

Relationship Between Lung Sound Power and Factors Related to the Onset of Asthma in Three-year-old Children

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(Received October 24, 2025; Accepted December 19, 2025)

Objective: Childhood asthma can lead to chronic obstructive pulmonary disease in adults, thus necessitating an early diagnosis and timely intervention from early childhood.

Methods: A retrospective study was conducted on parameters related to lung sound power in three-year-old healthy children. All cases were surveyed using the ATS-DLD questionnaire, which mainly covered items related to the history of wheezing, diagnosis of asthma/asthmatic bronchitis, and history of allergies, and then lung sounds were measured. From these data, the characteristics of inspiratory and expiratory sound power at this age were examined.

Results: There were correlations between the parameters related to lung sound power at the low- and middle-range frequencies. In addition, children with a history of wheezing or diagnosed with asthma/asthmatic bronchitis showed an increase in the power of inspiratory and expiratory sounds and the power ratio of inspiratory and expiratory sounds compared with children without such histories. Furthermore, the parameters of lung sound power correlated with those of the inspiratory sound spectrum.

Conclusions: Measurements of the power of inspiratory and expiratory sounds confirmed that three-year-old children with a history of wheezing or diagnosed asthma/asthmatic bronchitis had characteristic lung sounds even when healthy.

Key words: asthma, children, lung sound analysis, machine learning, sound power

ABBREVIATIONS

AI: artificial intelligence
ARI: acute respiratory tract infection
COPD: chronic obstructive pulmonary disease
RSV: respiratory syncytial virus
AUC: area under the curve
F₉₉: 99% of maximum point in breath sound spectrum
0 point: the maximum point of breath sound spectrum extracted from parameter analysis
FAP₀: analysis parameter of frequency at the 0 point
PAP₀: 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
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})]
RPF_{75p}: Ratio of power to (F_{99p} - F_{75p}) [= dB_{F_{75p}} / (F_{99p} - F_{75p})]
LF: low frequency area (100–200 Hz)
MF: middle frequency area (200–400 Hz)

I: inspiration

E: expiration

INTRODUCTION

Recently, many studies have suggested that childhood asthma and severe respiratory tract infections in infants are risk factors for chronic obstructive pulmonary disease (COPD) in adults [1, 2]. Furthermore, a preterm birth, which accounts for 6–10% of all births, is thought to be a risk factor for the development of both childhood asthma [3, 4] and a respiratory function decline in adults [5, 6]. Therefore, early diagnosis and appropriate intervention of pediatric respiratory diseases are important to prevent the onset and progression of lung function declining later in life.

However, it remains difficult for physicians to make a definitive diagnosis of asthma in young children [7]. Although a history of repeated wheezing is the most important information for diagnosing asthma [8], the appearance of wheezing differs from the results of lung function tests [9] and that it is difficult for guardians to make correct assessments overnight [10]. Furthermore, the evaluation of bronchial hyperresponsiveness is difficult to use in pediatric clinical practice because young children are unable to follow the exam-

iner's instructions [7, 8].

In recent years, respiratory sound analyses can be used to evaluate airway changes in young children as a safe and simple method [11, 12]. Recent advances in artificial intelligence (AI) technology have improved the ability to extract information related to clinical diseases from lung sounds [13, 14]. We have recently developed an automatic analysis software program that utilizes machine learning (ML) algorithms to perform reliable lung sound analyses in children [15] and have reported on the relationship between parameters of high-pitched inspiratory sounds and a history of wheezing and asthma/asthmatic bronchitis in three-year-old children [16], as well as the peculiarities of lung sounds in early infancy [17].

On the other hand, lung sound analyses based on the power of low- and middle-pitched sounds, which are less susceptible to the low-pass filter effect of the lungs and thorax, have shown good results in studies of asthma and airway inflammation in adults [18, 19]. Studies on acute bronchiolitis in infants also showed a good correlation between lung sound power and clinical symptoms [20, 21].

The present study analyzed parameters related to the respiratory sound power in healthy three-year-old children, investigated the characteristics of lung sound power at this age, and examined the relationship with factors related to the onset of asthma. Furthermore, the results of respiratory sound power were compared

with the results of the high-pitched inspiratory sound spectrum using a new software program [15, 16].

METHODS

Subjects

The subjects were healthy children who underwent infant health checkups at the age of three years old. Children who had severe respiratory, circulatory, or neurological diseases were excluded. As previously reported [22], all parents of participants agreed to participate in the study and completed the ATS-DLD questionnaire (Japanese version) [23]. The subjects were in a quiet room and lung sounds were collected while breathing at rest. The results of an analysis of the inspiratory sound spectrum of these children were reported by Mochizuki *et al.* [16].

The study protocol was approved by the institutional review board of Tokai University Hospital (No. 22R-136, approval date: October 20, 2022). In these studies, written informed consent was obtained from all parents.

Correction of lung sounds

Lung sounds were collected as previously reported [12, 24], using a commercially available lung sound analysis system (LSA-2020; Kenz Medico Co., Saitama, Japan) for ≥ 10 seconds in a quiet room (Fig. 1). A handheld microphone (BSS-01; Kenz Medico Co.) was placed in the second intercostal space along the midcla-

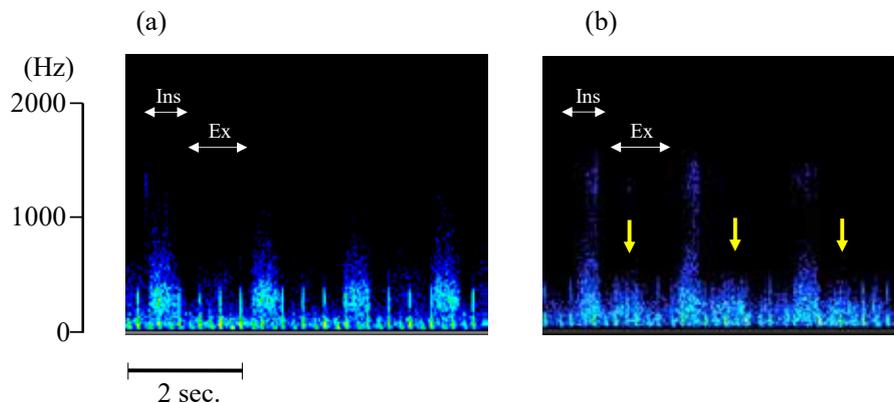


Fig. 1 Lung sound spectrogram of three-year-old children

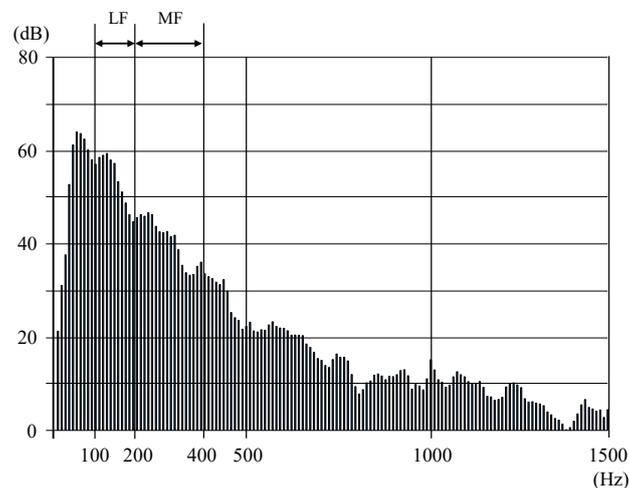


Fig. 2 Low frequency area and middle frequency area in lung sound spectrum

vicular line. An acoustic amplification unit was found to be effective for the analysis of inspiratory sounds in the range of 100–2500 Hz. The recorded lung sounds were analyzed using a fast Fourier transform. The sampling frequency was 10,240 Hz, and the spectrum was obtained using a Hanning window. We have a rule to measure at the best possible time every time, emphasize the importance of calm breathing, and work with parents to wait until the subject has calmed down.

The analysis of the inspiratory and expiratory sound power

As previously reported [18, 19], the median power of the low-frequency area (LF; 100–200 Hz) and middle frequency area (MF; 200–400 Hz) in the inspiration (I) and expiration (E) pairs were calculated from the lung sound spectrum (Fig. 2) and the median value of the samples of the three breath pairs was also calculated and used. The power ratio of expiration-to-inspiration sound (E/I) in the LF and MF were also calculated.

The analysis of the spectrum of inspiratory sounds

From the collected lung sound spectrogram, the examiner selected a 10-sec section that was considered optimal for measurement because it was free of noise and crying. From the inspiratory sounds within this section, the new analysis software program automatically selected a typical sample [16]. The lung sound parameters of the selected inhalation sounds were calculated automatically.

As a first step, to calculate the new parameters using the software created using ML, the analytical base point (0 point) was calculated from the spectrum of the subject's inhalation sounds. Next, the maximum frequency at 0 points was calculated as the FAP_0 (KHz) for convenience, and the basal lung sound power was calculated as the PAP_0 (dBm) [15]. Other lung sound parameters were also created using the 0 point in accordance with a previous lung sound analysis method. The index obtained by dividing the power (dB) at half the frequency from 100Hz to the 0 point by the frequency at the same time (F_{50}) was defined as RPF_{50p} , and the index obtained by dividing the power (dB) at three-quarters the frequency from 100Hz to the 0 point by the frequency at the same time (F_{75}) was defined as RPF_{75p} . Furthermore, two-thirds of the frequency from 100 Hz to 0 points was defined as A_{3p} , and the area from A_{3p} to the 0 point in the high-pitched region was defined as A_{3a} , A_{3a}/A_T was calculated by dividing this by the total area (A_T). The B_{4p} and B_{4a}/A_T ratios were calculated in the same manner [15].

Relationship between lung sound power and asthma onset factors

The ATS-DLD questionnaire was used to ascertain whether participants had acute respiratory tract infection (ARI) within the past week; a history of wheezing or allergic disease, a doctor's diagnosis of asthma/asthmatic bronchitis, respiratory syncytial virus (RSV) infection and hospitalization due to airway disease; a family history of allergies; and the presence or absence of smoking, pets, or air pollution in home (Appendix, Table A1) [23]. The results of this questionnaire were compared with the results for each parameter of lung

sound power.

Relationship between lung sound power and inhalation sound spectrum

The relationship between the parameters of inspiratory and expiratory sound power in low- and middle-range frequencies and the parameters of inspiratory sound spectrum in high-range frequencies were examined, focusing on the correlation.

Statistical analysis

Statistical analyses were conducted using the SPSS software program (IBM SPSS Statistics, Version 22 for Windows; IBM Corp., Armonk, N.Y., USA). Correlation coefficients were calculated using Pearson's correlation coefficient. The Mann-Whitney U-test was used to evaluate the differences between the two groups. The association of factors affecting lung sound parameters was examined by linear regression analysis using the forced entry method. Binary logistic regression analysis was performed to adjust for the association between lung sound parameters and confounding factors. $P < 0.05$ was considered significant. Data are expressed as the median, maximum and minimum values.

RESULTS

Subjects

Of the 145 healthy children who underwent three-year-old health checkups in Isehara City between January 1, 2023, and March 31, 2024, lung sounds were collected and analyzed in 139 children (median age, 3 years 0 month, old; boys: girls, 66: 73) [16]. An analysis was not possible in six children because they were crying during the measurement. In addition, parents of 28 (boys: girls, 16: 12) of the 139 children reported that their children had suffered from ARI within the past week despite having no obvious respiratory symptoms on the day of the examination.

Characteristics of lung sound power in three-year-old children

There was a correlation between the inspiratory sound power (I LF, I MF) and sex and weight, and the intensity of the inhalation sound tended to be louder in boys than in girls, and in lighter children than in heavier children (Table 1). In addition, children with higher respiratory rates tended to have greater increases in inspiratory and expiratory sound power than children with lower respiratory rates. However, no such relationship was found for E/I LF and E/I MF, which are clinically important parameters [19].

Furthermore, we investigated the correlation between the factors affecting lung sound parameters in a different manner. Each lung sound parameter was used as the dependent variable, and sex, weight, and respiratory rate were used as covariates to examine their influence using a forced-entry linear regression analysis. The lung sound parameters that were found to have a significant effect on the overall model fit were I LF ($F = 7.72$, $p < 0.001$, adjusted $R^2 = 0.133$), E LF ($F = 6.20$, $p < 0.001$, adjusted $R^2 = 0.106$), I MF ($F = 5.31$, $p = 0.002$, adjusted $R^2 = 0.110$), and E MF ($F = 4.28$, $p = 0.006$, adjusted $R^2 = 0.090$). In contrast, no significant effects were found for E/I LF ($F = 2.326$, $p = 0.078$, adjusted $R^2 = 0.029$) or E/I MF ($F = 0.852$,

Table 1 Relationship between sex, height and weight and each parameter in three-year-old children

		Sex (m: f)	Height (cm)	Weight (kg)	Respiratory Rate (/min)
I LF(dB)	CC	0.201	-0.109	-0.246	0.220
	P	0.018	0.213	0.004	0.009
E LF(dB)	CC	0.117	-0.060	-0.118	0.321
	P	0.171	0.497	0.177	< 0.001
E/I LF	CC	-0.060	0.033	0.095	0.145
	P	0.484	0.708	0.278	0.088
I MF(dB)	CC	0.177	-0.064	-0.151	0.239
	P	0.037	0.469	0.082	0.005
E MF(dB)	CC	0.074	-0.019	-0.074	0.273
	P	0.385	0.825	0.396	0.001
E/I MF	CC	-0.071	0.032	0.049	0.083
	P	0.404	0.713	0.577	0.334

Correlation coefficients (CC) were calculated by Pearson's correlation coefficient. Bold letter of p-value for CC shows a statistical significance.

Table 2 Relationship between the parameters of lung sound power in three-year-old children

		I LF	E LF	E/I LF	I MF	E MF	E/I MF
I LF	CC	-	0.509	-0.372	0.690	0.443	-0.119
	P	-	< 0.001	< 0.001	< 0.001	< 0.001	0.164
E LF	CC	0.509	-	0.611	0.377	0.742	0.451
	P	< 0.001	-	< 0.001	< 0.001	< 0.001	< 0.001
E/I LF	CC	-0.371	0.611	-	-0.228	0.392	0.596
	P	< 0.001	< 0.001	-	0.007	< 0.001	< 0.001
I MF	CC	0.690	0.377	-0.228	-	0.443	-0.378
	P	< 0.001	< 0.001	0.007	-	< 0.001	< 0.001
E MF	CC	0.443	0.742	0.392	0.443	-	0.663
	P	< 0.001	< 0.001	< 0.001	< 0.001	-	< 0.001
E/I MF	CC	-0.119	0.451	0.596	-0.378	0.663	-
	P	0.164	< 0.001	< 0.001	< 0.001	< 0.001	-

Correlation coefficients were calculated by Pearson's correlation coefficient. Bold letter of p-value for CC shows a statistical significance.

$p = 0.468$, adjusted $R^2 = -0.003$).

Furthermore, an examination of the regression coefficients and significance of each variable revealed significant relationships between I LF and respiratory rate, sex, and weight ($p = 0.049$, $p = 0.005$, and $p < 0.001$, respectively), E LF and respiratory rate ($p < 0.001$), I MF and respiratory rate, and sex ($p = 0.009$ and $p = 0.024$, respectively), E MF and respiratory rate ($p = 0.001$), and E/I LF and respiratory rate ($p = 0.032$). However, no significant effect was observed between E/I MF and respiratory rate.

In Table 2, significant correlations were found between lung sound parameters, for example, between I LF and E LF, and between I MF and E MF. Correlations were also found between the power of the low and middle ranges of inspiration, and between the power of the low and middle ranges of expiration (Table 2).

Relationship between questionnaire item and parameters of lung sound power

The correlation between the results of the ATS-DLD version of the questionnaire on asthma and allergies was examined for 139 children, and the results are shown in Table 3. In children with a history of wheezing (Q2: ever having wheezing, Q3: summary of questions on wheezing from ARI), even in the absence of respiratory symptoms, increases were observed in all six parameters of lung sound power at rest compared to children without such histories (Table 3). In chil-

dren who had been diagnosed with asthma/asthmatic bronchitis by a physician (Q7), significant increases were observed in the E LF, E MF, E/I LF, and E/I MF. Although no differences in any of the parameters were observed depending on whether the subject had a history of RSV infection or allergic diseases, an increase in I MF was observed in children with smokers in the home.

Considering the influence of confounding factors, responses such as the presence or absence of wheezing were used as the dependent variable in a binary logistic regression analysis, and the correlation with lung sound parameters was adjusted for the respiratory rate, sex, and weight. The results are presented in Table 4. Even after making adjustments, significant differences in E LF and E MF were observed in the children with a history of wheezing. Furthermore, the adjustment for E/I MF was significant in children with a history of asthma/asthmatic bronchitis (Table 4).

A comparison of children with and without a history of wheezing using receiver operating characteristic curves showed that, for E/I MF, the most trusted parameter to date [19], the AUC was 0.711, asymptotic significance was < 0.001 , and 95% confidence interval (0.616, 0.806). For E/I MF, the cutoff value for the presence or absence of a history of wheezing was calculated using Youden's index and was 0.202, with a sensitivity of 0.58 and a specificity of 0.80.

Because it has been reported that the history of ARI within a week affects the lung sounds of children with

Table 3 Results of the questionnaire and lung sound analysis in three-year-old children

	LF			MF		
	I LF (dB)	E LF (dB)	E/I LF	I MF (dB)	E MF (dB)	E/I MF
Wheezing [†] (+)	96.0 [§]	88.1	2.50	87.3	68.4	2.06
(n = 45)	(73.6, 118.6)	(64, 105.6)	(1.51, 3.55)	(73.0, 109.7)	(46.8, 105.3)	(1.17, 3.63)
Wheezing (-)	89.8	74.2	2.25	84.4	57.4	1.66
(n = 94)	(73.1, 127.2)	(60.0, 97.8)	(0.28, 3.25)	(66.9, 122.0)	(49.6, 86.9)	(0.17, 3.13)
P	0.002	< 0.001	< 0.001	0.044	< 0.001	< 0.001
Asthma (+)	92.9	83.0	2.56	84.7	66.2	2.11
(n = 20)	(73.6, 108.3)	(65.0, 105.6)	(1.51, 3.55)	(74.2, 109.4)	(46.8, 105.3)	(1.17, 3.13)
Asthma (-)	90.8	76.3	2.27	86.0	59.0	1.70
(n = 119)	(73.1, 127.2)	(60.0, 102.6)	(0.28, 3.47)	(66.9, 122.0)	(49.6, 89.7)	(0.17, 3.63)
P	0.627	0.019	0.017	0.959	0.023	0.006
RSV (+)	94.5	80.1	2.42	85.9	63.6	1.80
(n = 50)	(73.6, 113.8)	(62.3, 105.6)	(1.16, 3.38)	(73.0, 109.7)	(46.8, 95.4)	(1.01, 3.63)
RSV (-)	90.1	76.0	2.26	85.5	58.3	1.70
(n = 89)	(73.1, 127.2)	(60.0, 102.5)	(0.28, 3.55)	(66.9, 122.0)	(50.2, 105.3)	(0.17, 2.80)
P	0.148	0.069	0.186	0.495	0.063	0.227
Atopy [‡] (+)	91.6	82.4	2.32	85.1	61.5	1.85
(n = 28)	(77.6, 113.8)	(63.2, 102.6)	(1.58, 3.55)	(69.6, 109.7)	(46.8, 89.7)	(1.01, 2.80)
Atopy (-)	90.8	77.2	2.29	85.8	59.0	1.70
(n = 111)	(73.1, 127.2)	(60.0, 105.6)	(0.28, 3.47)	(66.9, 122.0)	(49.6, 105.3)	(0.17, 3.63)
P	0.551	0.312	0.495	0.815	0.470	0.537
Smoking (+)	92.9	75.9	2.27	90.3	61.3	1.56
(n = 34)	(80.5, 113.8)	(63.1, 102.6)	(1.68, 2.95)	(74.6, 109.7)	(50.2, 105.3)	(0.98, 2.80)
Smoking (-)	90.8	77.5	2.33	84.4	59.0	1.80
(n = 105)	(73.1, 127.2)	(60.0, 105.6)	(0.28, 3.55)	(66.9, 122.0)	(46.8, 95.4)	(0.17, 3.63)
P	0.251	0.808	0.273	0.012	0.619	0.096

†: Wheezing group: infants with positive responses for wheezing-related items (Question 2 or 3), ‡: Atopy group: infants with positive responses for atopy-related items (Question 10 or 11), §: Median (minimum, maximum). P values were calculated by Mann-Whitney U-test. Bold letter of p-value shows a statistical significance.

Table 4 Results of the multivariate comparison of outcomes in three-year-old children

Wheezing [†]	Unadjusted OR (95% CI)	P values	Adjusted OR [‡] (95% CI)	P values
E LF	0.930 (0.876–0.986)	0.016	0.932 (0.879–0.989)	0.021
E MF	0.939 (0.886–0.995)	0.033	0.938 (0.885–0.994)	0.030
Asthma	Unadjusted OR (95% CI)	P values	Adjusted OR (95% CI)	P values
E MF	0.942 (0.905–0.981)	0.004	N/A	N/A
E/I MF	N/A	N/A	0.179 (0.063–0.507)	0.001

†: Wheezing group: infants with positive responses for wheezing-related items (Question 2 or 3), ‡: Adjusted p was adjusted for sex, weight and respiratory rate. Factors were analyzed using logistic regression models with the forced entry method. Definition of abbreviations: OR = odds ratio; CI = confidence interval; N/A = not applicable.

a history of wheezing [15, 25], the 139 participants were divided into a group of 94 children with no history of wheezing and a group of 45 children with a history of wheezing, and the effects of ARI were examined in each group. The history of ARI, with or without a history of wheezing, did not significantly affect lung sound power. (data not shown).

Relationship between parameters of lung sound power and parameters of inspiratory sound spectrum

The relationships between the parameters of lung sound power and the parameters of inspiratory sound spectrum in all 139 subjects were examined. An inverse correlation was found between all lung sound power parameters and PAP₀, which is the basal lung sound power, and a positive correlation was found between all lung sound power parameters and FAP₀, which indicates the highest frequency (Appendix Table

B1). For other inspiratory sound parameters, correlations were found between I MF and A₃/A_T and B₄/A_T.

DISCUSSION

In this study, we investigated the characteristics of lung sound power in three-year-old children, using parameters related to low- and middle-pitched expiratory and inspiratory sound powers. This method has been previously examined in adult asthma patients [18, 19], children with asthma [26] and infants with RSV acute bronchiolitis [20, 21], and several new discoveries have been made using this method.

In analyses of lung sound power in infants, the respiratory rate, sex, and weight may be influential confounding factors. Although the adjusted R² was < 0.5 in all multiple regression analyses, this needs to be taken into consideration as a characteristic of lung sound power in children. However, the E/I rate has been used as a reliable parameter in adults [18,

19], and because the influence of respiratory rate, sex, and weight is minimal in infants, it is thought to be a parameter that will continue to deserve attention. Furthermore, as shown in Table 4, even after making adjustments, E/I MF showed significant results for the diagnosis of asthma/asthmatic bronchitis, suggesting that parameters related to lung sound power are meaningful in the clinical setting of pediatric respiratory diseases.

Interestingly, children with a history of wheezing or asthma/asthmatic bronchitis showed an increase in lung sound power, especially expiratory sound power. In our previous investigations of inspiratory sound spectrum [16], similar differences were observed in children with a history of wheezing or asthma/asthmatic bronchitis. It is important to note that these differences were observed on the day of the infant health checkups when the children were considered healthy. It has been reported that abnormalities in flow-volume curves are always observed in asthmatic patients before treatment, regardless of the presence or absence of respiratory symptoms [27]. It would be worthwhile to screen children for asthma by evaluating such constant findings through lung sound analyses during infancy.

Consistent with previous reports [16], no significant correlation was found between the presence of allergic disease and lung sound parameters. Previous reports have suggested that allergic asthma and RSV-induced asthma in young children may belong to different phenotypes [28, 29]. However, bronchial hyperresponsiveness, which is the main pathology of allergic asthma, indicates the reversibility of bronchial constriction, and it is also assumed that bronchial constriction may not exist in the healthy stage. As there are reports that RSV infection can trigger the onset of atopic asthma [30], this issue should also be addressed in the future.

Furthermore, it is interesting that there was a clear correlation between the power of inspiratory and expiratory sounds during tidal breathing. In chest auscultation and lung sound analyses of healthy adults and children, expiratory sounds are difficult to detect in normal breath sounds (so-called vesicular breath sounds) [31, 32]. When examining the power ratio of inspiratory and expiratory sounds, it is necessary to consider the mechanism by which normal inspiratory and expiratory sounds are generated. Although, many previous studies on expiratory adventitious sounds such as wheezes were reported [33, 34], there have been few reports of normal breath sounds [35], making this difficult to discuss. We speculate that the mechanisms of expiratory and inspiratory sounds differ fundamentally in terms of respiratory physiology. In other words, it is thought that the generation of lung sounds during inhalation is caused by airflow diverging from the central airway to the peripheral airway, whereas the generation of lung sounds during exhalation is caused by airflow merging from the peripheral airway to the central airway [31].

It is known that turbulence in the airway tubes is deeply involved in the generation of both normal breath sounds and adventitious sounds such as wheezes [31] and it has been speculated that the area of the airways where turbulence is likely to occur fluid-dynamically is around the fifth to seventh bronchial bifurcations [34]. As turbulence is the main mechanism of

sound generation, the generation of expiratory sounds may occur when expiratory air integrates at each bronchial bifurcation, causing turbulence upstream of the airways [31], and which has also been confirmed by 3D models [36]. In contrast, the airflow is divided at the bronchial bifurcation during inhalation, causing Karman vortices [37], and normal inspiratory sounds were generated as an integrated sound from multiple bronchial bifurcations. However, this study confirmed that, in a healthy airway, the power ratio of inspiratory and expiratory sounds during quiet breathing is constant. We speculated that when airway inflammation and/or narrowing is present, this balance is disrupted, and the generation of turbulence increases during expiration compared to inspiration [9].

Also of interest, there was a correlation between the parameters of lung sound power and the parameters of the inspiratory lung sound spectrum. Correlations were observed between the sound power parameters (E/I LF and E/I MF) [18], which suggest changes in low- and middle-pitched sounds, and the inspiration sound parameters (PAP_0 and FAP_0) [15], which suggest changes in high-pitched inspiratory sounds. These results indicate the reliability of lung sound analysis as a lung function test that can evaluate airway abnormalities individually.

Several limitations associated with the present study warrant mention. First, it was limited to three-year-old children, so it is not possible to conclude that this is a characteristic of the overall population of children. In addition, when analyzing the lung sounds of children, particularly young children, complex changes can occur such as periodic changes in breathing strength [17] and crying, making it difficult to measure as accurately as with older children. As the current method has limitations with regard to reproducibility, we plan to implement AI, among other tools, to confirm the breathing patterns of each children and extract the ideal lung sound spectrum.

Furthermore, regarding the phenotype classification of childhood asthma [28, 29], the current data did not allow sufficient consideration of the relationship between parameters related to lung sound power and atopic constitution or smoking at home. Since lung sound analyses in young children have only just begun, we plan to continue to consider multifaceted analysis methods.

CONCLUSION

A comparison of the results of lung sound power analysis [18] with the results of inspiratory sound spectrum analysis [15] showed that they had the same accuracy in the history of wheezing and diagnosing asthma/asthmatic bronchitis. Although these two methods involve different respiratory physiological evaluations, the reliability of both methods was proven because the same trends were observed.

In this report, we were able to characterize the power of lung sounds in infants and young children. However, because long-term observation was not conducted, we were unable to make a definitive diagnosis of bronchial asthma in the subjects. The fact that diagnosing asthma in infants and young children remains difficult [7, 8] is largely due to the inability to objectively and directly evaluate the lung function. We

would like to develop better diagnostic methods and criteria for infantile asthma utilizing multiple lung sound analysis methods, such as the analysis of high-pitched inspiratory sound spectrum and the analysis of low- and middle-pitched lung sound power. We believe that examining screening methods for declining lung function from an early age may be useful in preventing declining lung function later in life.

DATA AVAILABILITY STATEMENT

For further details beyond the data provided in the main text, please contact the corresponding authors.

FUNDING

This study received no support.

AUTHOR CONTRIBUTIONS

MI and HM conceptualized and designed the study, drafted the initial manuscript, and critically reviewed and revised the manuscript. TS, FN designed the data collection instruments. HF and MK carried out the initial analysis. YY and AU critically reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

CONFLICTS OF INTEREST

The authors have no conflicts of interest.

ACKNOWLEDGMENTS

We would like to thank Dr. Terufumi Shimoda, Department of Allergy, San Remo Rehabilitation Hospital, for his kind guidance in calculating the inspiratory and expiratory sound power.

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Appendix Table A1 Original questionnaire (translated to English)

Child' name _____ Address _____

Sex (1, Male 2, Female), Birthday (___/___/20___), Age ___years___month,

Height _____cm, Weight _____kg, Birth weight _____kg

Q1. Has your child recently caught an acute respiratory infection?
 1. He/She has not had an acute respiratory infection for a week.
 2. He/She recovered from an acute respiratory infection () days ago.
 3. He/She has an acute respiratory infection now.

Q2. When your child breathes, have you heard the sound of wheezing or whistling?
 (1, Yes 2, No)

Q3. When your child has had a cold, have you heard a wheezy or whistling sound?
 (1, Yes 2, No)

Q4. How many times has your child's chest sounded wheezy?
 (1, 0 times, 2, 1-2 times, 3, 3-6 times, 4, 7-12 times, 5, More than 13 times)

Q5. Has your child suffered from attacks characterized by difficulty breathing with wheezing or whistling?
 (1, Yes 2, No)

Q6. If yes, how many such attacks has your child had?
 (1, 0 times, 2, 1-2 times, 3, 3-6 times, 4, 7-12 times, 5, More than 13 times)

Q7. Has your child been diagnosed with bronchial asthma or asthmatic bronchitis by a physician?
 (1, Yes 2, No)

Q8. Has your child been diagnosed with an RS virus-induced respiratory infection?
 (1, Yes 2, No)

Q9. Has your child been hospitalized because of bronchial asthma, bronchitis or pneumonia?
 (1, Yes 2, No)

Q10. Does your child have any allergies?
 (1, Yes 2, No)

If yes and a blood test was performed, please select all that were positive.
 (1.Mites 2.House dust 3.Cedar Pollen 4.Cat dander 5.Egg white 6.Milk 7.Others ())

Q11. Has your child been diagnosed with atopic dermatitis by a physician?
 (1, Yes 2, No)

Q12. Do your child's family have any of the allergic diseases described below?
 Please connect the corresponding upper and lower words with a line.
 [Asthma, Allergic rhinitis (hay fever), Atopic dermatitis, Others]
 [Father, Mother, Siblings, Grandparents]

Q13. Is there anyone who smokes in your house? Please circle all that apply.
 (1, Father 2, Mother 3, Others 4, None)

Q14. What kind of domestic pets do you keep?
 (1, Dog 2, Cat 3, Others 4, None)

Q15. Is there a road with heavy traffic near the house?
 (1, Yes 2, No)

Q16. Has your child been diagnosed with COVID-19?
 (1, Yes 2, No)

Appendix Table B1 Relationship between the parameters of lung sound power and the parameters of inspiration in three-year-old children

		I LF	E LF	E/I LF	I MF	E MF	E/I MF
PAP ₀	CC	-0.233	-0.378	-0.193	-0.288	-0.394	-0.167
	P	0.006	< 0.001	0.023	< 0.001	< 0.001	0.049
FAP ₀	CC	0.279	0.490	0.271	0.266	0.514	0.309
	P	< 0.001	< 0.001	0.001	0.002	< 0.001	< 0.001
RPF _{50p}	CC	-0.032	-0.065	-0.041	0.039	-0.064	-0.099
	P	0.704	0.445	0.633	0.648	0.453	0.247
RPF _{75p}	CC	-0.081	0.012	0.088	-0.110	-0.059	0.032
	P	0.340	0.887	0.305	0.195	0.490	0.712
A _{3a} /A _T	CC	-0.083	-0.037	0.037	-0.211	-0.113	0.060
	P	0.332	0.666	0.668	0.013	0.186	0.481
B _{4a} /A _T	CC	-0.086	-0.078	-0.005	-0.222	-0.124	0.058
	P	0.316	0.360	0.953	0.009	0.146	0.499

Correlation coefficients were calculated by Pearson's correlation coefficient. Bold letter of p-value for CC shows a statistical significance.