facilitate the hospital turnover of infected patients, protect patients' family members, and reduce the risk of infection of healthcare professionals. On the other hand, no adverse events requiring medical intervention emerged during the telemonitoring period, suggesting that the occurrence of clinical deterioration in SARS-CoV-2–positive, clinically stable patients is uncommon. As such, further research in larger cohorts is warranted to validate our findings and determine the real cost-effectiveness of this approach.

In conclusion, we show that a hotel-based, telemedicine-enabled management represents a feasible and safe approach for patients with COVID-19 requiring long-term isolation. The widespread adoption of telemonitoring tools as alternatives to unnecessary or prolonged hospitalization gets particular relevance in the context of the ongoing second or third wave of COVID-19 in many countries. ■

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Characteristics of Children with Bronchopulmonary Dysplasia with Prolonged and/or Later-Onset Pulmonary Hypertension

To the Editor:

A common sequela of prematurity is bronchopulmonary dysplasia (BPD), characterized by impaired alveolar growth, airway inflammation, and airflow obstruction (1), which may affect up to 50,000 U.S. infants annually (2, 3). Pulmonary hypertension (PH) is an increasingly recognized comorbidity of BPD. Cohort studies estimate that 14–43% of infants with BPD will develop PH, which is associated with increased mortality (14–38%) (4). Few studies describe the natural history of PH in infants with BPD after neonatal intensive care unit (NICU) discharge. Two retrospective studies found that 24–34% of survivors still had PH at ∼3 years of age (5, 6), but it has not been observed in school-age children with BPD (7, 8). Given these studies, our first objective was to characterize preterm infants at risk for prolonged resolution of PH after 1 year of age.

Published guidelines recommend screening echocardiograms at 36 weeks postmenstrual age (PMA) for infants with moderate or severe BPD (9). One subsequent study did not identify any cases of PH after 40 weeks PMA (10), but another study found that 48% of PH cases were diagnosed after NICU discharge (6). Our second objective was to identify infants with negative screening echocardiograms who were subsequently diagnosed with PH.

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Methods

Charts for 758 subjects enrolled in an outpatient BPD clinical registry between 2008 and 2018 were retrospectively reviewed. Inclusion criteria included birth at <32 weeks gestation and a diagnosis of BPD (all severities) (2, 11). Caregivers were consented per the Johns Hopkins University Institutional Review Board. Echocardiogram findings were abstracted from the medical record. Subjects were classified as having PH if PH was present on any clinically obtained echocardiogram in the screening period (34–38 wk PMA) and/or follow-up period (>38 wk PMA). The diagnosis of PH was based on elevated right ventricular pressures defined by tricuspid regurgitation jet, patent ductus arteriosus (PDA) gradient, or systolic interventricular septal position. Of the 758 subjects, 57 subjects had echocardiograms only in the screening period, 197 only had them in the follow-up period, and 168 had them in both periods. For this study, we arbitrarily examined children who had PH resolve after 1 year of chronological age versus before 1 year of chronological age. Late-onset PH was defined as PH found in the follow-up period that was not observed during the screening period; infants were only included in this analysis if they had echocardiograms during both the

Table 1. Resolution of pulmonary hypertension

	Any Pulmonary Hypertension (*n* = *143*)	Resolution after 1 yr of Age (*n* = *25*)	Resolution before 1 yr of Age (*n* = *118*)	*P* Value
Sex, % female	46.9	52.0	45.8	0.57
Race/ethnicity, % non-White	69.2	60.0	71.2	0.27
Gestational age, mean ± SD (range), wk	26.0 ± 2.2 (23–32)	26.8 ± 2.9 (23–32)	25.9 ± 2.0 (23–30.7)	0.07
Birthweight, mean ± SD (range), grams	815 ± 295 (380–1,900)	957 ± 447 (420–1,900)	785 ± 243 (380–1,650)	0.008
Birthweight percentile, mean ± SD (range), %	40 ± 24 (1–94)	36 ± 23 (2–88)	41 ± 24 (1–94)	0.37
G-tube, % yes	55.9	92.0	48.3	<0.001
Nissen fundoplication, % yes	37.8	72.0	30.5	<0.001
Supplemental oxygen at discharge, % yes	65.0	72.0	63.6	0.42
Initial oxygen amount, mean ± SD (range), LPM	0.53 ± 0.43 (0.13–2.00) (*n* = 93)	0.94 ± 0.59 (0.13–2.00) (*n* = 18)	0.43 ± 0.31 (0.13–1.50) (*n* = 75)	<0.001
Age at home oxygen discontinuation, median (95% CI), yr	1.18 (1.12–1.34) (*n* = 93)	1.97 (1.59–3.95) (*n* = 18)	1.13 (1.02–1.18) (*n* = 75)	<0.001*
Diuretics, % yes	79.0	96.0	75.4	0.022
Tracheostomy, % yes	11.9	32.0	7.6	0.001
Home ventilator, % yes	10.5	32.0	5.9	<0.001
PDA requiring procedure, % yes	38.5	48.0	36.4	0.28
CSF shunt, % yes	10.5	20.0	8.5	0.09
Initial length of stay, mean ± SD (range), d	195 ± 125 (53–806)	296 ± 189 (92–806)	173 ± 95 (53–744)	<0.001
Outpatient vasodilator therapy, % yes†	24.5	44.0	20.3	0.012

Definition of abbreviations: CI = confidence interval; CSF = cerebrospinal fluid; LPM = liters per minute; PDA = patent ductus arteriosus; SD = standard deviation.
**P* value generated *via* Wilcoxon rank-sum test.
†Out of the 143 subjects, 30 subjects were on sildenafil alone, 4 were on sildenafil and bosentan, and 1 was on sildenafil and treprostinil.

Table 2. Late onset of pulmonary hypertension

	Negative Screen; Positive in Follow-Up (*n* = *27*)	Negative Screen; Negative in Follow-Up (*n* = *133*)	*P* Value
Sex, % female	40.7	42.1	0.90
Race/ethnicity, % non-White	59.3	62.4	0.76
Gestational age, mean ± SD (range), wk	25.7 ± 2.1 (23.1–32)	26.4 ± 2.2 (22.7–32)	0.14
Birthweight, mean ± SD (range), grams	787 ± 277 (470–1,590)	880 ± 332 (400–2,310)	0.17
Birthweight percentile, mean ± SD (range), %	41 ± 25 (4–89)	44 ± 25 (1–95)	0.70
G-tube, % yes	66.7	33.8	0.001
Nissen fundoplication, % yes	44.4	19.6	0.006
Supplemental oxygen at discharge, % yes	74.1	40.6	0.001
Initial oxygen amount, mean ± SD (range), LPM	0.48 ± 0.24 (0.13–1.00) (*n* = 20)	0.32 ± 0.23 (0.03–1.00) (*n* = 54)	0.010
Age at home oxygen discontinuation, median (95% CI), yr	1.31 (1.06–2.10) (*n* = 20)	0.81 (0.70–1.00) (*n* = 54)	0.034*
Diuretics, % yes	88.9	72.2	0.07
Tracheostomy, % yes	7.4	3.0	0.27
Home ventilator, % yes	7.4	3.0	0.27
PDA requiring procedure, % yes	48.2	27.1	0.030
CSF shunt, % yes	11.1	12.0	0.89
Initial length of stay, mean ± SD (range), d	211 ± 80 (95–452)	139 ± 63 (49–507)	<0.001

Definition of abbreviations: CI = confidence interval; CSF = cerebrospinal fluid; LPM = liters per minute; PDA = patent ductus arteriosus; SD = standard deviation.
**P* value generated *via* Wilcoxon rank-sum test.

screening and follow-up periods. Patient characteristics were compared using Chi-square tests, Wilcoxon rank-sum tests, and *t* tests (Tables 1 and 2). Censored data for time to PH resolution and time to late-onset PH were described using Kaplan-Meier analysis.

Results

Timing of resolution of PH. Of the 758 infants with BPD in the registry, 143 (18.9%) had PH during the screening period and/or during the follow-up period (Table 1). Of those with PH, the median age of resolution was 20 weeks after birth (Figure 1A). However, 25 infants (17.5%) had PH that resolved after 1 year of age. This prolonged resolution of PH was not associated with sex, race and/or ethnicity, gestational age, or birthweight percentile but was associated with heavier birthweight. In addition, those with PH that persisted after 1 year of age were more likely to receive gastrostomy tube placement and Nissen fundoplication than those with resolution of PH before 1 year of age. Although this prolonged PH was not associated with home

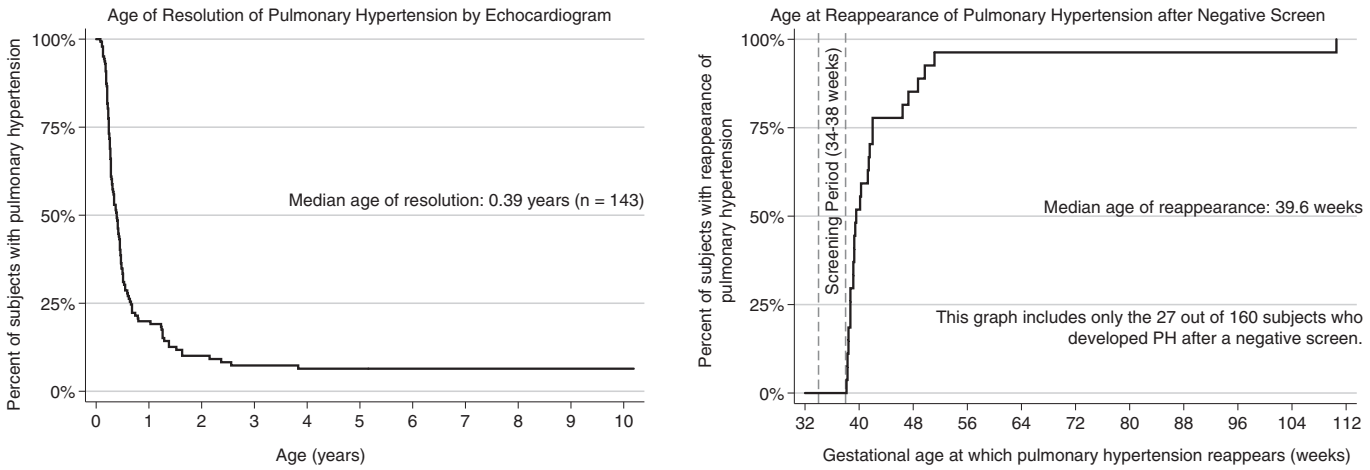

Figure 1. Resolution and reappearance of PH. PH = pulmonary hypertension.

supplemental oxygen, if supplemental oxygen was required, those with PH persisting after 1 year of age required a greater mean amount of oxygen with longer duration of use and were more likely to require tracheostomy and home ventilation. This prolonged PH was associated with increased diuretic and vasodilator use and a longer NICU admission (296 d vs. 173 d).

Subpopulation with late-onset PH. A total of 160 patients had negative or inconclusive echocardiograms during the screening period, 27 (16.9%) of whom developed echocardiographic evidence of PH in the follow-up period (Table 2). The median age of first positive echocardiogram was 39.6 weeks PMA (range, 38.1–110.6 wk PMA; Figure 1B). Late-onset PH was not associated with any demographic characteristics. Infants with late-onset PH were more likely to receive gastrostomy tube placement and Nissen fundoplication than infants with persistently negative echocardiograms. In addition, infants with late-onset PH were more likely to have received a procedural intervention for a PDA, have home respiratory support needs with longer duration of oxygen use, and have a longer initial NICU admission (211 d vs. 139 d). Time to resolution of PH did not differ between infants with early- versus late-onset PH ($P = 0.65$).

Discussion

This retrospective cohort study describes the natural history of PH in BPD, including subpopulations with more prolonged resolution of PH (after 1 yr of age) and late-onset PH. Our findings suggest that these subpopulations cannot be readily identified based on demographic characteristics, as there were no significant differences in gestational age, etc., and surprisingly, infants with more prolonged PH were counterintuitively heavier at birth. However, infants with PH that persisted after 1 year of age and those with late-onset PH did require increased home respiratory support, suggesting more severe lung disease. Although it is assumed that respiratory support requirements are a surrogate marker of lung disease, supplemental oxygen may also be a concomitant PH therapy. Gastrostomy tube placement and Nissen fundoplication are a common sequela of prematurity. Both were seen with increased frequency in PH persisting after 1 year of age and late-onset PH, which again likely reflects a marker of more severe disease. We found that PDAs receiving procedural intervention were more common with late-onset PH, and this may reflect that infants with hemodynamically significant PDAs may be at risk for the development of PH due to ongoing systemic-to-pulmonary shunting (12). Lastly, infants with late-onset PH had longer initial hospitalizations than infants with persistently negative echocardiograms. Therefore, it is reasonable to consider repeating screening echocardiograms in infants with BPD who remain hospitalized beyond the standard screening age of 36 weeks PMA, even if initially negative.

This study was limited by its retrospective nature, echocardiograms obtained for clinical reasons, and absence of control subjects without BPD. In addition, as resolution of PH likely occurred between echocardiograms, bias secondary to interval censoring may be present (13). Also, using echocardiograms to determine the presence of PH is a potential limitation, as cardiac catheterization is more accurate in determining presence as well as severity (14). In addition, during the study period, there was no standardized protocol for who was screened for PH at ~36 weeks PMA, so the overall prevalence, and particularly mild disease, may be underestimated.

Although PH affects a minority of premature infants with BPD, improving screening and follow-up guidelines to identify those at highest risk and better understanding of PH resolution and recurrence may improve outcomes and anticipatory guidance. Future prospective studies should focus on further clarifying risk factors for the development of disease as well as the ideal screening window to identify patients. ■

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Evaluation of Agreement on Presence and Severity of Tracheobronchomalacia by Dynamic Flexible Bronchoscopy

To the Editor:

Collapsibility of the lower airways, also known as tracheobronchomalacia (TBM), is an important cause of chronic cough, noisy breathing, and airway obstruction in childhood (1, 2). Symptoms of TBM include dyspnea, respiratory distress, wheezing, and/or a barky cough. Symptoms can be worse during periods of increased respiratory effort, such as during crying, coughing, increased activity, inflammation and/or infection (3). TBM has been linked to increased respiratory morbidity in the neonatal period and throughout childhood (4, 5).

The preferred method for evaluating central airway collapse is direct visualization via flexible bronchoscopy during spontaneous respiration. There are no widely accepted criteria for defining central airway collapse (6, 7), although a recent "Early View" Task Force report from the European Respiratory Society suggested using collapse of greater than 50% as diagnostic of tracheomalacia (1). Our study aims to evaluate agreement among pediatric pulmonologists on the presence and severity of TBM as assessed by using flexible bronchoscopy during spontaneous respiration.

Methods

Children who underwent transnasal flexible bronchoscopy during spontaneous respiration (Table 1) at Cincinnati Children's Hospital Medical Center (CCHMC) from January 1, 2015, to January 1, 2017, were eligible for enrollment. Bronchoscopies performed via an endotracheal tube, laryngeal mask airway, or tracheostomy tube were excluded from this study. This study was approved by the institutional review board at CCHMC. Thirty bronchoscopic videos were deidentified and edited (VaultStream EasyCut version 8.0) to include dynamic evaluation of the airway caudal to the vocal cords. Deidentified bronchoscopic video clips were affixed electronically on a secured server with a multiple-choice questionnaire, which was sent to 21 faculty and six senior fellows within the pulmonary division at CCHMC. Ten faculty and three fellows chose to participate.

Physician reviewers were asked to assess the edited bronchoscopic videos for the presence and severity of TBM. Reviewers were asked to rate the severity of collapse as none, mild, moderate, and severe on the basis of their clinical impressions (there were no defined criteria). Interrater reliability was assessed for consensus agreement with Cohen's

Table 1. Patient and procedure characteristics

	N (%)
Age at bronchoscopy, yr	
0–4	7 (23)
4–8	14 (47)
8–12	7 (23)
12+	2 (7)
Primary indication	
Wheezing	17 (57)
Chronic cough	15 (50)
Recurrent croup	13 (43)
Secondary indications	
Bronchiectasis	3 (10)
Stridor	3 (10)
Dyspnea on exertion	2 (7)
Recurrent bronchitis or pneumonia	2 (7)
Aspiration (known/suspected)	1 (3)
Upper airway obstruction	1 (3)
Clinical diagnosis by primary bronchoscopist	
Normal (no malacia segments)	4 (13)
Bronchomalacia only	6 (20)
Tracheomalacia only	11 (37)
Tracheobronchomalacia	8 (27)
Bronchoscope	
BF-XP160F (2.8-mm outer diameter)	26 (87)
BF-XP190F (3.1-mm outer diameter)	2 (7)
BF-P190 (4.2-mm outer diameter)	2 (7)