjects with a diagnosis of GERD had a positive pH-MII. This is a test that should find reflux presence regardless of acid suppressive therapy. As more risks of acid suppression with PPI are published, our understanding of the incidence and effect of GERD on the airway is important. This is further complicated by the proliferating data demonstrating the hazards and limited role of proton pump inhibitor (PPI) and anti-reflux surgery in managing airway anomalies (not including lung transplant).[12,20–25] Although diagnostic testing is not needed in all subjects to diagnose GERD or to mandate therapy trials, the low yield of positive findings in this study suggests that an improved protocol describing how and when to prescribe acid suppressive medication in airway conditions is needed.

The definition of GERD is based on a clinical diagnosis and often confirmed based on a pH-MII demonstrating 50-100 episodes of reflux in 24 h, symptom correlation, or evidence of esophagitis on EGD.[26] Even with such definitions many providers are still concerned when reflux is seen on an UGI study; however, a reflux event or multiple events are normal findings in children and adults on such studies. This study again demonstrated that an UGI is a poor study for GERD when correlating with an EGD or pH-MII to confirm abnormal acid exposure, esophagitis, or reflux presence in the esophagus. The evaluation for sensitivity/specificity regarding GERD out of interest in our dataset because the UGI continues to be misused as a diagnostic test for GERD and "reflux."[27,28] Further although the non-reflux associated diagnostic yield of UGI was low, in our population which includes patients with several genetic abnormalities, airway anomalies, and TEF/EA, the UGI remained useful to diagnose anatomic problems or concerns in 1/10 children. These results are helpful in planning interventions prior to anesthesia events in this cohort.

This study was limited by its retrospective nature and single center. Additionally, approximately 60% of our subjects were on a form of acid suppression at the time of their evaluations. This would potentially change the number of patients with abnormal EGD

TABLE 5 Testing paradigm in aerodigestive clinic

	Pre-clinic testing	Procedures with anesthesia	Result based follow-up testing
Original aerodigestive clinic testing paradigm	1. Chest X-Ray 2. UGI series if not done recently 3. Videofluoroscopic swallow study (VFSS) or fiberoptic endoscopic evaluation of swallowing (FEES)	1. Triple scope and probe (flexible bronchoscopy with lavage, MLB, EGD) and pH-MII Placement) 2. Consider chest CT	1. Consider manometry 2. Repeat testing as needed
Proposed aerodigestive modification	1. Chest X-ray 2. UGI series if not done recently 3. Videofluoroscopic swallow study (VFSS) or fiberoptic endoscopic evaluation of swallowing (FEES)	1. Triple scope (Flexible bronchoscopy with lavage, MLB, EGD) 2. Consider chest CT 3. Consider PH-MII if not local, unable to return to clinic, or to answer specific clinical question	1. Consider pH-MII to document adequate acid suppression therapy, ongoing clinical symptoms not treated 2. Consider manometry 3. Repeat testing as needed

mucosal abnormalities or with abnormal acid exposure in the esophagus. These are two but not the only criteria for GERD. With pH-MII probes, the number of reflux events would remain constant, and this may explain the elevated findings compared to some components of the North American general population.[18] To truly understand this question, we would need to wean acid suppression prior to the time of pH-MII in aerodigestive clinics prior to study.[12,29,30] Another limitation of our study may include our center's interpretation of pH-MII studies. Several centers vary their positive criteria for reflux regarding number of events and symptom correlation due to a lack of standardized metrics in pediatrics.[4,31] This study demonstrated that pH-MII-defined GERD diagnosis was higher, perhaps up to 2× the prevalence of the general population, but still overall relatively low regarding diagnostic yield. If other published standards, such as 72 events were used, in this study for children >1 year of age, the diagnosis of GERD or excessive esophageal acid exposure using pH-MII may have been lower.[31] Finally, this study primarily looked at the reflux evaluation and not the other components of aerodigestive care. Our center also does not routinely perform esophageal motility studies, but altered esophageal or pharyngeal motility is found in other disorders such as TEF/EA and cricopharyngeal achalasia in the aerodigestive population.[32] Therapies for such esophageal abnormalities, however, are sparse.[33,34]

Despite these limitations, the GI aerodigestive evaluation objectively defined gastrointestinal tract anomalies, evaluated symptom correlation, and found histologic abnormalities. In this cohort, GI providers were often able to wean children off of their acid suppressing medications. This was due to the fact that 60.7% of the patients who underwent EGD and that 74.6% of the subjects who underwent pH-MII had clinically suspected reflux but normal studies. The studies allowed weaning of medication in this population, however, future long term prospective study of this practice on airway condition is needed. We propose that providers think critically before empirically trialing H2 or PPI and make a clear plan to stop the medication if clinical improvement is not seen. Collaboration with aerodigestive clinics and GI providers can improve our use of H2 and PPI in this high-risk population.

Based upon this study's findings of lower radiographic and procedural yield, the authors propose a modification of the gastrointestinal testing algorithm in aerodigestive programs to maintain quality, decrease cost, and have testing that would provide improved clinical management in aerodigestive clinics. We propose that due to the need for anesthesia to complete pulmonary and ENT airway evaluations, EGD should continue to be considered. This is due to the importance of biopsy results and the potential risk of a second anesthesia at a later date, however, the benefit of weaning off PPI if GI studies are negative is also of benefit to the patient.[35,36] PPI have not been shown to be consistently effective for anything other than GI tract inflammation.[12,29,30,37]

With limited radiographic risk and a relative low cost, the data also supports continued use of the UGI to evaluate for suspected anatomic abnormalities in this specific high-risk aerodigestive population. We propose re-evaluating routine aerodigestive use of pH-MII due to its lower yield rate and additional cost (Table 5). We consider usage only in certain populations, but further study is needed. At the authors' center a pH-MII study, a test that does not require anesthesia when performed alone, is no longer routinely ordered until the results of aerodigestive triple-scope are complete or if there is a high suspicion of a symptom correlation from GERD by the aerodigestive team. Of note, this practice is only applicable if the patient and family can easily return in the future. If the triple scope procedure produces answers to the aerodigestive consultation, then skipping the pH-MII prevented a redundant test. If the triple scope does not provide answers for the diagnostic dilemma, then the pH-MII can be done later. The role of gastrointestinal motility evaluations should also be considered. Prospective study is needed to evaluate the safest and most effective diagnostic evaluation.

5 | CONCLUSION

Based upon our retrospective, single-center study, the GI testing in the aerodigestive clinic was more likely to find EGD histological abnormalities in populations with feeding difficulty, TEF/EA, or recurrent pneumonia and an abnormal pH-MII in children with a diagnosis of asthma or TEF/EA. The majority of pediatric patients referred to an aerodigestive clinic with a previous diagnosis of GERD were found to have a normal evaluation but were also on acid suppressive medication. This study suggests that antacid medications can be weaned. We propose that antacid medications should be used judiciously prior to aerodigestive evaluation and at our institution EGD is prioritized over ph-MII when appropriate. Prospective studies evaluating this question are needed. We continue to work toward the goal of the clinic to provide high quality multi-disciplinary care that complies with the healthcare's triple-aim and decrease costs of healthcare for medically complex children with aerodigestive needs.[38]

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CONFLICTS OF INTEREST

No financial relationships relevant to the article of interest are present. The authors disclose the following potential conflict of interest: Joel Friedlander, Robin Deterding, Jeremy Prager, and Emily DeBoer are co-founders of Triple Endoscopy, Inc. and are listed inventors on University of Colorado patent pending related to endoscopic methods and technologies. Emily DeBoer and Robin Deterding are consultants for Boeringer Ingelheim, not related to this project. Todd Wine's children hold stock in Pfizer. Dr. Deterding is co-founder of Now Vitals, Inc. and creator of two patents: 1) Computing systems for determing vital information and 2) Personalized health care wearable sensor systems.

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