

Changes in Lung Sounds During the Acute Stage of RSV Acute Bronchiolitis in Infants

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Objective: Changes in the respiratory function over time in respiratory syncytial virus (RSV)-induced acute bronchiolitis were evaluated by a lung sound analysis.

Methods: We retrospectively examined changes in lung sound parameters over time in 54 children (median age, 7 months) diagnosed with RSV acute bronchiolitis. We evaluated the power of inspiratory and expiratory sounds using a conventional method and analyzed the frequency characteristics of inspiratory sounds using new automated analysis software program. We examined changes in these lung sound parameters over time during and after hospitalization and compared these data with those of age-matched healthy children.

Results: In 138 lung sound samples from 54 infants, the power of inspiratory and expiratory sounds was greatest within 4 days after the onset and improved over time. In contrast, the greatest changes in inspiratory sound parameters were observed at 5 to 10 days after the onset of RSV acute bronchiolitis. Some lung sound parameters in patients with RSV acute bronchiolitis did not return to normal even by 14 days after the onset.

Conclusions: This finding is considered a characteristic of RSV acute bronchiolitis in infants and is meaningful in terms of post-treatment management.

Key words: acute bronchiolitis, infants, lung sound analysis, machine learning, RSV

INTRODUCTION

Acute bronchiolitis caused by respiratory syncytial virus (RSV) is common in infants younger than 2 years of age and can become severe in some cases [1, 2]. Although damage to the airways is significant, no specific treatment for the acute phase has been established [3, 4]. Furthermore, it has been reported that RSV acute bronchiolitis can trigger the onset of childhood asthma [5], which may have a significant impact on the decline of the respiratory function [6] and the onset of chronic obstructive pulmonary disease (COPD) in the future in affected children. The damage caused by RSV infection is severe [7], and young children who are anatomically and immunologically immature may sometimes suffer permanent damage. However, there are few objective reports on the persistence and temporal changes of airway disorders after RSV acute bronchiolitis.

On the other hand, the possibility of lung sound analysis has been studied as a lung function test for infants and young children [8–10], because they are simple, non-invasive, and do not require the subject's cooperation [11]. In recent years, lung sound analysis

methods have made remarkable progress with the advent of artificial intelligence (AI), and the use of AI has also been reported in the field of pediatric clinical practice [12–15]. Its application in the evaluation of airway narrowing associated with asthma is currently progressing [23], and the analysis of adventitious respiratory sounds is also being investigated for the diagnosis of respiratory diseases in children [24]. The clinical application of this technology in pediatric patients with respiratory diseases is also expanding. As the major advantages of performing a lung sound analysis include the fact that it is non-invasive, simple, and does not require labored breathing [25], lung sound analyses are expected to be an effective means of evaluating the lung function of infants who cannot undergo normal lung function tests.

In this study, we aimed to confirm the persistence of airway damage in infants with RSV acute bronchiolitis and examined the time-dependent changes in various parameters obtained by lung sound analysis in patients hospitalized with RSV acute bronchiolitis. In addition, we compared their results with healthy infants with the same age.

METHODS

Subjects

From June 1, 2021, to December 31, 2022, a retrospective observational study was conducted on infants under 2 years of age who were admitted to our hospital for treatment of RSV acute bronchiolitis and whose parents consented to this study. In accordance with previous reports [16, 17], the severity of acute bronchiolitis, SpO₂ at the time of admission, and length of hospitalization were also confirmed.

As a control for comparison, infants of the same age who underwent infant health checkups in Isehara City between January 8 and March 7, 2025, and whose parents consented to this study were used as controls, and lung sound analysis was performed in the same manner.

This study was reviewed and approved by the Institutional Review Board (IRB) of Tokai University School of Medicine (IRB number; 21R126, 22R136). All parents of the children included in this study provided their written informed consent at the first visit, and they opted out of attending our outpatient clinic from the start of this study (March 1, 2025).

Diagnosis of RSV acute bronchiolitis

The diagnosis of acute bronchiolitis was as previously reported [18, 19]. That is, the diagnosis was made by multiple pediatric specialists on the basis of the following: (1) age was under 24 months and no wheezing history, (2) RSV antigen test was positive, (3) presence of respiratory symptoms, wheezes and/or rhonchi, and (4) clear decrease in SpO₂ and/or clear signs of hyperinflation on chest radiography. All patients underwent nasopharyngeal swab viral antigen testing for RSV (RSV Imunace®, Tauns Co., Izunokuni City, Japan). As previously reported, severity was assessed using the severity score of De Boeck *et al.* [20].

Lung sound analyses

Lung sound analyses were performed for all participants, as described previously [8, 9]. Lung sounds were measured in the supine or sitting position while awake and were acquired using a handheld microphone for ≥ 10 s. The microphone was placed on the right upper anterior chest at the second intercostal space along the mid clavicular line. Each personal lung sound parameter was analyzed conventionally, using a sample with a median value from three tidal breaths.

A sound acquisition of the inspiration and expiration was performed using an LSA-2020 sound spectrometer (Kenz Medico Co., Saitama, Japan). The sound-amplifying unit was set to be effective for analyzing sounds in the range of 100–3,000 Hz. The recorded sounds were analyzed using fast Fourier transformation. The sampling frequency was 10,240 Hz, and the spectra were obtained using a Hamming window.

The power of the low frequency area (100–200 Hz) (LF) and middle frequency area (200–400 Hz) (MF) during inspiration (I) and expiration (E) was calculated from the breath sound spectrum. The power ratio of the expiratory sound to the inspiratory sound (E/I) in the LF and MF was also calculated [21].

The analysis of frequency characteristics of inspira-

tory sounds was performed using software developed using machine learning (ML), and the reliability of this method has previously been reported [15, 22]. The parameter calculation method involves first calculating the analytical base point (0 point), from the spectrum of the subject's inspiratory sound. Next, the highest frequency at the 0 point was calculated as FAP₀ (KHz) for convenience, and the basal lung sound power was calculated as PAP₀ (dBm) [15]. Other lung sound parameters were also created using the 0 point in accordance with the previous lung sound analysis method. In other words, the index obtained by dividing the power (dBm) at 1/2 the frequency from 100 Hz to the 0 point by the frequency at the same time (F₅₀) was defined as RPF_{50p}, and the index obtained by dividing the power (dBm) at 3/4 the frequency by the frequency at the same time (F₇₅) was defined as RPF_{75p}. Furthermore, 2/3 of the frequency from 100 Hz to 0 point was defined as A_{3p}, and the area from A_{3p} to 0 point in the high-pitched region was defined as A_{3a}, and A_{3a}/A_T was calculated by dividing this by the total area (AT). B_{4p} and B_{4a}/A_T were calculated in the same manner.

Evaluation by lung sound analysis

Based on lung sound data from patients with RSV acute bronchiolitis during hospitalization and outpatient care, the changes over time in each parameter of frequency characteristics in inspiratory sounds, the power of expiratory and inspiratory sounds and the power ratio of expiratory/ inspiratory sounds were analyzed. These data were compared with the results of lung sound analysis of healthy children of the same age.

Statistical analysis

Statistical analyses were conducted using SPSS software program (IBM SPSS Statistics, ver. 22 for Windows; IBM Corp., Armonk, NY, USA). To analyze repeated measurements of lung sound parameters, generalized estimating equations (GEE) were used to examine changes in lung sound parameters over time in patients with RSV bronchiolitis. An unstructured correlation was specified to account for within-subject correlation, and the model included time and body height. The Mann-Whitney U test was used to assess differences between patients with RSV bronchiolitis and healthy children. In comparison of the six groups, Bonferroni correction test was used as the criterion for significant differences, and $p < 0.01$ was considered significant. Table data are expressed as median, maximum and minimum values.

RESULTS

Subjects

Fifty-four infants (male: female = 32: 22, median age; 7 months) with RSV acute bronchiolitis underwent lung sound analyses. Finally, a total of 138 measurements (average 2.6 times) were obtained (Table 1). In 54 children with RSV acute bronchiolitis, 44 (81.5%) had fever, 51 (94.4%) had cough, 51 (94.4%) had wheezing, and 12 (22.2%) had pneumonia diagnosed with chest X-ray. The median acute bronchiolitis severity score was 3.0, and the median SpO₂ at admission was 95.5%. Data on the power of the initial lung

Table 1 Profiles of RSV acute bronchiolitis infants and age-matched healthy infants

	Bronchiolitis infants (n = 54)	Healthy infants (n = 34)	p
Age (months)	7.0 [§] (0.5, 22)	7.0 (7.0, 9.0)	0.722
Sex (m:f)	32: 22	18: 16	0.266
Weight (kg)	8.5 (2.8, 13.7)	8.1 (6.9, 10.0)	0.967
Height (cm)	68.9 (47.3, 89.5)	68.9 (60.7, 74.5)	0.652
Severity of bronchiolitis [†]	3.0 (0, 10.0)	—	—
Onset to Hospitalization (days)	4.0 (1.0, 13.0)	—	—
Hospitalization Days (days)	7.0 (3.0, 14.0)	—	—

[§]: Median (minimum, maximum), [†]: Acute bronchiolitis severity score by De Boeck *et al.* (Reference No. 20), P values were calculated by Mann-Whitney U-test.

sounds for 32 of the 54 patients are also included in the report by Kuruma *et al.* [16]. None of the infants with acute bronchiolitis had a history of wheezing.

Using the GEE, time was classified into three groups based on the clinical course (hyperacute phase: within 4 days of onset, acute phase: 5–11 days, and recovery phase: ≥ 12 days), and changes in lung sound parameters were examined.

To facilitate comparison with the control group, lung sound samples were divided into five groups based on the number of days since the onset of bronchiolitis (within 4 days of onset; n = 26, 5–7 days; n = 39, 8–10 days; n = 26, 11–13 days; n = 25, and ≥ 14 days [14–26 days]; n = 22). As controls for comparison, 34 healthy infants of the same age (m: f = 16: 18, median age; 7 months) whose parents consented to the study were used. These infants had no fever, cough, or other respiratory adventitia, and no history of recurrent wheezing, chronic lung disease such as asthma or hospitalization (Table 1).

Evaluation of RSV acute bronchiolitis by the power of inspiratory and expiratory sounds

Differences among the three groups of RSV acute bronchiolitis were examined using GEE. Height was used as a covariate, and the analysis focused on the main inspiratory sound parameters PAP₀ and FAP₀, and the main lung sound power parameters E/I LF and E/I MF. The results showed that there was no significant change in lung sound power over time among the three groups, however, a tendency for E/I MF to decrease over time was observed (Table 2 and 3). Furthermore, similar results were observed in pairwise comparisons among the three groups (Table 4).

In contrast, when comparing the five groups including healthy children, the power of expiratory sounds (E) and inspiratory sounds (I) and the expiratory/inspiratory power ratio (E/I ratio) tended to decrease over time (Table 5). In comparison, the E LF and E MF in the last group (≥ 14 days group) that continued to be observed for RSV acute bronchiolitis showed

significantly higher values.

Evaluation of RSV acute bronchiolitis by frequency characteristics in inspiratory sounds

In the analysis of frequency characteristics in inspiratory sounds using the ML lung sound analysis software program [15, 22], PAP₀ in the acute phase of RSV acute bronchiolitis was the lowest among the three groups. FAP₀ was highest in the acute phase. However, the GEE showed no significant differences from early hospitalization to discharge in any of the three groups (Table 2, 3 and 4).

In contrast to the control group, the PAP₀ and FAP₀ values on days 5–7 and 8–10 after onset were significantly different from those in the control group. However, no significant differences were observed in the FAP₀ values within 4 days after onset (using Bonferroni correction test, Table [6]. In addition, the PAP₀ values in the last group (≥ 14 days) of acute bronchiolitis group were significantly different from those in the control group (p = 0.001) (Table 6).

DISCUSSION

Although most children suffer from RSV respiratory tract infections by 2 years of age, there are quite a few cases that become severe. Furthermore, it has been reported that RSV respiratory tract infection may be related to the onset of asthma [5, 26, 27] and COPD [28]. However, there are many unknowns regarding the healing process over time.

It is significant that this study clarified the characteristics of airway disorders during the acute and recovery phases of RSV acute bronchiolitis. This study confirmed that, in RSV acute bronchiolitis, the power of both inspiratory and expiratory sounds was highest in the early stages of infection and decreased over time. Previous reports have also shown that patients in the acute phase have a clear increase in expiratory sound power due to damage caused by airway inflammation compared to patients in the recovery phase [16, 17]. Previous studies on lung sound power have reported

Table 2 Regression coefficients for parameters of lung sounds over time after bronchiolitis infection using generalized estimating equations (n = 54)

[PAP₀]			95% Wald CI		Hypothesis testing		
Parameter	B	S.E.	Lower limit	Upper limit	Wald chi-square	Degrees of freedom	P value
(Intercept)	6.054	0.948	4.197	7.912	40.805	1	< 0.001
Hyperacute	0.134	1.568	-2.939	3.207	0.007	1	0.932
Acute	-1.499	1.156	-3.765	0.766	1.682	1	0.195
Recovery	Reference	—	—	—	—	—	—
Height	0.004	0.007	-0.008	0.017	0.429	1	0.512

Note: Scale, 20.117

[FAP₀]			95% Wald CI		Hypothesis testing		
Parameter	B	S.E.	Lower limit	Upper limit	Wald chi-square	Degrees of freedom	P value
(Intercept)	1.823	0.049	1.728	1.918	1407.147	1	< 0.001
Hyperacute	-0.005	0.082	-0.165	0.156	0.003	1	0.955
Acute	1.490	0.078	-0.004	0.302	3.649	1	0.056
Recovery	Reference	—	—	—	—	—	—
Height	< 0.001	0.001	0.000	0.000	0.832	1	0.362

Note: Scale, 0.113

[E/I LF]			95% Wald CI		Hypothesis testing		
Parameter	B	S.E.	Lower limit	Upper limit	Wald chi-square	Degrees of freedom	P value
(Intercept)	2.523	0.185	2.160	2.886	185.552	1	< 0.001
Hyperacute	0.057	0.244	-0.421	0.534	0.054	1	0.816
Acute	0.328	0.211	-0.086	0.741	2.408	1	0.121
Recovery	Reference	—	—	—	—	—	—
Height	-0.001	< 0.001	-0.001	< 0.001	7.350	1	0.007

Note: Scale, 0.656

[E/I MF]			95% Wald CI		Hypothesis testing		
Parameter	B	S.E.	Lower limit	Upper limit	Wald chi-square	Degrees of freedom	P value
(Intercept)	1.895	0.201	1.500	2.289	88.621	1	< 0.001
Hyperacute	0.609	0.325	-0.029	1.246	3.499	1	0.061
Acute	0.415	0.244	-0.062	0.893	2.912	1	0.088
Recovery	Reference	—	—	—	—	—	—
Height	0.002	< 0.001	< 0.001	0.003	4.331	1	0.037

Note: Scale, 1.000

B: Regression Coefficient, S.E.: Standard Error, CI: Confidence Interval.

Table 3 Changes of estimated marginal means in parameters of lung sounds over time after bronchiolitis infection using generalized estimating equations (n = 54)

	Group 1 Hyperacute (≤ 4 days)	Group 2 Acute (5–11days)	Group 3 Recovery (≥ 12 days)
E/I LF			
Mean	2.52	2.79	2.46
S.E.	0.13	0.13	0.18
95% Wald CI	2.27, 2.77	2.54, 3.04	2.10, 2.82
E/I MF			
Mean	2.61	2.42	2.01
S.E.	0.21	0.16	0.20
95% Wald CI	2.21, 3.02	2.12, 2.73	1.62, 2.39
PAP ₀			
Mean	6.50	4.87	6.37
S.E.	1.23	0.72	0.79
95% Wald CI [§]	4.10, 8.90	3.46, 6.28	4.81, 7.92
FAP ₀			
Mean	1.81	1.96	1.81
S.E.	0.07	0.06	0.05
95% Wald CI	1.68, 1.94	1.85, 2.08	1.72, 1.91

S.E.: Standard Error, CI: Confidence Interval, [§]: Lower and Upper Limits.**Table 4** Comparison of lung sound parameters among three groups after bronchiolitis infection using generalized estimating equations (n = 54)

E/I LF	Difference in the mean	95% Wald CI	p value
Group 1 vs Group 2	-0.271	-0.621, 0.080	0.130
Group 1 vs Group 3	0.057	-0.421, 0.535	0.816
Group 2 vs Group 3	0.328	-0.086, 0.741	0.121
E/I MF			
Group 1 vs Group 2	0.193	-0.369, 0.755	0.501
Group 1 vs Group 3	0.609	-0.029, 1.246	0.061
Group 2 vs Group 3	0.415	-0.062, 0.893	0.088
PAP ₀			
Group 1 vs Group 2	1.633	-1.242, 4.508	0.266
Group 1 vs Group 3	0.134	-2.939, 3.207	0.932
Group 2 vs Group 3	-1.500	-3.765, 0.766	0.195
FAP ₀			
Group 1 vs Group 2	-0.154	-0.340, 0.033	0.106
Group 1 vs Group 3	-0.005	-0.165, 0.156	0.955
Group 2 vs Group 3	0.149	-0.004, 0.303	0.056

Group 1: Hyperacute phase (≤ 4 days), Group 2: Acute phase (5–11days), Group 3: Recovery phase (≥ 12 days), CI: Confidence Interval.

Table 5 Comparison of lung sound power over time after bronchiolitis infection with control values

Days from Onset (days)	< 4	5–7	8–10	11–13	> 14	Controls
Sample Size (n)	26	39	26	25	22	34
Power of I LF	116.4 [§] (81.3, 147.7)	102.9 (85.4, 137.5)	95.6 (81.5, 129.6)	98.4 (84.4, 130.7)	97.4 (74.3, 140.7)	88.7 (75.3, 121.5)
P [†]	< 0.001	< 0.001	0.009	0.005	0.063	
Power of E LF	105.4 (73.7, 135.3)	99.7 (72.2, 142.4)	97.3 (71.4, 136.4)	85.7 (69.8, 120.4)	86.0 (67.5, 137.2)	74.1 (62.6, 103.9)
P	< 0.001	< 0.001	< 0.001	0.001	0.002	
Log E/I LF	2.59 (1.30, 4.74)	2.67 (1.58, 4.32)	2.64 (1.94, 4.81)	2.39 (0.66, 3.01)	2.56 (0.28, 5.04)	2.25 (1.12, 2.94)
P	0.034	0.002	0.001	0.234	0.038	
Power of I MF	102.3 (84.6, 131.7)	100.0 (74.0, 137.4)	91.8 (68.1, 127.9)	94.0 (77.3, 120.0)	93.4 (77.3, 112.1)	87.3 (68.8, 112.2)
P	< 0.001	< 0.001	0.074	0.053	0.169	
Power of E MF	97.8 (57.4, 133.7)	89.1 (47.0, 138.5)	92.8 (52.7, 132.3)	67.3 (44.5, 110.1)	63.3 (47.1, 124.0)	58.3 (46.1, 82.8)
P	< 0.001	< 0.001	< 0.001	0.003	0.009	
Log E/L MF	2.38 [¶] (1.14, 4.18)	2.09 (1.03, 4.90)	2.42 (0.89, 4.98)	1.87 (-0.06, 2.52)	1.54 (0.98, 4.26)	1.60 (1.89, 10.62)
P	< 0.001	< 0.001	< 0.001	0.149	0.237	

[§]: Median (minimum, maximum). [†]: P values were compared with control data by Mann-Whitney U-test. Using Bonferroni correction test, differences in the comparison among the six groups were considered significant at $p < 0.01$.

Bold p-values indicate that comparisons among the six groups were significantly different compared to the control group.

Table 6 Comparison of inspiratory sound parameters after bronchiolitis infection with those of controls

Days from Onset	< 4	5–7	8–10	11–13	> 14	Controls
Sample Size (n)	26	39	26	25	22	34
PAP ₀	6.23 [§] (0.53, 17.45)	5.44 (-5.26, 20.01)	4.97 (-2.0, 12.18)	5.46 (-1.67, 11.88)	7.64 (-1.47, 12.71)	9.0 (1.92, 12.99)
P [†]	0.005	< 0.001	< 0.001	< 0.001	0.001	
FAP ₀	1.86 (1.03, 2.49)	1.95 (1.44, 2.49)	1.91 (1.0, 2.49)	1.84 (1.49, 2.49)	1.77 (1.51, 2.49)	1.67 (1.23, 2.26)
P	0.045	< 0.001	0.002	0.006	0.037	
RPF _{50p}	2.70 (1.40, 4.13)	2.52 (0.96, 4.09)	2.10 (1.11, 4.29)	2.17 (0.96, 3.57)	2.35 (1.18, 3.39)	1.93 (1.06, 4.04)
P	0.006	0.098	0.509	0.480	0.177	
RPF _{75p}	3.31 (1.04, 5.22)	2.86 (0.6, 4.60)	2.56 (0.81, 5.36)	3.18 (0.57, 4.56)	2.81 (0.71, 4.19)	2.60 (0.59, 5.98)
P	0.192	0.542	0.919	0.545	0.940	
A _{3a} /A _T	12.69 (4.85, 17.68)	12.30 (5.32, 17.58)	11.38 (5.52, 17.17)	12.89 (4.91, 21.77)	11.67 (3.32, 16.78)	12.93 (3.80, 18.80)
P	0.676	0.588	0.225	0.747	0.397	
B _{4a} /A _T	7.34 (2.25, 11.05)	6.80 (1.77, 10.71)	6.45 (2.56, 10.02)	7.50 (1.52, 13.19)	6.40 (1.05, 9.79)	6.75 (1.89, 10.62)
P	0.512	0.544	0.674	0.550	0.580	

[§]: Median (minimum, maximum). [†]: P values were compared with control data by Mann-Whitney U-test. Using Bonferroni correction test, differences in the comparison among the six groups were considered significant at $p < 0.01$.

Bold p-values indicate that comparisons among the six groups were significantly different compared to the control group.

a significant correlation between sound intensity and airway inflammation [21]. It is understandable that the power of inspiratory and expiratory sounds changes over time, as shown in this study.

Because the median number of days between the onset of symptoms and hospitalization in this report was the fourth day, the damage caused by RSV acute bronchiolitis is thought to be significant from around the fourth day after onset of symptoms. Previous reports have suggested that the increase in lung sound power in RSV acute bronchiolitis is due to damage to the bronchial mucosa and the production of highly viscous sputum [29, 30]. It has been pointed out that this increase in sound power may be related to rhonchi (a low-pitched, persistent adventitious respiratory sound) [31, 32], and this increase in lung sound power is thought to directly reflect airway damage.

In contrast, the parameters of inspiratory sounds increased in many cases even after hospitalization, and abnormal values were observed even on the 10th day after onset, close to the time of discharge, after which the parameters gradually improved. Unlike adventitious respiratory sounds, such as wheezes and rhonchi, heard during expiration, the analysis of frequency characteristics in inspiratory sounds has been studied using measurements obtained during resting breathing [8, 9]. Taking advantage of lung sound analysis with excellent sensitivity [15, 22], this approach aims to objectively detect subtle airway abnormalities in symptom-free period. However, it has been pointed out that the influence of airflow (L/sec) on inspiratory sounds is large [8, 15].

In the acute phase of acute bronchiolitis, it is presumed that the tidal volume decreases due to significant air trapping, and the decrease in inspiratory airflow leads to insufficient ventilation [17]. Therefore, it is understandable that the abnormality of inspiratory sound is not clear during the exacerbation phase; rather, the greatest changes are seen during the period of improvement. However, there are many unknowns regarding the cause of inspiratory sounds, which are mainly alveolar breath sounds, thought to be due to turbulence during inspiration [33]. Because elucidating the pathogenesis of RSV acute bronchiolitis is believed to be important for considering the physiological causes of abnormalities in lung sounds, we plan to continue our research in the future.

The most clinically significant finding of this study is that the inspiratory and expiratory sounds of the patients did not return to normal, even close to the date of discharge. The median time from onset to hospitalization was 4 days, and the median length of hospitalization was 7 days; it was estimated that the time to discharge was approximately 11 days after the onset. However, in this study, it is noteworthy that significant differences were observed between the inspiratory and expiratory sound parameters and healthy children, more than 14 days after onset. Although the time was divided into three groups and changes in lung sound parameters were analyzed using a GEE, no significant differences were observed among the groups. This may be related to the presence of severe airway damage caused by RSV infection at all phases.

Pathological findings of RSV acute bronchiolitis include necrosis of bronchial epithelial cells, hyperplasia

of bronchiolar epithelium, infiltration of monocytes and T cells into the bronchi, and infiltration of neutrophils between blood vessels and bronchi [30, 34]. We have previously reported a significant correlation between the E/I value and the severity score of RSV acute bronchiolitis [16]. Previous studies on lung sounds in healthy infants have shown abnormalities in lung sound parameters in infants with a history of RSV infection [11, 22]. However, it is unclear how long the damage from a single RSV infection lasts and what types of children are more likely to sustain damage from RSV infection. Understanding the long-term condition of the airways after RSV infection is important for the infant's subsequent lung function, and lung sound analyses appear to be useful for this purpose.

This study had some limitations. Because it was a retrospective observational study, the timing and frequency of lung sound measurements for hospitalized patients with RSV acute bronchiolitis were not consistent. If the study had been designed prospectively, consistent frequency and timing of measurements might have allowed for more definitive conclusions. Future studies based on lung sound measurements from the date of onset for each patient are desirable.

Furthermore, although it has been reported that the high-pitched region of the spectrum of inspiratory sound as alveolar respiratory sounds increases due to airway narrowing [10, 35], it was not possible to provide an answer to the more fundamental question of whether a similar mechanism occurs in RSV acute bronchiolitis [16, 17]. It was speculated that the increase in expiratory sound intensity in acute bronchiolitis is mainly due to the influence of viscous sputum [16, 17]; however, the abnormality in inspiratory sound in this study was speculated to be due to a different mechanism. The cause of normal inspiratory sounds in lung sound analyses has not yet been clarified [33], which is a major problem and will be addressed in the future.

CONCLUSION

It is necessary to continue to evaluate individual patients with airway damage caused by RSV infection, even after discharge from the hospital. In this study, we utilized a lung sound analysis, which is simple, safe, and can directly assess the state of the airway [21, 22]. We confirmed the changes in lung sounds over time from the acute to the recovery phase of RSV acute bronchiolitis. Observing the progression of airway obstruction and dynamic changes in respiratory physiology in RSV acute bronchiolitis is expected to provide great benefit in the future in understanding airway symptoms and improving treatment through lung sound analysis.

Furthermore, comparing infants with healthy children of the same age, our results suggest that respiratory tract damage persists in infants with RSV acute bronchiolitis even after discharge from the hospital, which is important and confirms the need for follow-up observation. We plan to continue using lung sound analyses to investigate the characteristics of the respiratory condition in infants with RSV acute bronchiolitis.

DATA AVAILABILITY STATEMENT

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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AUTHOR CONTRIBUTION

Takashi Matsushita: conceptualization, data collection and writing-original draft.

Kaiga Chinami: data collection and software.

Kota Hirai: data collection and software.

Fumio Niimura: methodology, writing- review and editing.

Hiroyuki Furuya: writing- original draft and formal analysis.

Yoshiyuki Yamada: methodology and formal analysis.

Atsushi Uchiyama: supervision, writing-review and editing.

Hiroyuki Mochizuki: methodology, conceptualization, supervision, writing- review and editing and data curation.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest in association with the present study.

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Consent

The authors confirm that written informed consent was obtained from all participants in this study. The consent process involved explaining the purpose of using participants' images in this study, the extent of their publication, and assurances that their identities and personal information would remain confidential.

TRANSPARENCY STATEMENT

The lead author (HM) affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and any discrepancies from the study as planned have been explained.

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ABBREVIATIONS

AI: artificial intelligence

GEE: generalized estimating equations

ML: machine learning

COPD: chronic obstructive pulmonary disease

RSV: respiratory syncytial virus

0 point: the maximum point of breath sound spectrum extracted from parameter analysis

AUC: area under the curve

F_{99} : 99% of maximum point in breath sound spectrum

FAP_0 : analysis parameter of frequency at the 0 point

PAP_0 : analysis parameter of power at the 0 point

A_T : total area under the curve of 100 Hz to the 0 point

A_{3a} : third area under the curve divided into 3 parts

B_{4a} : fourth area under the curve divided into 4 parts

A_{3a}/A_T : Ratio of high-pitched third area to total area

B_{4a}/A_T : Ratio of high-pitched fourth area to total area

$dB F_{50p}$: dB at F_{50p}

$dB F_{75p}$: dB at F_{75p}

RPF_{50p} : Ratio of power to $(F_{99p}-F_{50p})[= dB F_{50p}/(F_{99p}-F_{50p})]$

RP_{F75p} : Ratio of power to $(F_{99p}-F_{75p})[= dB F_{75p}/(F_{99p}-F_{75p})]$

E LF: the expiratory sound power in a low-frequency range

I LF: the inspiratory sound power in a low-frequency range

E MF: the expiratory sound power in a mid-frequency range

I MF: the inspiratory sound power in a mid-frequency range

E/I LF: the expiratory-to-inspiratory sound power ratio in a low-frequency range

E/I MF: the expiratory-to-inspiratory sound power ratio in a mid-frequency range

EXPLANATION OF TABLES

Table 1: Patient profile

Table 2: Regression coefficients for lung sound parameters over time after bronchiolitis infection using generalized estimating equations ($n = 54$)

In all parameters, the generalized estimating equations showed no significant differences among the three groups.

Table 3: Changes of estimated marginal means in parameters of lung sounds over time after bronchiolitis infection using generalized estimating equations ($n = 54$)

No significant differences were observed for sound power or inspiratory sound parameters; however, each parameter tended to change over time.

Table 4: Comparison of lung sound parameters among three groups after bronchiolitis infection using generalized estimating equations ($n = 54$)

No significant differences were observed in the comparison of acoustic power and inhalation sound parameters between the three-phase pairs.

Table 5: Comparison of lung sound power over time after bronchiolitis infection with those of controls

Significant changes over time were observed for each parameter among the six groups. The Bonferroni correction test was used as the criterion for significant differences, with $p < 0.01$ indicating statistical significance.

Table 6: Comparison of inspiratory sound parameters after bronchiolitis infection with those of controls

Significant changes over time were observed for each parameter among the six groups. The Bonferroni correction test was used as the criterion for significant differences, with $p < 0.01$ indicating statistical significance.

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