Upper Airway Pathology Contributes to Respiratory Symptoms in Children Born Very Preterm

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Objective To evaluate the role of upper airway dysfunction, indicated by altered vocal quality (dysphonia), on the respiratory symptoms of children surviving very preterm birth.

Study design Children born <32 weeks of gestation participated in 2 separate assessments during midchildhood. The first visit assessed voice quality by a subjective evaluation using the Consensus Auditory-Perceptual Evaluation of Voice and a computerized analysis of the properties of the voice via the Acoustic Voice Quality Index. The second assessment recorded parentally reported respiratory symptoms and measures of lung function, including spirometry, lung volumes, oscillatory mechanics, and a cardiopulmonary exercise test.

Results Preterm children (n = 35; median gestation 24.3 weeks) underwent paired voice and lung assessments at approximately 11 years of age. Preterm children with dysphonia (n = 25) reported significantly more respiratory symptoms than those with normal voices (n = 10) including wheeze (92% vs 40%; $P = .001$) and asthma diagnosed by a physician (60% vs 10%; $P = .007$). Lung function outcomes were generally not different between the dysphonic group and the group with normal voice ($P > .05$), except for the oscillatory mechanics measures, which were all at least 0.5 z score lower in the dysphonic group (Xrs_8 mean difference = −0.91 z scores, $P = .003$; f_{res} = 1.06 z scores, $P = .019$; AX = −0.87 z scores, $P = .010$; Rrs_8 = 0.63 z scores, $P = .068$).

Conclusions The upper airway may play a role in the respiratory symptoms experienced by some very preterm children and should be considered by clinicians, especially when symptoms are in the presence of normal lung function and are refractory to treatment. *(J Pediatr 2019;213:46-51)*.

Lung disease is the most prevalent cause of early life morbidity for survivors of preterm birth.[1] Although alveolarization continues through childhood, lung disease persists. Reduced[2,3] and declining[4] lung function are reported in preterm survivors and approximately 50% of children born before 32 weeks of gestation have recurrent respiratory symptoms such as wheeze.[2,5,6] Commonly, such children are diagnosed with asthma, often based solely on parentally reported symptoms. However, structural and functional upper airway pathologies such as paradoxical adduction of the vocal cords during inspiration (vocal cord/laryngeal dysfunction), exercise induced laryngomalacia, arytenoid prolapse, and vocal cord immobility, can also result in a high-pitched inspiratory stridor commonly described as "wheeze."[7] Children presenting with upper airway dysfunction often present with dysphonia ("hoarseness"), either as a result of the abnormality itself or of compensatory use of the laryngeal musculature, which may also contribute to airway narrowing.[8] Such upper airway dysfunction can contribute to respiratory symptoms that appear "refractory" to asthma treatment.

Upper airway damage may be a candidate for ongoing respiratory symptoms in preterm survivors with normal lung function. Intubation injury, prolonged endotracheal intubation, obstructive apneas, and reduced upper airway muscle tone requiring noninvasive ventilation (continuous positive airway pressure)[9] and even vocal cord paralysis during surgical ligation of a patent ductus arteriosus[10] are common events in the neonatal intensive care unit, resulting in upper airway damage.[11] Indeed, significant pathology of the larynx[8] and a high incidence of dysphonia (>60% of children)[12] has been described. It remains unknown if the commonly reported asthma-like symptoms are associated with upper airway abnormalities in preterm children. The aim of this study was to explore the relationship between dysphonia, respiratory symptoms, and lung function in very preterm children. We hypothesized that dysfunction of the upper airway manifesting as disturbance to vocal quality would be associated with increased respiratory symptoms.

Methods

The data reported in this study are not exclusive. Individual participants are a subset of preterm born children who had participated in 2 previously published larger cohort studies recruited from the same neonatal care centre: a respiratory

AVQI	Acoustic Voice Quality Index
CAPE-V	Consensus Auditory-Perceptual Evaluation of Voice

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assessment ("the lung study") and a voice assessment ("the voice study").[2,13] A concise summary of participant details, assessment methodologies, and the approach to the analysis of the data used in this study are defined below.

Participants

Preterm children, born less than 32 weeks of gestation, were recruited from the King Edward Memorial Hospital neonatal discharge database in Perth, Western Australia during childhood.[2,13] Bronchopulmonary dysplasia was defined according to the 2001 National Heart, Lung and Blood Institute workshop report as the requirement for at least 28 days supplemental oxygen, with severity assessed at 36 weeks of gestational age.[14] Approval for each study was obtained from the Princess Margaret Hospital Human Research Ethics Committee. The data sets of both studies were cross-matched, and 35 participants were identified as participants in both studies.

Assessment of Voice

Clinical voice assessments were conducted by a speech pathology doctoral candidate with clinical and research experience in the treatment of pediatric voice disorders.[13] Clinical voice assessments consisted of a subjective judgement of the qualities of the vocal signal, using the Consensus Auditory-Perceptual Evaluation of Voice (CAPE-V)[15]; and a computerized analysis of the acoustic properties of the sound produced by the larynx and resonated through the vocal tract, the Acoustic Voice Quality Index (AVQI).[16]

A visual analogue scale is used to rate dysphonia severity on the CAPE-V.[8,15] The overall dysphonia severity categorization was, therefore, assigned to each participant based on their CAPE-V score. The AVQI score is used for discriminating normal from dysphonic voices. The threshold for pathology in English-speaking children is 3.46, with a higher value representing a more severe deviation in the vocal signal.[17] The AVQI score was used to confirm the presence of dysphonia for each participant.

Assessment of Lung Function and Symptomatology

Assessment of lung function consisted of forced expiratory flows and volumes by spirometry, assessment of inspiratory flow volume loops, lung volumes by multiple breath nitrogen washout, and respiratory system mechanics via the forced oscillation technique (I2M, Chess Medical, Ghent, Belgium). All lung function testing was carried out in accordance with the American Thoracic Society/European Respiratory Society standards[18-21] and as previously described.[2] All lung function data influenced by anthropometrics were expressed as z scores. An incremental exercise test was conducted on a treadmill in line with a modified Balke protocol[22] and flow limitation during exercise was assessed as described by O'Dea et al.[23]

Respiratory symptom data was obtained by caregiver-proxy via a modified International Study of Asthma and Allergies in Childhood questionnaire[24] and a 3-month respiratory symptoms questionnaire.[25] Neonatal data, including duration of invasive mechanical ventilation, frequency of intubation, number of surfactant doses, antenatal steroid exposure, days of supplemental oxygen, and continuous positive airway pressure, was abstracted form medical records and the neonatal discharge database at King Edward Memorial Hospital.

Statistical Analyses

All statistical analyses were carried out using SPSS v 22 (SPSS Inc, Chicago, Illinois). Results are presented as mean and SD or as median and IQR depending on data distribution. A P value of $<.05$ was considered statistically significant. Depending on data distribution, independent t tests, Mann-Whitney U tests, or χ^2 tests were used to assess the differences between the normal voice and dysphonic groups. A nonparametric correlation was used to assess the relationship between dysphonia severity (using both the subjective CAPE-V score and objective AVQI score as outcome measures) and all lung outcomes and neonatal factors. Multicollinearities between neonatal predictors were accounted for by using residuals of independent regressions of the collinear variables as previously described by our group.[4]

Results

Study Participants

Thirty-five very preterm children with median (range) gestation of 24.3 (22.0-31.0) weeks were included in this study. When categorized according to voice quality, 10 participants were normophonic. Of the remaining 25 children, 11 presented with mild and 14 with moderate to severe dysphonia. Demographic and neonatal information are summarized in **Table I**. Age, height, and weight were equivalent, across the groups, at initial voice and lung assessment.

Dysphonia and Neonatal Variables

Children with dysphonia were born at a significantly lower gestational age compared with those children with normal voices ($P = .001$). Consequently, children with dysphonia were also smaller at birth than those without dysphonia but were more appropriate for gestational age (birthweight z score increased in the dysphonic group; $P = .022$). As a result of lower gestational age, children with dysphonia also required more intubations, increased days of mechanical ventilation, and oxygen supplementation in the neonatal period, compared with those children with normal voices (**Table I**; $P < .05$).

Consistent with our previously published data on the full voice cohort,[12] increasing dysphonia severity (assessed by CAPE-V and AVQI score) was predicted by lower gestational age ($r = 0.681$; $P < .001$ and $r = 0.483$; $P = .004$, respectively), increased days of mechanical ventilation ($r = 0.464$; $P = .011$, and $r = 0.451$; $P = .017$, respectively), and increased number of intubations (CAPE-V $r = 0.396$; $P = .033$). These data also demonstrated a positive association between dysphonia severity and increased days of supplemental oxygen after accounting for gestational age and days of mechanical ventilation (AVQI $r = 0.423$; $P = .013$).

Table I. Neonatal and visit demographics for the very preterm participants

Characteristics	No dysphonia	Any dysphonia	Mild dysphonia	Moderate/severe dysphonia
Number of participants	10	25	11	14
Sex, n (%) male	6/10 (60.0%)	11/25 (44.0%); $P = .392$	8/11 (72.7%)	3 (21.4%)
Neonatal demographics				
BPD diagnosis, n (%)	4/10 (40%)	23/25 (92%); $P = .001$*	9/11 (81.8%)	14/14 (100%)
Gestational age (wk)	27.0 (25.5-30.3)	24.0 (24.0-24.4); $P = .001$*	24.2 (24.0-26.3)	24.0 (23.0-24.3)
Birthweight (g)	908 (760-1010)	665 (585-750); $P = .004$*	690 (585-1120)	648 (565-730)
Birthweight z score, mean (SD)	−0.66 (0.63)	−0.06 (0.79); $P = .022$*	−0.13 (0.92)	0.00 (0.70)
Number of NICU intubations	2.0 (1.0-3.0)	4.0 (3.0-7.0); $P = .017$*	4.0 (2.0-5.0)	5.0 (4.0-7.0)
Duration of mechanical ventilation (d)	4.3 (3.1-6.9)	35.0 (25.0-60.5); $P = .007$*	25.0 (3.8-42.8)	36.0 (28.3-67.0)
Duration of CPAP (d)	5.21 (1.3-24.7)	19.5 (6.0-24.8); $P = .460$	19.5 (3.5-24.8)	18.4 (6.0-26.0)
Duration of oxygen (d)	24.0 (5.0-60.0)	104 (96-142); $P = .003$*	98.0 (45.0-130.0)	107.0 (103.0-172.0)
Antenatal steroids administered, n (%)	10 (100%)	17/25 (68.0%); $P = .074$	8 (72.7%)	9 (64.3%)
PDA, n (%)	3/10 (30%)	15/25 (60%); $P = .109$	5 (45.5%)	10 (71.4%)
Surgical ligation	0/10 (0%)	3/25 (12 %)	0 (0%)	3 (21.4%)
Lung test demographics				
Age (y)	10.5 (0.5)	10.7 (0.5); $P = .355$	10.6 (0.5)	10.7 (0.6)
Height (cm)	138.1 (6.6)	140.5 (7.8); $P = .363$	141.1 (7.1)	140.1 (8.5)
Weight (kg)	31.0 (5.0)	33.0 (8.0); $P = .389$	33.2 (5.4)	32.8 (9.7)
Voice test demographics				
Age (y)	11.0 (1.0)	10.8 (1.8); $P = .696$	10.6 (1.4)	10.9 (2.1)
Time between lung and voice visits (y)	0.49 (1.1)	0.11 (1.7); $P = .460$	0.04 (1.45)	0.17 (1.95)

BPD, bronchopulmonary dysplasia; *CPAP*, continuous positive airway pressure; *NICU*, neonatal intensive care unit; *PDA*, patent ductus arteriosus.
Neonatal demographics of participants expressed as median (IQR), unless stated. Participant demographics at date of lung and voice testing expressed as means (SD).
Differences in demographics information between children with and without dysphonia were assessed using an independent t test, Mann-Whitney U test, or χ^2 test as appropriate. BPD defined as the requirement for at least 28 days supplemental oxygen prior to 36 weeks of gestational age.
*Represents significant difference between the normal voice participants and those with dysphonia ($P < .05$).

Dysphonia and Respiratory Symptoms

Children with dysphonia had a history of significantly more respiratory symptoms than children with normal voices including previous wheeze (92% vs 40%), asthma diagnosis (60% vs 10%), and prior prescription of asthma medication (72% vs 30%) such as bronchodilator, inhaled corticosteroid, and/or nonsteroidal anti-inflammatories (Table II).

A positive correlation was established between CAPE-V severity score and several asthma-like symptoms including past wheeze (r = 0.381; $P = .042$), exercise symptoms in the last 3 months (r = 0.386; $P = .042$), and use of asthma medication in the last 3 months (r = 0.477; $P = .014$). The only significant respiratory symptom correlated with increased AVQI score was use of asthma medication in the last 3 months (r = 0.414; $P = .021$).

Dysphonia and Lung Function

Forced Flows and Volumes by Spirometry. There were no significant differences in forced expiratory flows and volumes (spirometry) between children with dysphonia and those with a normal voice (Table III). Similarly, the proportion of children with abnormal inspiratory loops or dynamic flow limitation on exercise was not different between the 2 groups. No significant correlation was demonstrated between dysphonia severity as per CAPE-V and AVQI scores, and any of the spirometric factors ($P > .05$).

Gas Trapping from Multiple Breath Washout (Lung Volumes). Gas trapping or hyperinflation, as indicated by the ratios of residual volume to total lung capacity and functional residual capacity to total lung capacity, were not significantly different between children with and without dysphonia, nor significantly correlated with AVQI or CAPE-V score ($P > .05$).

Respiratory System Mechanics (Forced Oscillation Technique). All forced oscillation outcomes were at least 0.5 z scores more abnormal in the dysphonic group than the group with normal voice (Table III); where 0.5 z scores is deemed a clinically relevant threshold. Increased CAPE-V severity

Table II. Respiratory symptoms and dysphonia severity in very preterm children

	No dysphonia	Any dysphonia	Mild dysphonia	Moderate/severe dysphonia
Respiratory symptoms				
Wheeze ever	4/10 (40%)	22/24 (91.7%); $P = .001$*	10/11 (90.9%)	12/13 (92.3%)
Asthma diagnosis ever	1/10 (10%)	15/25 (60.0%); $P = .007$*	6/11 (54.5%)	9/14 (64.3%)
Asthma medication ever	3/10 (30%)	18/25 (72.0%); $P = .041$*	8/11 (72.7%)	10/14 (71.4%)
Respiratory symptoms at rest past 3 mo	1/10 (10%)	3/24 (12.5%); $P = .837$	1/11 (9.1%)	2/13 (15.4%)
Respiratory symptoms on exertion past 3 mo	2/10 (20%)	12/24 (50.0%); $P = .105$	5/11 (45.5%)	7/13 (53.8%)
Asthma medication usage past 3 mo	0/10 (0%)	8/25 (32.0%); $P = .052$	2/11 (18.2%)	6/14 (42.9 %)
Inhaled corticosteroid in past 3 mo	0/10 (0%)	5/25 (20.0%); $P = .146$	2/11 (18.2%)	3/14 (21.4 %)

Respiratory symptoms expressed as N (% responding yes to questionnaire).
The difference in proportion of children with respiratory symptoms was assessed in children with and without dysphonia via χ^2 analysis. Asthma medication includes bronchodilators, inhaled corticosteroid, and/or inhaled nonsteroidal anti-inflammatory therapy. Respiratory symptoms at rest or on exertion are defined as parentally reported wheeze, excessive cough, and/or shortness of breath.
*Represents significant differences between participants with normal voices and those with dysphonia ($P < .05$).

Table III. Lung function outcomes and dysphonia severity in very preterm children

	No dysphonia	Any dysphonia	Mild dysphonia	Moderate/severe dysphonia
Forced flows and volumes (spirometry)				
N successful/total	10/10	24/25	11/11	13/14
FEV_1 z score	−0.81 (0.58)	−0.96 (1.07); $P = .580$	−1.08 (1.08)	−0.87 (1.08)
FEF_{25-75} z score	−1.32 (0.93)	−1.59 (1.04); $P = .472$	−1.61 (1.16)	−1.58 (0.98)
FVC z score	0.07 (0.72)	−0.11 (1.09); $P = .602$	0.12 (1.21)	−0.30 (0.99)
FEV_1/FVC z score	−1.24 (0.90)	−1.27 (0.94); $P = .928$	−1.37 (1.15)	−1.19 (0.76)
Abnormal inspiratory loop, n (%)	2/10 (25.0%)	6/19 (31.6%); $P = .732$	4/10 (40.0%)	2/9 (22.2%)
Dynamic flow limitation on exercise, n (%)	3/6 (50%)	12/20 (60%); $P = .664$	6/9 (66.7%)	6/11 (54.5%)
Gas trapping (multiple breath washout)				
N successful/total	8/10	24/25	11/11	13/14
RV/TLC	25.77 (6.74)	22.43 (8.52); $P = .275$	22.06 (8.96)	22.74 (8.48)
FRC/TLC	56.98 (5.43)	55.30 (7.65); $P = .508$	55.80 (6.83)	54.88 (8.53)
Respiratory mechanics (FOT)				
N successful/total	10/10	17/25	9/11	8/14
Rrs_8 z score	−0.08 (0.67)	0.55 (1.05); $P = .068$	0.53 (1.10)	0.58 (1.08)
Xrs_8 z score	−0.06 (0.51)	−0.85 (0.72); $P = .003$*	−0.87 (0.77)	−0.83 (0.72)
f_{res} z score	0.41 (0.85)	1.47 (1.36); $P = .019$*	1.34 (1.55)	1.61 (1.20)
AX z score	−0.02 (0.64)	0.89 (1.06); $P = .010$*	0.79 (1.21)	1.00 (0.94)

FEF, forced expiratory flows; *FOT*, forced oscillation technique; *FRC*, functional residual capacity; *RV*, residual volume; *TLC*, total lung capacity.
Differences in lung function outcomes between children with and without dysphonia were assessed using an independent t test or χ^2 test as appropriate.
*Represents a difference between children with and without dysphonia ($P < .05$).

score was significantly correlated with higher resonant frequency (f_{res}) (r = 0.546; $P = .009$) and area under the reactance curve (*AX*) (r = 0.563; $P = .006$), as well as worse (more negative) respiratory system reactance at 8 Hz (Xrs_8) (r = −0.542; $P = .009$). Respiratory system resistance at 8 Hz (Rrs_8) was not different between those children with dysphonia or normal voice (r = 0.398; $P = .066$). The only forced oscillation outcome to significantly correlate with the AVQI severity score was f_{res} (r = 0.394; $P = .046$). None of the forced oscillation technique outcomes were predicted by any neonatal factors ($P > .05$).

Discussion

Survivors of preterm birth commonly report respiratory symptoms such as cough, wheeze, and shortness of breath throughout life; particularly when exercising.[2] These ongoing symptoms have been largely attributed to chronic lung disease. We assessed the contribution of both the lungs and the upper airway to these symptoms and found that respiratory symptoms are associated with dysphonia, in conjunction with normal lung function in some participants, as depicted in the **Figure**. These preliminary findings highlight the possible role of the upper airway (with or without a contribution from the lung) in the ongoing respiratory symptoms experienced by survivors of very preterm birth.

Our data show that in this population of former very and extremely preterm neonates, survivors that reported respiratory symptoms of wheeze, recent exercise symptoms, and/or use of asthma medication during the 3 months prior to participation in the study had more severe dysphonia. Dysphonia in typically developing term-born children predominantly follows enthusiastic use of the vocal mechanism (shouting and use of voice in play) and is usually mild, transient, and resolves during puberty when laryngeal changes occur.[26] In contrast, recent studies suggest that children born very preterm (<32 weeks of gestation) have a more severe dysphonia that persists beyond childhood and likely reflects underlying laryngeal pathology resulting from invasive intubation and ventilation in the neonatal intensive care unit.[8,11] Such children often adopt a compensatory mechanism, supraglottic hyperfunction, which can add further injury.[8]

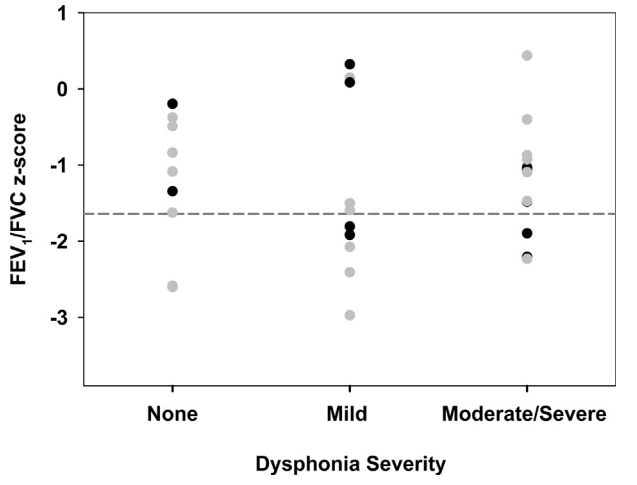

Figure. Airway obstruction (FEV_1/FVC z score as a surrogate marker) and dysphonia severity in very preterm children. Black dots represent preterm children reporting respiratory problems when exercising in the 3 months preceding the lung visit. Dashed line represents the lower limit of normal. Typical "healthy" populations average zero z scores (SD of 1). Data indicate that a number of children have lung function in the normal range (<−1.64 z scores) but report respiratory symptoms when exercising. *FEV_1*, forced expiratory volume in 1 second; *FVC*, forced vital capacity.

The symptoms of upper airway pathologies and vocal cord dysfunction are often misdiagnosed and mistreated as asthma, which can lead to increased prescription of medication and healthcare utilization. Clinically, an alternative diagnosis to asthma should be considered in cases of exercise-induced breathlessness that is not managed effectively with inhaled corticosteroids and pre-exercise β-agonists (bronchodilator).[27] Indeed, upper airway dysfunction and pattern disordered breathing are well known differentials of 'exercise-induced asthma'.[28-30] Less well known is the possibility of airway-narrowing laryngeal pathology arising from intubation, and our data suggest that these differentials should be considered in very preterm populations presenting with these asthma-like symptoms, particularly in those with normal lung function and no bronchodilator response.

Referral to a speech pathologist may improve symptoms. The role of speech pathologists in the management of laryngeal and upper airway disorders is well established[31] but less well known outside the field of laryngology.[32] A speech pathologist specializing in voice and upper airway disorders is trained to remediate faulty respiration and phonation as well as other disorders affecting the larynx such as vocal cord dysfunction and chronic cough.[33,34] Some preliminary evidence about the efficacy of surgical and behavioral management of dysphonia as a symptom of upper airway abnormalities has demonstrated improved voice outcomes in some preterm children and includes breathing training as part of the intervention.[35,36] However, concurrent reductions in respiratory symptoms in this population are yet to be studied and evidence-based interventions are required. It could be hypothesized that, if changes in upper airway structure and/or function underlie improvements in dysphonia severity, that respiratory symptoms in those children with normal lung function may also improve.

Increased severity of dysphonia was observed in preterm born children with a recent history of asthma medication usage (which may include bronchodilator, inhaled corticosteroid, or nonsteroidal anti-inflammatory therapy). There is a known association with inhaled corticosteroid use and dysphonia,[37,38] in some cases causing significant voice disturbance. The current recommendation is to balance vocal health with asthma management by taking the minimum dose of inhaled corticosteroid to achieve control of asthma symptoms.[38] Although we cannot definitively rule out that the dysphonia observed in this study is a consequence of inhaled corticosteroid usage, it appears unlikely because only 20% of the dysphonic group were receiving this medication in the preceding 3 months, and only 2 of the participants (both in the severe dysphonia group) were on inhaled corticosteroid at the time of testing. We suggest it is more likely that upper airway obstruction as an outcome of premature birth, which is currently underdiagnosed, may contribute to the respiratory symptoms in preterm children resulting in prescription of inhaled corticosteroids. A parallel could be drawn with vocal cord dysfunction, which is often misdiagnosed as exercise-induced asthma despite the more recent development of specific diagnostic tools.[39] Consequently, we suggest that primary care practitioners should be alert for laryngeal pathology as a contributing or causative factor in respiratory symptoms reported by preterm children.

A strength of our study is that respiratory and voice data were analyzed together in survivors of preterm birth. However, our data are limited by the retrospective nature, small sample size, and the lapsed time between respiratory and voice assessments. At present, it is unclear whether voice quality in preterm children changes over time. The current evidence suggests that dysphonia is persistent in preterm children. However, individual variability has been observed and it cannot be determined whether voice quality was stable between study participations. Future prospective studies should be considered to establish further links between breathing problems, lung function, and the role of the upper airway. Our preliminary data do, however, suggest that preterm children would benefit from a coordinated approach to care of the airway. A multidisciplinary team, consisting at of a respiratory physician and an otolaryngologist, would evaluate the contribution of upper and lower airway symptoms to lung function and voice, and refer for therapy as appropriate. In the absence of such a team, primary care practitioners who manage preterm children with hoarse voices should have a high index of suspicion of the potential for upper airway pathology to contribute to respiratory symptoms and refer to both specialties to differentially diagnose upper and/or lower airway pathology.

We showed that decreased total respiratory system compliance (indicated by lower Xrs_8 and AX), measured by the forced oscillation technique, was associated with more severe dysphonia in survivors of very preterm birth. It is unclear if these findings are associated with the earlier gestational age (and consequent neonatal intensive care unit treatments) leading to respiratory disease, or if the forced oscillation technique may play a role in delineating between upper and lower airway disease. Perhaps underutilized in this area, the forced oscillation technique has previously been shown to detect and quantify upper or central airway diseases including tracheal stenosis,[40] tracheoesophageal fistula,[41] laryngeal obstruction,[42] and vocal cord dysfunction; though separation of inspiratory and expiratory impedances to examine the flow dependence during each phase of the respiratory cycle would likely yield most information in this group of patients, rather than the averaged data outputted by most commercial devices, including in this study. These pilot data advocate for the use of the forced oscillation technique during future studies to potentially delineate the origin of airway obstruction.

In summary, we have shown that respiratory symptoms are associated with dysphonia, in conjunction with normal lung function in some very and extremely preterm children. Our findings suggest that the upper airway and dysfunctional

breathing may play a role in the respiratory symptoms experienced by some very preterm children and should be considered if symptoms are refractory to treatment and in the presence of normal lung function. ■

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