



Original article

Evaluation of airflow limitation using a new modality of lung sound analysis in asthmatic children



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ABSTRACT

Background: Reliable assessment of not only symptoms but also lung function is essential in asthma management. We developed a new technology for analyzing lung sounds and assessed its clinical usefulness in asthmatic children.

Methods: Forty-four children underwent lung sound recording with simultaneous airflow measurement using a sensor on the upper right anterior chest. We calculated a sound parameter index from the amplitude of inspiratory lung sounds at 700 Hz (ic700). ic700 were compared depending on flow and body size. In addition, 184 asthmatic children and 16 non-asthmatic children underwent lung sound analysis and lung function test in an asymptomatic state. In the asthma group, 135 children received treatment continually. The untreated asthma group included 28 children who had never received treatment continually and 21 children who had not been treated for at least 1 year. The asthmatic children were divided into four classes according to asthma severity. ic700 were compared depending on spirometric parameters and asthma severity classification.

Results: The influences of flow and body size were negligible for ic700. ic700 correlated with FEV₁%, MMF and FEF50 ($r = -0.436$, -0.339 and -0.302 , respectively). There was a significant difference of ic700 between asthmatic and non-asthmatic children ($p < 0.001$), and ic700 correlated with the classification of asthma severity ($p < 0.001$). The ic700 scores of the severe group were higher than those of the intermittent group and non-asthmatic children.

Conclusions: It was possible to evaluate airway dysfunction of asthma using ic700, which was calculated non-invasively by analyzing lung sounds alone, without measuring body size and airflow.

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Introduction

Asthma control should include not only clinical manifestations, but also objective parameters of airflow limitation and airway inflammation.¹ Reliable assessment of asthma control is essential to manage asthma efficiently.² Therefore, objective monitoring will be a useful tool in the management of small asthmatic children. However, for small children, it is not easy to perform lung function tests.

Lung sound analysis is a non-invasive method that does not require the cooperation of small children. Airway inflammation and airflow limitation affect breath sounds even in the absence of adventitious sounds.^{3–5} Recent developments in signal processing methods have improved the possibility of extracting physiologically and clinically relevant information from lung sounds.^{3–5} It has been reported that acoustic transfer characteristics may be affected by airway wall compliance, airway diameter and energy dissipation caused by respiratory motion.^{6–8}

We reported our indices of lung sound analysis that uses acoustic transfer characteristics of the pulmonary system, which were measured at 2 points, namely, trachea and chest surface, while evaluating asthmatic children. Our acoustic indices were not affected by body size and airflow.⁹ We also reported that our index

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of lung sound analysis correlated with C-ACT score and indicated the level of control of asthma in this journal in 2013.¹⁰ Subsequently, we attempted to simplify this measurement and developed a new index that requires the measurement of lung sounds at only one location on the chest surface and can also avoid the effects of body size and airflow. In this study, we investigate whether this new index of lung sound analysis can detect flow limitation.

Methods

Subjects and study design

We examined 44 healthy children (age: median 10 years, from 5 to 15 years; height: median 136 cm, from 113 to 171 cm; weight: median 33 kg, from 17 to 60 kg) and recorded lung sounds with airflow. All the patients changed their breath pattern, involving alternation between shallow and deep breathing. Lung sounds were recorded at the upper right anterior chest at the second intercostal space on the midclavicular line, using a sound sensor (MA-300; FUKUDA DENSHI, Tokyo, Japan) fixed with tape (H260; NIHON KOHDEN, Tokyo, Japan) on the chest wall. Airflow was measured using a Lilly-type flow meter, Lung Sound Analyzer (LSA-2000; KENZMEDICO, Saitama, Japan). The analog signal output of airflow was taken from LSA-2000 and recorded with lung sounds on a hard disk. Lung sounds were compared depending on airflow, height and weight.

In addition, 184 outpatients in Minami Wakayama Medical Center and 16 non-asthmatic children were examined. The non-asthmatic children were attendees at a regular health examination. The subjects' baseline characteristics are listed in Table 1. The diagnosis and classification of asthma were made according to international guidelines.^{11,12} A total of 135 asthmatic children with mild, moderate and severe persistent asthma were treated continuously with inhaled corticosteroid and/or leukotriene receptor antagonists. The untreated asthma group included 28 children who had never received treatment continually and 21 children who had not been treated for at least 1 year.

All participants underwent lung sound recording for at least 20 s. After this recording, all participants underwent lung function testing (CHEST GRAPH HI-105; CHEST, Tokyo, Japan). All the tests were performed during the asymptomatic period. The asymptomatic period is defined as the period without any respiratory or systemic symptoms including asthma attack, upper or lower respiratory infections and upper respiratory infections with cough. It was also ensured that the breath sounds did not include wheezes or crackles on the basis of auscultatory findings or the findings of breath sound analysis.

Written informed consent was obtained from all the studied subjects or their legal guardians, and the study protocol was approved by the ethics committee of our institution.

Table 1
Patient characteristics.

	Total (n = 200)	Asthma (n = 184)	Non-asthma (n = 16)
Gender M/F	117/83	108/76	9/7
Median age (years)	10.6	11.6	7.4
Range (years)	4.3–15.1	4.3–15.1	6.0–14.9
Median height (cm)	138.0	139.0	123.3
Range (cm)	97.2–172.4	97–172	106–166
Median weight (kg)	33.3	34.1	21.5
Range (kg)	14.3–95.0	14.3–95.0	19.2–54.0

Sound recording and signal processing

A schematic block diagram of the recording system is presented in Fig. 1. Lung sounds were recorded at the upper right anterior chest at the second intercostal space on the midclavicular line, using a sound sensor (MA-300; FUKUDA DENSHI) fixed with tape (H260; NIHON KOHDEN) on the chest wall. The audio signal was digitized at 48 kHz and 24 bits per sample by an audio interface (Fireface UC; RME, Germany), and recorded on a hard disk of a notebook PC (Let's Note CF-C1; Panasonic, Osaka, Japan). The lung sounds were recorded in a quiet room for at least 20 s while the patients were able to breathe quietly.

Prior to sound analysis, we carefully listened to all recordings and reviewed the spectrogram to exclude noise such as friction and environmental noise. Since the audio signal of inspiratory breath sounds has greater amplitude than that of expiration, the inspiratory and expiratory phases can be identified.

Lung sounds were re-sampled at 6 kHz, and 512-point fast Fourier transformation (FFT) was performed with 75% overlap into adjacent segments, using a Hanning data window. Values of the index, which will be explained in the following section, were calculated for all inspiratory lung sounds, and then the median was calculated.

Index of chest at 700 Hz (ic700)

To avoid the effects of the influence of airflow on lung sounds, we used wide band power of breath sounds between 150 and 1550 Hz instead of measuring airflow directly. We determined the predicted value of sub-band power by regression analysis using the wide band power in normal subjects.¹³ The frequency band of the sub-band power is between 650 and 750 Hz. We calculated the difference of lung sound power by subtracting the predicted value from the measured sub-band power of lung sounds. We called the difference of sub-band power (which has a central frequency of 700 Hz) ic700.

We set 0 dB of ic700 as the average power of lung sounds in normal subjects.

The lung sound power of asthmatic subjects who do not receive appropriate treatment is much larger than normal. The ic700 of these subjects was greater than normal.

Statistical analyses

The patients' demographic data are presented as median and range. The ic700 values are presented as median, range and mean $\pm$ SEM. Comparisons of ic700 between non-asthma and asthma groups were carried out using the unpaired *t*-test. The correlation coefficients were determined using Pearson's product–moment correlation coefficient. Comparisons of ic700 and spirometric parameters among all groups of asthma severity were made using the Kruskal–Wallis test. Values of *p* < 0.05 were considered statistically significant.

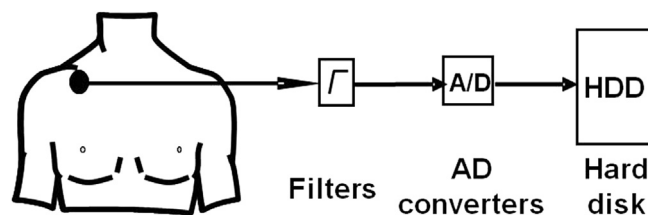


Fig. 1. Block diagram of the recording system. Breath sounds are measured at one location on the chest wall. The breath sounds are amplified and high-pass-filtered. Then, the breath sounds are converted from analog to digital form, and stored on a hard disk. A/D, analog-to-digital converter; HDD, hard disk.

Table 2
Spirometric parameters.

	Asthma (n = 184)				Non-asthma (n = 16)
	Intermittent (n = 88)	Mild (n = 68)	Moderate (n = 23)	Severe (n = 5)	
%FEV ₁	89.1 ± 12.1%	85.6 ± 13.5%	83.6 ± 15.5%	88.9 ± 20.1%	108.5 ± 23.5%
FEV ₁ %	88.8 ± 5.9%	88.0 ± 6.4%	85.2 ± 8.4%	85.7 ± 4.6%	90.8 ± 4.7%
%MMF	90.4 ± 22.9%	85.2 ± 26.2%	77.0 ± 27.9%	79.5 ± 25.8%	112.2 ± 12.1%
%PEF	101.8 ± 18.5%	97.8 ± 20.4%	88.1 ± 19.8%	99.6 ± 26.0%	108.9 ± 18.5%
%FEF50	91.6 ± 22.5%	87.0 ± 25.6%	78.3 ± 29.2%	84.6 ± 22.5%	116.4 ± 21.9%
%FEF75	88.0 ± 29.0%	82.6 ± 31.0%	78.0 ± 34.6%	72.4 ± 36.5%	130.8 ± 69.0%

Results

Relationship of lung function test and severity of asthma

Table 2 shows that spirometric parameters correlated with the classification of asthma severity. There were no significant differences among these groups.

Influence of airflow and body size on ic700 was reduced

Figs. 2 and 3 show that the power at 700 Hz of lung sounds was influenced by airflow and body size (flow $r = 0.47$ (x-axis is a log scale), body height $r = -0.35$, body weight $r = -0.33$). However, as shown in Figs. 2 and 3, these influences on ic700 could be reduced (flow $r = 0.23$ (x-axis is a log scale), body height $r = -0.19$, body weight $r = -0.19$).

Difference in ic700 between non-asthma and asthma groups

Fig. 4 shows the distributions of ic700 for non-asthma and asthma groups. The mean ic700 scores were -0.4 ± 1.1 dB for non-asthma and 0.8 ± 1.8 dB for asthma, with a significant difference between them ($p = 0.001$).

Scatter diagram of ic700 in non-asthma and untreated asthma groups

Fig. 5 shows the distributions of ic700 for 16 cases of non-asthma and 28 cases of untreated asthma that had never received continual treatment. The median ic700 scores were -0.3 dB (range: min. -2.4 dB, max. 2.1 dB) for non-asthma and 2.1 dB (range: min. 0.7 dB, max. 4.3 dB) for untreated asthma. There was a significant difference between them ($p = 0.001$).

All except one of those without asthma showed ic700 of less than 1 dB, while all except three of the untreated asthma subjects showed ic700 greater than 1 dB.

Relationship of ic700 and spirometric parameters in untreated asthma group

For the 49 subjects in the untreated asthma group, including 28 children who had never received continual treatment and 21 children who had not been treated during asymptomatic periods for at least 1 year, median ic700 was 0.93 dB (range: max. 4.2 dB, min. -2.4 dB).

On pulmonary function tests for the 49 subjects in the untreated asthma group, median %FEV₁ (FEV₁/FVC) was 89.8% (range: max. 112.6%, min. 51.4%), median FEV₁% (FEV₁/FVC) was 85.7% (range: max. 100.0%, min. 58.7%), median %PEF (PEF/predicted PEF $\times 100$) was 91.3% (range: max. 124.1%, min. 52.4%), median %MMF (MMF/predicted MMF $\times 100$) was 72.4% (range: max. 135.8%, min. 22.6%), median %FEF50 (FEF50/predicted FEF50 $\times 100$) was 74.1% (range: max. 144.7%, min. 22.5%) and median %FEF75 (FEF75/predicted FEF75 $\times 100$) was 66.2% (range: max. 148.9%, min. 18.6%).

ic700 negatively correlated with FEV₁% ($r = -0.436$, $p = 0.0017$) (Fig. 6), %MMF ($r = -0.339$, $p = 0.01$) (Fig. 7) and %FEF50 ($r = -0.302$, $p = 0.035$) (Fig. 8). ic700 did not correlate with %FEV₁, %PEF and %FEF75.

Relationship of ic700 and severity of asthma

All of the 200 subjects were compared for ic700. Fig. 9 shows that ic700 correlated with asthma severity. The mean ic700 scores were -0.4 ± 1.1 dB for non-asthmatics, 0.3 ± 1.7 dB for intermittent, 1.1 ± 1.7 dB for mild, 1.7 ± 1.8 dB for moderate and 2.0 ± 1.8 dB for severe asthma. There was a significant difference in ic700 among these groups ($p < 0.001$).

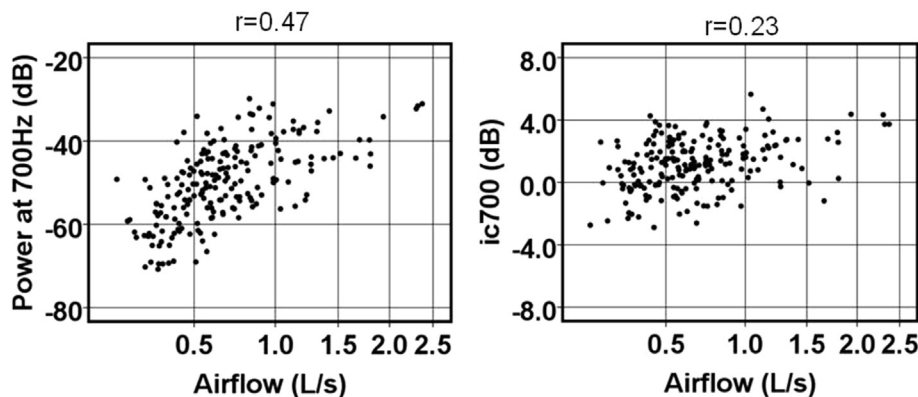


Fig. 2. Influence of airflow on ic700 was reduced. ic700, index of chest at 700 Hz.

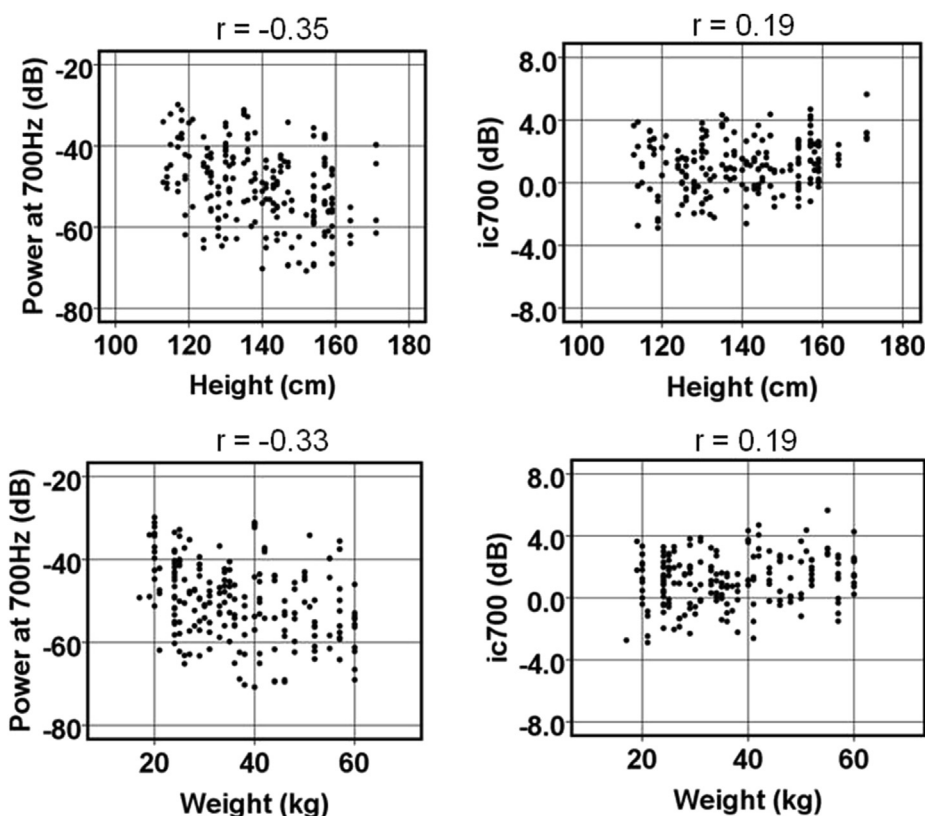


Fig. 3. Influence of body size on ic700 was reduced. ic700, index of chest at 700 Hz.

Discussion

We previously reported that changes of acoustic transfer characteristics in the acoustic transition region of the pulmonary system and the spectral shape of tracheal sounds correlated with asthmatic symptoms and indicated the level of asthma control.¹⁰

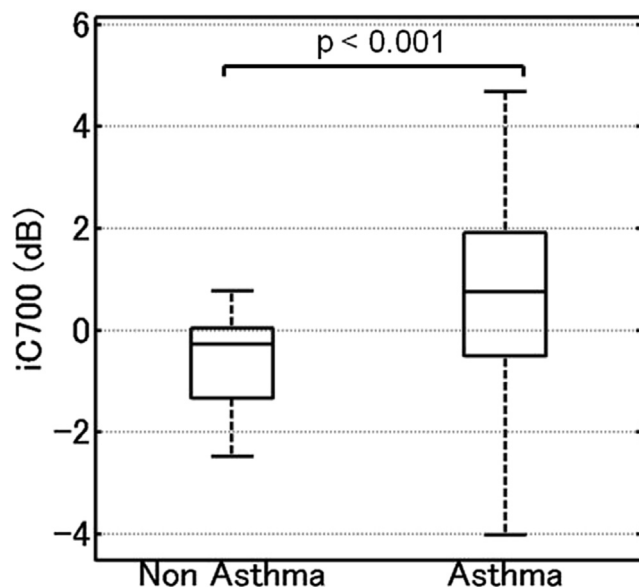


Fig. 4. Difference in ic700 between non-asthma and asthma groups. There was a significant difference in ic700 between non-asthma and asthma groups ($p = 0.001$). ic700, index of chest at 700 Hz.

The present study demonstrated that the analysis of lung sounds may indicate airway obstruction and/or airflow limitation in childhood asthma. Many studies on changes of breath sounds in asthmatic conditions that are caused by changes of breath sound generation or transmission have been reported.⁷ These reports accord with the findings of this study.

In 2009, we found that differences in the highest-frequency inspiratory breath sounds (HFI), that is, the intensity of inspiratory lung sounds, could reflect airway obstruction in asymptomatic asthmatic children.⁵

The intensity of lung sounds is affected by individual differences (age, height, weight and airflow), so we attempted to avoid the effect of these differences. In our previous studies in 2013, we analyzed the acoustic index of lung sounds at two locations.

We attempted to avoid the above-mentioned individual differences by subtracting the intensity of lung sounds between two points. In the present study, we measured the acoustic index of lung sounds at one location on the chest surface and simplified the measurement. The intensity of measured lung sounds is influenced by airflow.

For our new index, we intended to avoid the effects of airflow and body size of the examined subjects. We successfully avoided the effects of airflow by using the relationship of the sub-band and the wide band intensity of the lung sounds. Effects of body size were also avoided by our previously reported method; thus, these assessments were carried out by analyzing breath sounds at one point alone.

In this study, we evaluated the airflow limitation of asymptomatic asthmatic children by using our new index. Figs. 6–8 show that there are significant correlations of ic700 with airway narrowing. Fig. 5 shows that the distribution of ic700 of the untreated asthma group was higher than that of the non-asthmatic group.

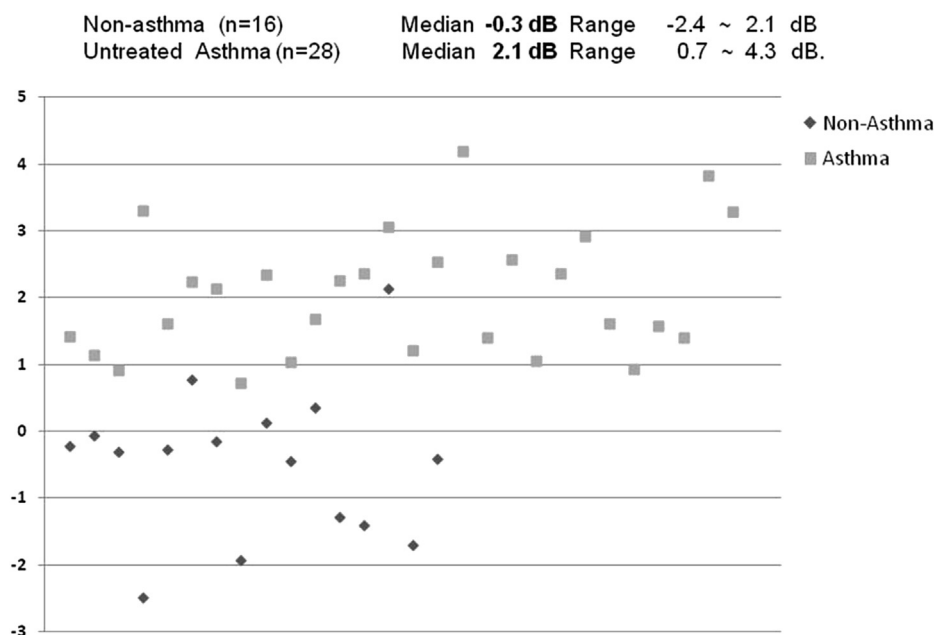


Fig. 5. Scatter diagram of ic700 in non-asthma and untreated asthma groups. The median ic700 scores were -0.2 dB (range: min. -2.4 dB, max. 2.1 dB) for non-asthma and 1.0 dB (range: min. 0.7 dB, max. 4.3 dB) for untreated asthma, with a significant difference between them ($p = 0.001$). ic700, index of chest at 700 Hz.

Figs. 4 and 9 show that there are significant differences in ic700 between normal and asthmatic children with rather stable asthma. In addition, ic700 correlated with the classification of asthma severity. When intermediate-frequency components of lung sounds are transferred to the chest wall, ic700 becomes larger, implying that there is airway narrowing.

Malmberg and coworkers¹⁴ also reported a significant difference in the frequencies of baseline lung sounds between healthy subjects and patients with asthma or COPD. Shreur et al.¹⁵ reported that, at similar levels of airway obstruction, changes in both the frequency and the intensity of sound with airflow were higher in asthmatics than in normal subjects. These studies showed the lung sound characteristics while airflow and volume were standardized

during acutely induced airway obstruction. These findings also suggest that lung sounds in asthmatics simply reflect the degree of airway obstruction and the changes in their breath sound transmission. Morphological changes in asthma, such as increased airway wall thickness, may enhance the change of lung sounds even at a similar change in FEV₁.¹⁶

Matsumoto et al. quantitatively assessed airway wall thickening and its clinical implications in asthma by computer tomography.¹⁷ Airway wall thickening should include histological airway structural changes, such as sub-basement membrane thickening, increases of mucous gland and goblet cells, increased airway wall thickness hyperplasia and increased vascularity, that is, chronic inflammation. These inflammatory changes are assumed to

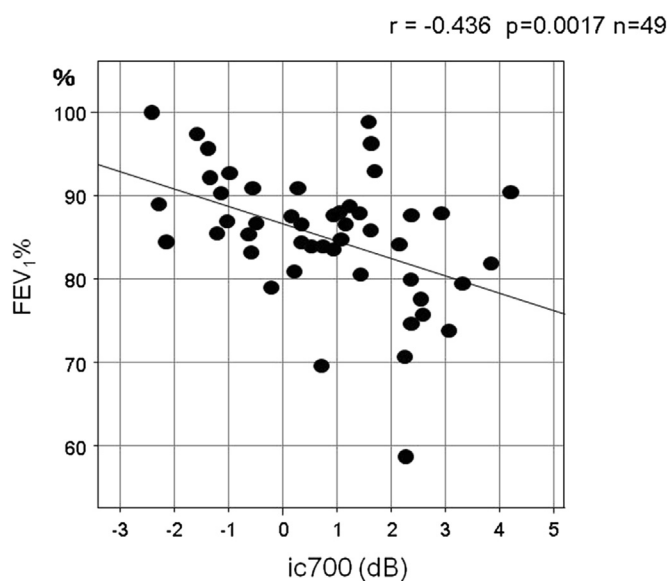


Fig. 6. Relationship of ic700 and FEV₁%. ic700 was negatively correlated with FEV₁% ($r = -0.436$, $p = 0.0017$). ic700, index of chest at 700 Hz.

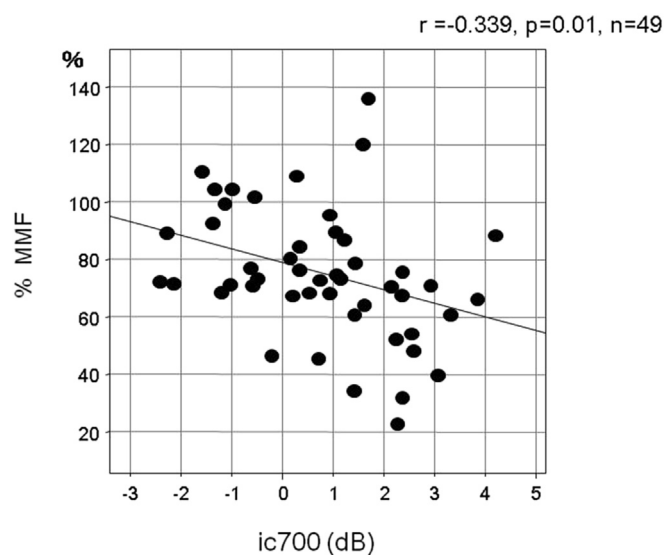


Fig. 7. Relationship of ic700 and %MMF. ic700 was negatively correlated with %MMF ($r = -0.339$, $p = 0.01$). ic700, index of chest at 700 Hz.

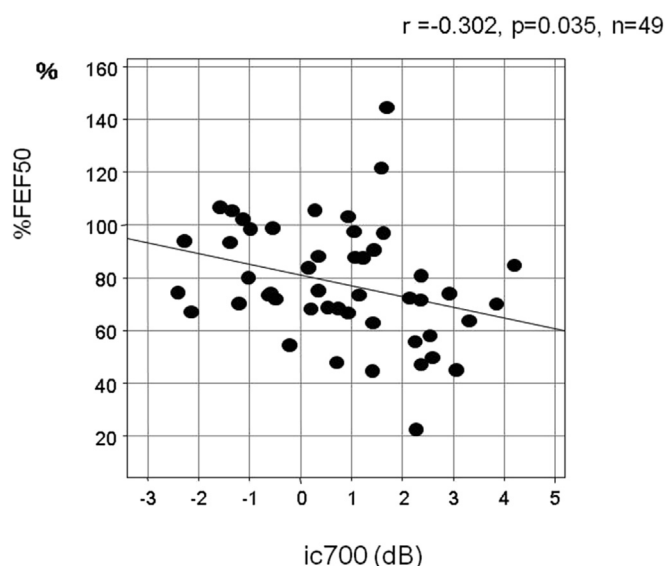


Fig. 8. Relationship of ic700 and %FEF50. ic700 was negatively correlated with %FEF50 ($r = -0.302$, $p = 0.035$). ic700, index of chest at 700 Hz.

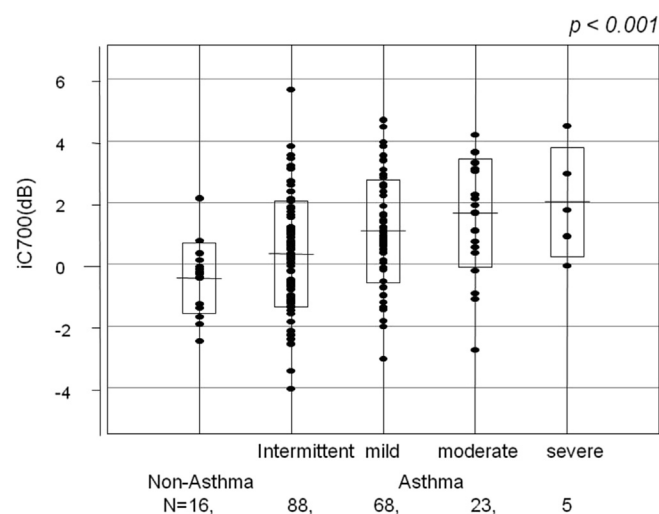


Fig. 9. Relationship of ic700 and asthmatic classification. There was a significant difference in ic700 among asthmatic classification groups ($p < 0.02$). ic700, index of chest at 700 Hz.

increase the stiffness of the airway; thus, the intensity of sound transmission can be increased.

We chose the index to be 700 Hz of inspiratory phase as the parameter of chronic asthmatic airway change. In bronchial challenge tests, acutely induced bronchospasm causes bronchial narrowing without the above-mentioned chronic inflammatory changes. Pasterkamp et al.¹⁸ reported that, in bronchial challenge tests, the intensity of lung sounds below 400 Hz decreased and that of sounds above 1000 Hz increased; however, those between 500 and 1000 Hz changed less than in the other frequency ranges.

In this study, we showed that ic700 will be useful for evaluating airway obstruction in asthmatic children. As an index of bronchial

change in asthma, ic700 may be more sensitive than spirometry. We assume that ic700 reflects breath sound generation and transmission in asthmatic children. Further studies will be needed to evaluate the correlation between ic700 and the effect of ICS treatment. This evaluation should include parameters of airway inflammation such as NO, or airway resistance measured by an oscillation method. ic700 may be more sensitive than spirometry as an index for the assessment of bronchial obstruction in asthma.

We analyzed chest breath sounds along with flow at the mouth and developed a novel index, ic700. We found that ic700 had good ability to evaluate chronic bronchial dysfunction in asthmatic children. We can assess ic700 non-invasively by analyzing breath sounds alone without measuring body size and airflow. We conclude that ic700 is easy to measure and may be a useful clinical parameter to assess chronic bronchial inflammatory changes in asthmatic children, non-invasively.

Conflict of interest

CH, KM and YN received a research grant from Panasonic Corporation. ME, MY and NH are employees of Panasonic Corporation.

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