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ORIGINAL ARTICLE

Chest radiological patterns predict the duration of mechanical ventilation in children with RSV infection

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Abstract
Background RSV-infected children demonstrate various radiographic features, some of which are associated with worse clinical outcomes.
Objective To investigate whether specific chest radiological patterns in RSV-infected children with acute respiratory failure (ARF) in the peri-intubation period are associated with prolonged duration of mechanical ventilation.
Materials and methods We included RSV-infected children <1 year of age admitted with ARF from 1996 through 2002 to the pediatric intensive care unit at Massachusetts General Hospital. Their chest radiographs were evaluated at three time-points: preintubation (day −1) and days 1 and 2 after intubation. Univariate and multiple logistic regressions models were utilized to investigate our objective.
Results The study included 46 children. Using day 1 chest radiograph findings to predict duration of mechanical ventilation of >8 days, a backward stepwise regression arrived at a model that included age and right and left lung atelectasis. Using day 2 chest radiograph results, the best model included age and left lung atelectasis. A model combining the two days' findings yielded an area under the ROC curve of 0.92 with a satisfactory fit (P=0.95).
Conclusion Chest radiological patterns around the time of intubation can identify children with RSV-associated ARF who would require prolonged mechanical ventilation.

Keywords RSV infection · Pediatric ICU · Mechanical ventilation · Chest radiograph · Outcome

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Introduction

Infection caused by respiratory syncytial virus (RSV) is a leading cause of hospitalization in the US for infants younger than 1 year [1]. It has been estimated that more than 120,000 infants in the US are hospitalized annually with RSV infection [2, 3]. RSV infection in infants causes significant morbidity, as 7–21% of these hospitalized infants require mechanical ventilation [4, 5].

Several studies in RSV-infected children have investigated risk factors associated with a more severe clinical course [5–18]. Younger age at presentation, lower weight on admission, prematurity, early ventilatory parameters, associated congenital heart disease, chronic lung disease, immunodeficiency, specific neuroendocrine profile, specific polymorphisms, and elevated liver transaminases have all been associated with longer duration of mechanical ventilation in RSV-infected children [5–32]. A few studies have investigated chest radiological patterns in both ventilated and nonventilated patients with bronchiolitis [17, 19–26, 33, 34]. We have retrospectively investigated whether specific chest radiological patterns in RSV-infected children with acute respiratory failure – immediately prior to endotracheal intubation and during the first 2 days after endotracheal intubation – are associated with a prolonged duration of mechanical ventilation [27].

Materials and methods

The Institutional Review Board for human subjects of the Massachusetts General Hospital approved the study. We conducted a retrospective medical record review of children aged 1 year and younger admitted with RSV infection and acute respiratory failure to the pediatric critical care unit at Massachusetts General Hospital, a tertiary care medical center, during the years 1996 through 2002.

Children with RSV infection were identified from the records of the clinical virology laboratory for specimens for the given year. In addition the key words "respiratory syncytial virus bronchiolitis," "respiratory syncytial virus pneumonia," and "respiratory syncytial virus infection" were entered into the computerized hospital medical record database and the medical records were retrieved. The medical records of all these children were reviewed. From these records, all children requiring mechanical ventilation for acute respiratory failure secondary to RSV infection were identified. Children excluded from this analysis included those who were premature and those who had chronic lung disease, superadded bacterial infection of the lungs, concomitant heart disease, upper airway problems, chest wall/spinal anomalies, or episodes of aspiration pneumonia or other respiratory infections requiring prior hospitalization to the PICU.

Study methods

The medical records were reviewed for data regarding patient characteristics, including age at admission, gestational age at birth and significant medical history. Data pertaining to the duration of mechanical ventilation (in days) were retrieved from the medical records. For the purpose of this study, a day was defined to represent a single calendar day.

During the study period, our ventilatory strategy was similar to that described by others in the literature [24]. We used pressure-controlled time-cycled ventilation, aiming at a pH of >7.25 and an arterial oxygen saturation between 88% and 92%. In children with atelectasis, we used positive end expiratory pressure, attempting to prevent further loss of lung volume. Other means of mechanical ventilation, such as high-frequency oscillatory ventilation, were not used during the years included in our study. All children received adequate analgesia and sedation. Neuromuscular blockades were occasionally used when thought indicated by the attending physician. Bronchodilators were used only when it was thought that patients had a therapeutic response after an initial dose. Hydration and electrolytes were closely monitored to maintain normal levels. Children were assessed daily for their ability to wean ventilatory parameters.

Radiological evaluation

An independent pediatric radiologist blinded to the children's clinical outcome variables evaluated all chest radiographs. Chest radiography in the study subjects was not done routinely but at the discretion of the bedside intensivist managing the child. In cases of multiple chest radiographs on a given day the chest radiograph with the most significant radiological findings was used for the study. The preintubation chest radiograph was the last chest radiograph taken prior to endotracheal intubation. Chest radiographs were evaluated by the pediatric radiologist using standardized definitions for endotracheal tube position, atelectasis, interstitial lung disease, pneumothorax, pneumomediastinum, pleural effusion, and evidence of hyperinflation in various lung lobes. Atelectasis was defined as the presence of a transient pulmonary parenchymal opacity, which was associated with loss of lung volume when it involved a large portion of a lobe [35]. As it is difficult to differentiate atelectasis from pneumonia and focal edema or hemorrhage, the opacity was deemed to represent atelectasis when there was no air bronchogram within the opacity, there were no general signs of vascular fluid overload, and the opacity was absent within 48 h on subsequent chest radiographs. Pleural effusion was defined as thickening of the pleural line and/or blunting of the costophrenic angle. A pneumothorax was defined as the presence of an air pocket within the pleural space, as evidenced by visualization of the visceral pleural line and/or more indirect signs (hyperlucency of hemithorax, sharp outline cardiomediastinal border, deep sulcus sign). Pneumomediastinum was defined as the presence of air in the mediastinum as suggested by the presence of air overlying the heart and mediastinum, with or without associated soft-tissue emphysema. Interstitial lung disease was defined as the presence of an increase in linear markings in the lungs that could not be explained by the normal bronchovascular markings. Hyperinflation was defined as hyperlucency of a portion of the lung, associated with hyperexpansion (displacement of fissures, cardiomediastinal shift; Fig. 1).

Fig. 1 Chest radiograph in mechanically ventilated RSV-infected infant shows the presence of right upper lobe atelectasis, left lower lobe atelectasis and hyperinflation of the right middle and lower lobes of the lung (*arrows*)

All the different lung lobes were separately evaluated by the radiologist blinded to the clinical outcome.

Statistics

Our primary outcome variable was the total days of mechanical ventilation dichotomized at >8 days using the value at the 75th percentile. For the outcome variable, the demographic variables and chest radiograph findings at each time-point (pre-intubation, i.e. day −1, and days 1 and 2 after intubation) were subjected to univariate analysis using the Fisher exact test. Logistic regressions models were built for the outcome at each time-point using the demographic variables and radiographic findings that reached the 0.10 level of significance in the univariate analysis. Subsequently, a single model was derived for the outcome variable in a stepwise analysis that potentially included all significant terms from the regressions at each time-point. The model's goodness-of-fit was evaluated using the Hosmer-Lemeshow chi-squared test and the area under the receiver operating curve (ROC) [36].

Results

A total of 46 children out of 68 children with RSV-associated disease requiring mechanical ventilation were eligible for the study. There were 22 girls and 24 boys. There were 30 Caucasians, 6 African-Americans, 8 Hispanics, and 2 others. The median age for the study cohort was 37.5 days (range 6–272 days). Besides acute respiratory failure, no other organ dysfunction was noted in any of these children. The median duration of mechanical ventilation was 6 days. A prolonged duration of mechanical ventilation (>8 days) was recorded for 14 children.

Preintubation chest radiographs were not available for 21 children. A postintubation day 2 chest radiograph was unavailable for one child. None of the chest radiographs showed evidence of pneumomediastinum. Pneumothorax and pleural effusion were only noted for one patient each; therefore these findings were not considered further.

Univariate analysis

Table 1 presents the number and percentage of chest radiographs with atelectasis, interstitial lung disease and hyperinflation at each given time-point. Right lung atelectasis was common at day −1 and day 1 (52% and 43%, respectively) and was exhibited by most chest radiographs (89%) by day 2. The right upper lobe was affected most often (Fig. 1). Left lung atelectasis appeared in approximately a quarter of all chest radiographs at days −1 and 1, but on day 2 it was seen in the majority of radiographs (71%). The left upper lobe and left lower lobe were affected at roughly the same rate (47% versus 49% of patients, respectively).

Table 2 shows the number and percentage of specific radiological findings associated with prolonged duration of mechanical ventilation (>8 days). In addition, the odds of having the particular outcome given the chest radiograph

Table 1 Radiological findings in mechanically ventilated children with RSV infection.

Radiological finding	Day −1 (*n*=25)	Day 1 (*n*=46)	Day 2 (*n*=45)
	n (%)	*n* (%)	*n* (%)
Location of atelectasis			
Right upper lobe	10 (40)	19 (41)	38 (84)
Right middle lobe	8 (32)	6 (13)	18 (40)
Right lower lobe	4 (16)	2 (4)	16 (36)
Any right lobe	13 (52)	20 (43)	40 (89)
Left upper lobe	2 (8)	4 (9)	21 (47)
Lingula	2 (8)	2 (4)	5 (11)
Left lower lobe	5 (20)	10 (22)	22 (49)
Any left lobe	6 (24)	12 (26)	32 (71)
Any lobe of left or right lung	13 (52)	22 (48)	41 (91)
Interstitial lung disease	6 (24)	20 (43)	16 (36)
Hyperinflation	19 (76)	33 (72)	34 (76)

Table 2 Chest radiological findings in children with prolonged mechanical ventilation (>8 days).

Radiological finding	Day −1 (*n*=7)		Day 1 (*n*=14)		Day 2 (*n*=14)	
	n (%)	OR	*n* (%)	OR	*n* (%)	OR
Location of atelectasis						
Right upper lobe	4 (57)	2.7	10 (71)	6.4**	13 (93)	3.1
Right middle lobe	3 (43)	2.0	5 (36)	17.2**	8 (57)	2.8
Right lower lobe	2 (29)	3.2	1 (7)	2.4	5 (36)	1.0
Any lobe in the right lung	5 (71)	3.1	11(79)	9.4***	14 (100)	–[a]
Left upper lobe	0 (0)	–[a]	3 (29)	8.5	9 (64)	2.8
Lingula	1 (14)	2.8	2 (14)	–[a]	3 (21)	4.0
Left lower lobe	3 (43)	6.0	6 (43)	5.2*	10 (71)	4.0
Any lobe in the left lung	3 (43)	3.8	8 (57)	9.3***	13 (93)	8.2
Either lung	5 (71)	3.1	11 (79)	7*	14 (100)	–[a]
Interstitial lung disease	2 (29)	1.4	8 (57)	2.2	7 (50)	2.4
Hyperinflation	6 (86)	2.3	11 (79)	1.2	12 (86)	1.9

OR unadjusted odds of having the outcome if the finding was present, *%* percentage of children with prolonged mechanical ventilation who exhibited the finding.
*P<0.05, **P<0.01, ***P<0.005.
[a] Could not calculate due to empty cells.

finding are presented at each time-point. Atelectasis in both the right and left lungs on day 1 was associated with extended duration of mechanical ventilation (both $P<$ 0.005; Table 2). All children who were mechanically ventilated for >8 days showed atelectasis in either lungs on day 2 (Table 2). Interstitial lung disease and hyperinflation were not significantly associated with prolonged duration of mechanical ventilation. In addition, the low position of the endotracheal tube, which could have contributed to worsening atelectasis, did not correlate with our outcome variable.

Multivariate analyses

Using day 1 chest radiograph findings to predict a duration of mechanical ventilation of >8 days, a backward stepwise regression arrived at a model including age and atelectasis in any lobe of the right and left lung (Table 3). Using day 2 chest radiograph results, the best model included age and atelectasis in any lobe of the left lung. A model combining the two days' findings that included age, atelectasis in any lobe of the right lung at day 1 and atelectasis in any lobe of the left lung at day 2 performed well, yielding an area under the ROC curve of 0.92 (Fig. 2). The model fit satisfactorily (P=0.95), correctly classifying 84% of the cases.

Table 3 Independent predictors of prolonged duration of mechanical ventilation (>8 days).

Factor	Adjusted OR	95% CI	*P*-value
Age <31 days	24.53	2.19–274.81	0.009
Day 1 right lung atelectasis	07.97	1.22–52.210	0.030
Day 2 left lung atelectasis	34.80	1.64–740.22	0.023

Discussion

The principal observation from this institution-specific study is that the presence of specific chest radiological patterns after airway intubation in RSV-infected children with acute respiratory failure identified those who would subsequently have a prolonged clinical course. We found that atelectasis was the predominant chest radiological finding in these children. Children with areas of lung atelectasis on day 1 and day 2 after intubation required prolonged mechanical ventilation for >8 days. Surprisingly, the severity of hyperinflation and/or interstitial lung disease, which many physicians consider the hallmark of

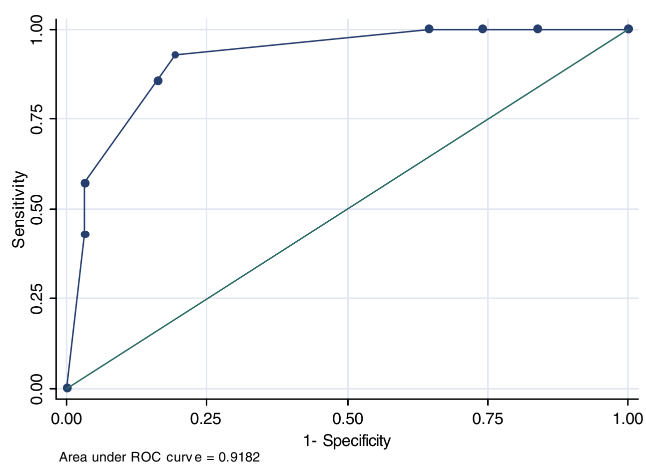

Fig. 2 Receiver operating curve (ROC) where a model combining age, right lung atelectasis at day 1 and left lung atelectasis at day 2 yield an area under the ROC curve of 0.9182. The model fit satisfactorily (P=0.9539), correctly classifying 84% of the cases

RSV infection, did not correlate well with our outcome end-point. Further, our study indicates that pneumothorax and pleural effusion are relatively uncommon among mechanically ventilated children with RSV infection.

In children with RSV infection it is well documented that atelectasis and infiltrates are common findings on chest radiographs [22–26], and children with these findings are more likely to be symptomatic. Willson et al. [25] found that atelectasis and infiltrates are common findings on chest radiographs among infants hospitalized for respiratory viral infection. However, only 14% of the children in the study cohort had respiratory failure and the timing of the appearance of atelectasis and infiltrates in the patients' clinical course was not clearly defined. Further, the study included patients with underlying chronic conditions, which could have affected their chest radiograph findings. Similarly, Lebel et al. [26] found that the appearance of new infiltrates (mostly atelectasis) during mechanical ventilation correlates with a longer duration of mechanical ventilation in patients with acute bronchiolitis. However, that study did not focus specifically on patients with RSV infection and did not specify when during the course of mechanical ventilation the chest radiographs were evaluated. Tasker et al. [24], in the retrospective phase of their study in 45 infants with RSV infection, found that during the initial 48 h of mechanical ventilation, four-quadrant alveolar consolidation on chest radiographs correlated well with an alveolar arterial oxygen gradient of >300 mmHg and a mean airway pressure of >10 cm H_2O. Subsequently, in the prospective phase of their study in 44 infants, they demonstrated that ventilatory parameters in the first 24 h of mechanical ventilation correlate with PICU length of stay. Their report, however, did not include statistical analysis about the effects of various radiological findings (i.e. atelectasis, hyperinflation, interstitial lung disease and others) on the duration of mechanical ventilation [29]. Roe et al. [37] in their literature review described, in addition to presenting pictures of chest radiographs of infants with severe RSV infection, the spectrum of lower respiratory tract chest radiographic findings in 45 PICU patients. The findings ranged from marked diffuse consolidation in all quadrants without hyperinflation to bilateral hyperinflation without consolidation.

Our study cohort with acute respiratory failure represented only the ones who were the most symptomatic, and it is possible that atelectasis is the predominant chest radiological finding in this subset of patients. We excluded from our study all children with risk factors such as secondary bacterial infection of the lungs, chronic lung disease, congenital heart disease, upper airway anomalies, immunocompromised status, chest wall or spinal anomalies and past episodes of aspiration pneumonia. We thought that an underlying lung disease could cause abnormal chest radiological patterns that could subsequently confound the study analyses.

In our study, atelectasis, when combined in a model with young age (<31 days), is an independent predictor of prolonged duration of mechanical ventilation. We speculate that the worsening atelectasis following airway intubation is multifactorial; it could be related to the process of airway intubation, mechanical ventilation strategies, worsening lung disease, increasing accumulation of respiratory tract secretions, worsening airway edema, poorly developed respiratory clearance mechanisms and a narrow-dimension endotracheal tube placed in an already small airway. Unfortunately, the retrospective nature of our study and the limited number of patients whose preintubation chest radiographs were available (n=25) precludes us from clarifying this matter.

Friis et al. [20] showed that abnormal chest radiological findings in the form of lobar or segmental consolidations occur more frequently in RSV-infected children younger than 6 months. Similarly, Wang et al. [30] found that pulmonary consolidation on the chest radiograph obtained at admission was one of the factors associated with a complicated hospitalization. Similarly, our study suggests that an abnormal radiological pattern on chest radiographs is more likely to be seen in the sicker and younger cohort among RSV-infected children.

Virkki et al. [33] compared radiological findings and host response markers with the etiology of infection in 256 children with pneumonia. The combination of an alveolar infiltration and CRP >80 mg/l, even though specific for bacterial pneumonia, was of only poor to modest clinical value because of a low positive likelihood ratio. Additionally, interstitial infiltrates are not a reliable indication of solely viral pneumonia, as two-thirds of the 254 hospitalized patients had alveolar infiltrates on chest radiographs. Half of the children with interstitial infiltrates as the sole radiographic finding had bacterial infection. However, in our study, atelectasis was identified in only 9% of the study cohort [34] and it excluded patients with bacterial coinfection.

In addition to the findings on chest radiographs, in our study, younger age was an independent risk factor for a worse course in RSV-infected children presenting with acute respiratory failure, and this finding is in accordance with the results of other studies [30]. This is contrary to the findings of Tissing et al. [7], who in a prospective study identified on multivariate analyses that only low weight was an independent risk factor for prolonged mechanical ventilation. Our results emphasize that the presence of atelectasis in an intubated RSV-infected infant younger than 31 days is associated with prolonged duration of mechanical ventilation.

The limitation of our study is that only 54% of the study cohort had preintubation chest radiographs. The study was conducted in a tertiary referral center where the majority of the patients in the study requiring mechanical ventilator support for RSV infection were transferred from outside referring community-based hospitals where (1) either the chest radiographs prior to intubation were not sent to our institution as part of the records, and/or (2) a significant number of these patients required emergent airway intubation based on the clinical picture where there was insufficient time to perform a preintubation chest radiograph. Even though the final model in this study is significant, logistic regression requires larger sample sizes than ordinary least squares regression (linear) for correct inference. It is possible that the small sample size in our study affected the predictive modeling. This study was also limited in its scope to address whether a different ventilatory technique or bacterial coinfection would make a difference in the type of chest radiological findings in these patients.

Conclusion

Chest radiological patterns on day 1 and day 2 after intubation can help identify children who will require a prolonged mechanical ventilation of more than 8 days. Being aware of these radiological patterns early in the course of the disease process might help the bedside clinician to guide the families and the PICU staff to identify children who might have a prolonged duration of mechanical ventilation.

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