



New insight into the assessment of asthma using xenon ventilation computed tomography

Jae-Woo Jung, MD, PhD^{*,†,‡}; Jae-Woo Kwon, MD^{*,†}; Tae-Wan Kim, MD^{*,†}; So-Hee Lee, MD^{*,†}; Kyung-Mook Kim, MD^{*,†}; Hye-Ryun Kang, MD, PhD^{*,†}; Heung-Woo Park, MD, PhD^{*,†}; Chang-Hyun Lee, MD, PhD[‡]; Jin-Mo Goo, MD, PhD[§]; Kyung-Up Min, MD, PhD^{*,†}; and Sang-Heon Cho, MD, PhD^{*,†}

^{*} Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea

[†] Institute of Allergy and Clinical Immunology, Seoul National University Medical Research Center, Seoul, Korea

[‡] Department of Internal Medicine, Chung-Ang University College of Medicine, Seoul, Korea

[§] Department of Radiology, Seoul National University College of Medicine and Institute of Radiation Medicine, Seoul National University Medical Research Center, Seoul, Korea

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ABSTRACT

Background: Image analyses include computed tomography (CT), magnetic resonance imaging, and xenon ventilation CT, which is new modality to evaluate pulmonary functional imaging.

Objective: To examine the usefulness of dual-energy xenon ventilation CT in asthmatic patients.

Methods: A total of 43 patients 18 years or older who were nonsmokers were included in the study. Xenon CT images in wash-in and wash-out phases were obtained at baseline and after inhalation of methacholine and salbutamol. The degrees of ventilation defects and xenon trappings were evaluated through visual analysis.

Results: Ventilation defects and xenon trapping were significantly increased and decreased after methacholine challenge and salbutamol inhalation, respectively ($P < .005$). The ventilation abnormalities were not significantly related to the percentage of forced expiratory volume in 1 second (FEV₁) or the ratio of FEV₁ to forced vital capacity. Xenon trappings after salbutamol inhalation were negatively related to the scores of the asthma control test, wheezing, or night symptoms, with statistical significance ($P < .05$), whereas, FEV₁ showed no significant correlation with symptom scores. Baseline FEV₁ was significantly lower and dyspnea and wheezing were more severe in the non–full reversal group than in the full reversal group after salbutamol inhalation in xenon CT ($P < .05$). The degree of ventilation defects were positively correlated with FEV₁ improvement after 3 months of treatment ($P = .02$).

Conclusion: The results of this study suggest that xenon ventilation CT can be used as a new method to assess ventilation abnormalities in asthma, and these ventilation abnormalities can be used as novel parameters that reflect the status of asthma control and symptom severity.

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Introduction

Asthma is a reversible airway obstructive disease that is characterized by chronic airway inflammation, increased airway responsiveness to variable stimuli, and airway remodeling.¹ Because the relationships of airway obstruction with the degree of inflammation and clinical symptoms have not yet been fully elucidated, it is still difficult to assess the severity of asthma correctly.²

Pulmonary functions tests, clinical symptoms, and inflammatory markers are widely used to assess asthma control and severity.³ However, asthma severity cannot be classified using a single parameter because asthma is a disease caused by a combination of heterogeneous parameters. A combination of spirometric measurements, clinical symptoms, and degrees of activity restriction is currently used to classify clinical states. There are correlations and discrepancies between such parameters because each parameter reflects a different aspect of the clinical states.³

Imaging studies used to assess asthma severity includes chest radiography, computed tomography (CT), and magnetic resonance imaging (MRI). Chest radiography often reveals hyperinflation at the time of an acute asthma attack but then reveals normal findings in the absence of symptoms.⁴ High-resolution CT is widely used to assess remodeling and airway obstructions by providing images of

Reprints: Sang-Heon Cho, MD, PhD, Seoul National University Hospital, 101 28 Yeongseon-Dong, Jongno-Gu, Seoul 110-744, Korea; E-mail: shcho@snu.ac.kr.

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air trappings and centrilobular prominence and to determine airway wall thickness and lung structure.^{5,6} However, these CT results are limited to structural analyses. Thus, functional analysis has recently been attempted by imaging ventilation. In particular, MRI is widely adopted for use in studying lung ventilation through oxygen enhancement or hyperpolarized gas, such as helium 3 or xenon 129.^{7–10}

Xenon ventilation CT using dual source and dual energy is a new modality for lung function imaging,^{11–15} which allows for the visualization of lung ventilation and quantification of regional ventilation defects and xenon trappings. Dual-energy CT refers to the use of CT data representing 2 different energy spectra and allows for the possibility of classifying and differentiating tissue to obtain material-specific images. In this study, the differentiation of xenon from lung tissue and image of pure xenon ventilation without lung structure can be possible without additional radiation.¹¹ There are several studies that have used xenon ventilation CT in patients with diseases accompanied by structural abnormalities, such as chronic obstructive pulmonary disease,¹² congenital hyperlucent lung lesions,¹⁶ bronchiolitis obliterans,¹³ and bronchial atresia.¹⁷ However, there have only been a few studies using xenon ventilation CT in asthmatic patients.^{11,18}

This study was designed to evaluate dynamic changes of xenon distribution in a steady state, bronchoconstriction, and recovery state to analyze correlations between clinical indices and quantitative measures of airway obstruction and to examine the usefulness of xenon ventilation dual-energy CT in asthmatic patients.

Methods

Study Participants

A total of 43 patients with newly diagnosed asthma 18 years or older who were nonsmokers were included in the study. Asthma was diagnosed when (1) cough, dyspnea, and wheezing manifested and (2) a provocative concentration of methacholine causing a 20% decrease in forced expiratory volume in 1 second (FEV₁) (PC₂₀) was less than 16 mg/mL by methacholine challenge testing. Patients with moderate-to-severe bronchiectasis or tuberculosis-destroyed lungs and patients who previously used the inhaled bronchodilators or steroids for

asthma were excluded from the study. Asthma severity and quality of life were assessed using the visual analog scale (VAS), Asthma Control Test (ACT), and the Quality of Life Questionnaire for Adult Korean Asthmatics (QLQAKA).¹⁹ There were 21 men (51.2%) and 22 women (48.8%). The mean (SD) age of the patients was 45.02 (12.30) years. The mean FEV₁ percentage, VAS score, ACT score, and QLQAKA score of the patients were 84.21% (16.83%), 7.61 (1.69), 21.48 (3.54), and 68.77 (9.86), respectively (eTable 1). This study was approved by the institutional review board of our hospital (H-0904-033-278), and written informed consent was obtained from each participant.

Protocol for Xenon Ventilation CT

We used the same protocol for xenon ventilation CT as in a previous study.¹² During the wash-in phase, patients inhaled a mixture of 30% xenon and 70% oxygen for 1 minute through a xenon gas rebreathing system (AZ-726; Anzai Medical, Tokyo, Japan) and a face mask (King Systems, Noblesville, Indiana) and then inhaled 100% oxygen during the wash-out phase. The mask was connected to a sensor that monitored the concentrations of tidal carbon dioxide and xenon. Respiratory rate, oxygen saturation, and blood pressure were monitored throughout CT. Wash-in-phase CT scans were taken when the exhaled xenon concentration reached 30% (Fig 1A). Wash-out-phase CT scans were taken when the exhaled xenon concentration became 0% after discontinuation of xenon and administration of oxygen. Xenon ventilation CT was performed using a dual-energy scanner (Somatom Definition; Siemens Medical Solutions, Forchheim, Germany) while patients held their breath. Unenhanced CT was performed before xenon inhalation. A minimum radiation dose was used to reduce the radiation hazard. The volume CT dose index of a single xenon-enhanced CT scan was 2.76 mGy. The mean (SD) total radiation dose that the patients were exposed to was 10.00 (1.26) mSv.

Xenon Ventilation CT After Methacholine Challenge and Salbutamol Inhalation

Xenon ventilation CT was performed in 3 steps (Fig 1B): FEV₁ and forced vital capacity (FVC) were measured before the start of each step. Baseline xenon ventilation CT was performed first. Then,

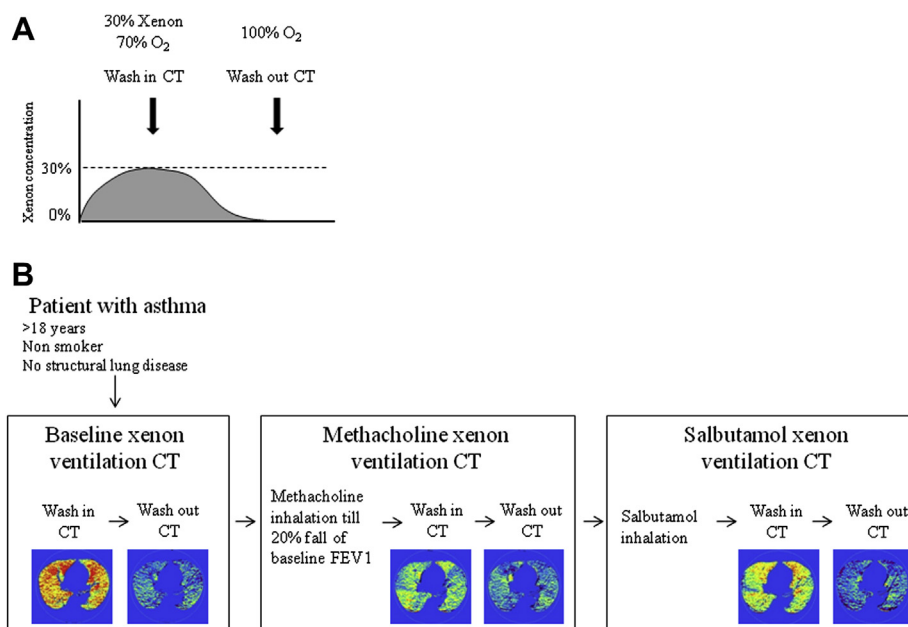


Figure 1. Flow of xenon ventilation computed tomographic (CT) scan. A, Xenon CT images in wash-in and wash-out phases were obtained. B, Xenon CT images at baseline and after inhalation of methacholine and salbutamol were obtained.

methacholine challenge was started at 0.25, 0.625, 1, 4, and 16 mg/mL, depending on which concentration was closest to each patient's PC₂₀ and then increased until FEV₁ decreased by 20%.²⁰ Immediately after a 20% decrease, methacholine xenon ventilation CT was performed. Thereafter, 2 puffs of salbutamol (Ventolin; GlaxoSmithKline, Bredford, England) was administered using the spacer, and after 15 minutes salbutamol xenon ventilation CT was then performed again.

Visual Analysis of Ventilation Defects and Xenon Trappings

Two independent radiologists (C.H.L. and K.N.J., with 12 years and 5 years of experience in chest CT interpretation, respectively) performed visual analyses after preparing the CT images on a PACS work station (Radmax; Marotech, Seoul, Korea) in consensus. The reviewers were masked to the clinical information and the interventions. Coded maps were processed to be displayed in blue, cyan, green, yellow, or red, depicting the increasing amounts of xenon.¹² A ventilation defect was defined as the lung area where inhaled xenon gas did not spread evenly in a wash-in phase shown as an area with blue, indigo, or violet colors (Fig 2) and a xenon trapping as lung area where xenon attenuation was detected after exhaust of xenon gas through oxygen inhalation in a wash-out phase shown as an area containing a red, orange, or yellow color (Fig 2). Ventilation defects were scored for the wash-in phase, and the degree of xenon trappings were scored for the wash-out phase. Lobe-based analyses were performed, depending on the xenon-enhanced patterns. The extent of ventilation defect and xenon trapping was evaluated on a 10-point scale according to the proportion of the areas showing ventilation defect and xenon trapping in each lobe (0, 0%–10%; 1, 10%–20%; 2, 20%–30%; 3, 30%–40%; 4, 40%–50%; 5, 50%–60%; 6, 60%–70%; 7, 70%–80%; 8, 80%–90%; 9, 90%–100%; 10, 100%). For an assessment of the extent of ventilation defect and xenon trapping for each study participant, total scores were calculated. The extent of ventilation defect and xenon trapping were expressed in the range of 0 to 50 points.

Statistical Analysis

All statistical analyses were performed using SPSS statistical software, version 17.0 (SPSS Inc, Chicago, Illinois). Continuous variables were expressed as mean (SD). All statistical differences

were determined using the χ^2 test, Fisher exact test, *t* test, and Mann-Whitney test. The paired *t* test was applied to compare the differences between changes in the variables after the administration of methacholine and salbutamol. The Spearman rank correlation coefficient was used for correlation analysis. *P* < .05 was considered statistically significant.

Results

Case Presentation of a Patient With Typical Changes in Xenon Ventilation Patterns

Figure 2 shows a 2-phase, 3-step xenon ventilation CT image taken from a 50-year-old woman with asthma. On the wash-in-phase image, small ventilation defects were observed at baseline, and new patchy ventilation defects developed after methacholine inhalation. Although the patchy defects improved slightly after salbutamol inhalation, new defects developed. On the wash-out-phase images, xenon trappings, which were not seen at baseline, increased after methacholine inhalation but improved after salbutamol inhalation.

Changes After Inhalation of Methacholine and Salbutamol

Mean FEV₁ percentage values were 84.09% (17.01%) at baseline, 63.53% (15.33%) after methacholine challenge, and 85.29% (16.73%) after salbutamol inhalation; the differences were statistically significant (*P* < .001). eFigure 1 shows the changes in ventilation defects and xenon trappings on the xenon CT images taken during each step. Ventilation defects significantly increased after methacholine challenge and significantly decreased after salbutamol inhalation (*P* < .005 for each). Xenon trappings were also significantly increased after methacholine challenge and significantly decreased after salbutamol inhalation (*P* < .005 for each).

Discordance Between Xenon Ventilation CT and Spirometry

FEV₁ percentage revealed no significant correlation with ventilation defects (*r* = −0.010, *P* = .95) or xenon trappings (*r* = 0.167, *P* = .31) (eFig 2). The FEV₁/FVC ratio also revealed no significant correlation with ventilation defects (*r* = 0.062, *P* = .69) or xenon trappings (*r* = −0.032, *P* = .84).

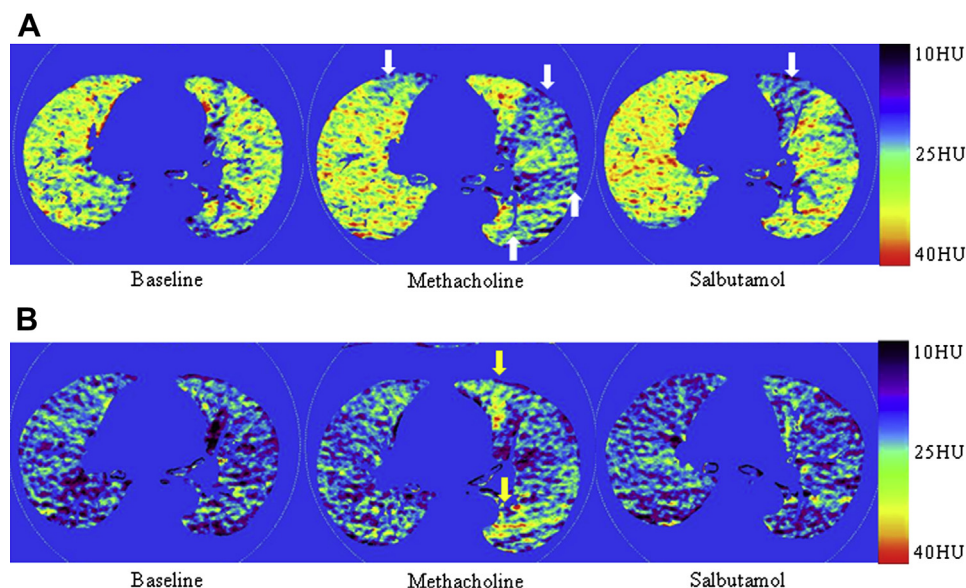


Figure 2. Typical imaging of xenon ventilation computed tomographic (CT) scan. A, Ventilation defect in wash-in phase. B, Xenon trapping in wash-out phase. Color-coded maps were processed to be displayed in blue, cyan, green, yellow, or red, depicting increasing amounts of xenon. On the wash-in-phase image, new patchy ventilation defects developed after methacholine inhalation and the patchy defects improved slightly after salbutamol inhalation (white arrows). On the wash-out-phase images, xenon trappings increased after methacholine inhalation but improved after salbutamol inhalation (yellow arrows).

Correlations Between Xenon Ventilation CT and Symptom Scores of Asthma

FEV₁ percentage revealed no significant correlation with the symptom scores or QLOAKA scores (Table 1). Xenon ventilation CT scans taken after salbutamol inhalation showed that xenon trappings had a significant, negative correlation with the total ACT score ($r = -0.395$, $P = .03$) or wheezing and the night symptoms score (QLQAKA or ACT) ($P < .05$).

The baseline xenon CT scans showed a significant, negative correlation with the log PC₂₀ ($r = -0.399$, $P = .01$). However, FEV₁ percentage revealed no significant correlation with the log PC₂₀.

Difference According to the Reversibility of Ventilation Defect After Salbutamol Inhalation

No significant differences were found in FEV₁ between the baseline values and those obtained after salbutamol inhalation ($P > .05$). Patients were categorized as those who fully returned to baseline (full reversal group, $n = 20$) and those who did not (nonreversal group, $n = 20$) (Table 2). The full reversal group exhibited FEV₁ levels at 91.00% of the baseline value, and the nonreversal group exhibited FEV₁ levels at 79.67% of the baseline value. This difference was statistically significant ($P = .02$). The dyspnea and wheezing score were significantly more severe in the nonreversal group than in the full reversal group ($P < .05$).

Prediction of Treatment Responsiveness

To find predictors of improvement in pulmonary function 3 months after treatment, we investigated the correlations between the improvement in FEV₁ and various parameters in 22 patients (Fig 3). The degree of ventilation defects was positively correlated with FEV₁ improvement after 3 months of treatment ($P = .005$). Such correlations were observed between the improvement in FEV₁ and the PC₂₀ values ($P = .005$) and the proportions of eosinophils in the induced sputum ($P = .03$). However, no significant correlation was found between the improvement in FEV₁ and FEV₁ at baseline.

Discussion

This study using xenon ventilation CT revealed that xenon ventilation significantly changed in asthmatic patients after inhalation of methacholine (a bronchoconstrictor) and salbutamol (a bronchodilator), and ventilation defects and xenon trapping were the independent markers that are not correlated with the pulmonary functions tests. Although pulmonary function was not correlated with asthma symptoms, xenon trappings after salbutamol inhalation were significantly correlated with various clinical symptoms, and ventilation defects at baseline reflect airway hypersensitivity and predict therapeutic responses.

In our study, severe asthma status was induced through methacholine challenge because radiologic findings were inconclusive in

Table 1
Correlation with asthma symptoms

Variable	FEV ₁ percentage		Xenon trapping on salbutamol xenon CT	
	<i>r</i>	<i>P</i> value	<i>R</i>	<i>P</i> value
VAS score	0.191	NS	−0.090	NS
Total ACT score	0.156	NS	−0.395	.03
Total QLQAKA score	0.031	NS	−0.104	NS
Wheezing score (QLQAKA)	−0.123	NS	−0.416	.03
Night symptom score (QLQAKA)	0.033	NS	−0.401	.04
Night symptom score (ACT)	−0.048	NS	−0.507	.007

Abbreviations: ACT, Asthma Control Test; CT, computed tomography; FEV₁, forced expiratory volume in 1 second; NS, not significant; QLQAKA, the Quality of Life Questionnaire for Adult Korean Asthmatics; VAS, the visual analog scale.

Table 2

Difference according to reversibility of ventilation defect after salbutamol inhalation^a

Variable	Full reversal group at xenon CT (n = 20)	Nonreversal group at xenon CT (n = 20)	<i>P</i> value ^b
Baseline FEV ₁ percentage	91.00 (78.67)	78.67 (14.68)	.02
Baseline xenon CT, ventilation defect	9.40 (7.23)	4.25 (4.15)	.01
Salbutamol xenon CT, ventilation defect	4.70 (4.40)	8.45 (5.63)	.02
Difference of ventilation defect ^c	−4.70 (4.07)	4.20 (3.02)	<.001
Dyspnea score (QLQAKA)	4.33 (0.9)	3.54 (0.88)	.03
Wheezing score (QLQAKA)	4.73 (0.59)	3.69 (0.95)	.003

Abbreviations: CT, computed tomography; FEV₁, forced expiratory volume in 1 second; QLQAKA, the Quality of Life Questionnaire for Adult Korean Asthmatics.

^aTest results are presented as mean (SD).

^b*P* value refers to the comparison of the values between the full reversal group and the nonreversal group.

^cDifference of ventilation defect between baseline and salbutamol xenon ventilation CT.

asthmatic patients with mild asthma symptoms. Through serial salmeterol xenon CT, improvement of xenon ventilation abnormality xenon ventilation was then assessed in terms of bronchial dilatation and symptomatic improvement through salbutamol inhalation at severe asthma status. In addition, ventilation defects and air trappings were assessed using 2-phase xenon CT.

There have been numerous studies on ventilation defects in asthmatic patients using hyperpolarized helium 3 MRI. It has been reported that ventilation defects observed on MRI are significantly correlated with clinical severity and spirometric measurements.¹⁰ Samee et al²¹ assessed ventilation defects in response to methacholine and exercise using hyperpolarized helium 3 MRI. Several investigators have suggested that because airflow obstruction caused by the administration of methacholine is persistent and occurs recurrently at the same obstruction site in the lungs of asthmatic patients, such obstruction may attributed to a fixed lesion.^{7,22} Although functional analysis using hyperpolarized helium 3 MRI is helpful in elucidating the pathophysiology of asthma, MRI has some limitations in clinical use. Hyperpolarized helium 3 MRI is not easily available, the equipment is expensive, and helium processing requires high costs. In addition, the resolution of MRIs decreases in the presence of air, and it requires much more time and has difficulty in diagnosing parenchymal lung diseases unlike CT scans.

Xenon ventilation CT has recently been used to provide additional information on lung function.²³ Xenon ventilation CT enables us to discriminate between lung tissue and inhaled radiodense xenon by using the dual-energy technique.^{23–25} However, there have been few studies on xenon ventilation CT. Chae et al¹¹ have documented that, in asthmatic patients, ventilation defects on xenon ventilation CT images reflect severe airflow limitation more accurately and are significantly correlated with airway wall thickening. They stated that FEV₁ percentage varies, depending on the absence or presence of ventilation defects. However, their study had some limitations because of the small number of patients, the assessment of only wash-in-phase ventilation defects, and no determination of the correlations between ventilation defects and clinical parameters.

Our study revealed dynamic changes in lung ventilation with the administration of a bronchoconstrictor (methacholine) and a bronchodilator (salbutamol). Ventilation defects and xenon trappings did not occur diffusely but in a patchy fashion. One of the striking findings in our study is that xenon ventilation abnormalities, including xenon ventilation defects and xenon trappings, were not significantly correlated with FEV₁ percentage, FVC percentage, or the FEV₁/FVC ratio. Xenon ventilation abnormalities were observed

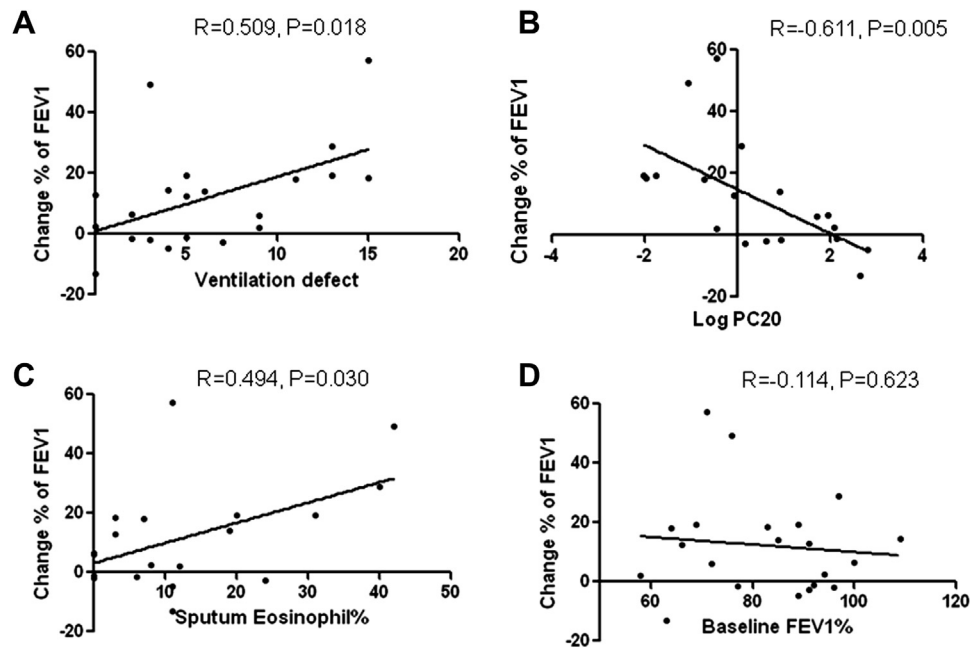


Figure 3. Correlation of percentage change in forced expiratory volume in 1 second (FEV₁) after 3 months of asthma medication with other clinical parameters. A, Ventilation defect; B, log provocative concentration of methacholine causing a 20% decrease in FEV₁; C, sputum eosinophils proportion; D, baseline FEV₁. Improvements in FEV₁ after 3 months of treatment became higher as ventilation defects at baseline increased ($P = .02$), and significant relationships were found between improvements in FEV₁ and baseline FEV₁.

in some asthmatic patients with normal pulmonary function, but such abnormalities were not observed in some asthmatic patients with decreased pulmonary function. These results mean that xenon ventilation abnormalities reflect pathologic conditions in the small airways unlike FEV₁, which reflects pathologic conditions in the medium-to-large airways.

FEV₁ is known to be the criterion standard for airflow obstruction evaluation. FEV₁ percentage, an objective and reproducible marker, plays an important role in the diagnosis and treatment of asthma.²⁶ However, some patients with normal FEV₁ experience severe asthma symptoms.²⁷ Previous studies have pointed out that there are no significant correlations among pulmonary function, respiratory symptoms, quality of life, and airway inflammation.^{28,29} In particular, spirometric parameters mainly reflect medium-to-large airway obstruction but have some limitations in evaluating peripheral small airway obstruction. In addition, the spirometric parameters are not significantly related to asthma symptoms.^{28,29} Because of these shortcomings, there have been many studies searching for new methods of evaluating asthma symptoms and asthma control.

Our study indicated that the ACT scores and the severity of wheezing were significantly correlated with xenon trappings but not with FEV₁ percentage. These results imply that xenon trappings that remain after salbutamol inhalation are significantly correlated with quality of life and asthma symptoms. Therefore, xenon ventilation CT has a higher sensitivity for detecting small airway obstruction than spirometry and thus compensates for the limitations of FEV₁ alone.

The 2002 Global Initiative for Asthma guidelines define asthma as acute and chronic inflammation of the whole airways, including airways of 2 mm or smaller. Asthma symptoms are induced by the inflammation and obstruction of the small airways and in patients with difficult-to-treat asthma or severe or fatal asthma, these are confirmed by CT, transbronchial lung biopsy, and autopsy.^{1,2} Peripheral airway obstruction can be evaluated using quantitative measures of airway obstruction by using xenon ventilation CT. Ventilation heterogeneity might better correlate with small airway

function instead of the large airways (FEV₁) and the degree of large airway bronchomotor tone (FEV₁/FVC). Spirometric parameters for small airway obstruction, such as the ratio of residual volume to total lung capacity and forced expiratory flow between 25% and 75% of vital capacity, would have been more helpful to prove the correlation between small airway function and ventilation heterogeneity^{30,31} if they had been included in the study.

In our study, it was found that ventilation abnormalities were correlated with airway hyperresponsiveness but not with eosinophilic airway inflammation and that ventilation defects were useful for predicting posttreatment FEV₁ improvement. These results imply that ventilation defects represent complete airway obstruction, which is relieved after treatment along with improvements in pulmonary function. Therefore, xenon ventilation CT can be used to select asthmatic patients who may require aggressive treatment. In our study, asthmatic patients were categorized as those who fully recovered and those who did not; the latter had worse pulmonary function and more severe asthma symptoms than the former. This means that, despite complete improvement in pulmonary function, persistent asthma symptoms may be attributed to the remaining ventilation defects. Therefore, it is thought that although FEV₁, a parameter for large airways, may improve rapidly, ventilation defects recover slowly.

Xenon, an anesthetic agent, has anesthetic effects at higher concentrations and can induce adverse reactions, such as headache, nausea, and somnolence.³² None of our patients experienced unconsciousness or a decrease in oxygen saturation, but some of them experienced somnolence or dizziness. CT carries a risk of exposure to radiation. However, with advances in CT technologies, CT can be performed with lower doses of radiation and shorter times. For these reasons, xenon ventilation CT can be used to evaluate lung physiology (to obtain information on emphysema, bronchiectasis, and mass lesions) and can be used to predict asthma severity and to evaluate asthma control. Golin et al³³ have advocated that newly developed topical inhalers should reach the peripheral airways to produce therapeutic effects. Because xenon ventilation CT is useful for assessing ventilation abnormalities in

the peripheral small airways, it can be used to perform clinical trial on newly developed inhalers.

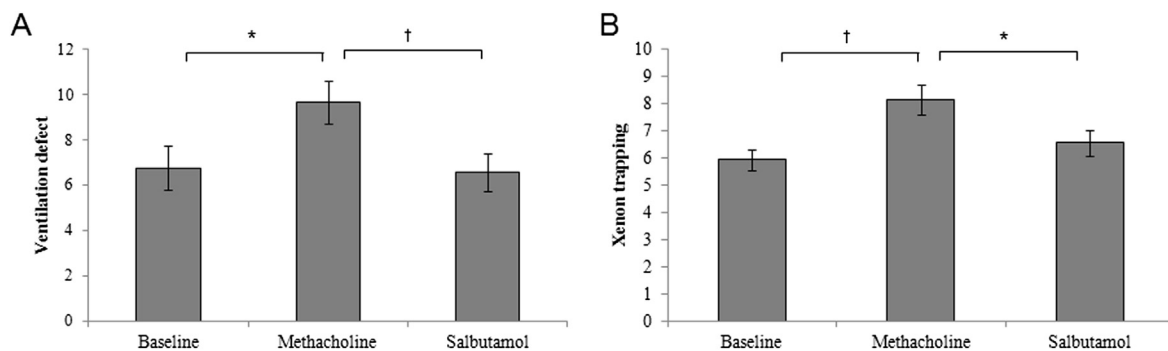
Taken together, air trappings described in previous studies using CT can be subdivided into ventilation defects and xenon trappings in 2-phase xenon CT. Ventilation defects represent complete airway obstruction with no ventilation, and xenon trappings represent the check-valve type of obstruction of the airways. In our study, ventilation defects represent therapeutic responses, whereas xenon trappings represent asthma symptoms. These results indicate that the 2 parameters have different clinical implications. In conclusion, xenon ventilation CT can be used as a new imaging method to assess ventilation abnormalities and asthma severity and control in asthmatic patients.

Supplementary Data

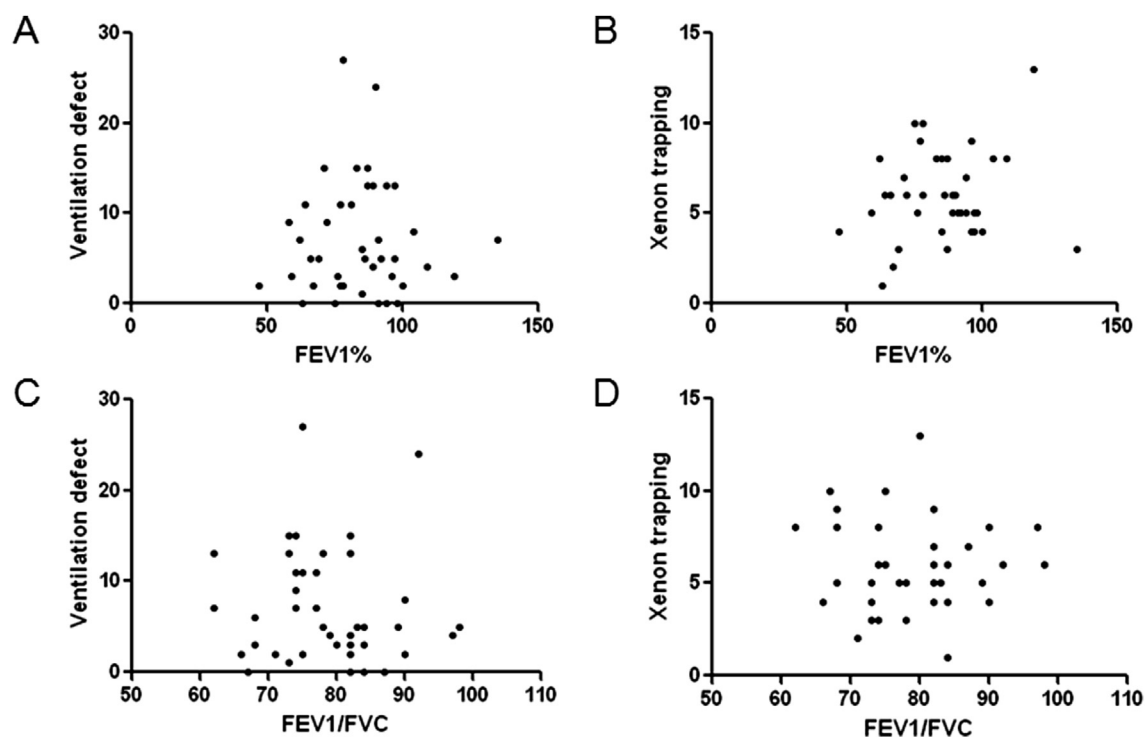
Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.anaai.2013.04.019>.

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eFigure 1. Change according to methacholine and salbutamol inhalation. A, Ventilation defect; B, Xenon trapping. Ventilation defects and xenon trapping were significantly increased and decreased after methacholine challenge and salbutamol inhalation. * $P < .001$, † $P < .005$.



eFigure 2. Discordance between ventilation abnormality and forced expiratory volume in 1 second (FEV₁) percentage or ratio of FEV₁ to forced vital capacity (FVC). A, FEV₁ and ventilation defect; B, FEV₁ and xenon trapping; C, FEV₁/FVC ratio and ventilation defect; D, FEV₁/FVC ratio and xenon trapping. The ventilation abnormalities were not significantly related to FEV₁ percentage or the FEV₁/FVC ratio.

eTable 1

Demographic and clinical characteristics

Characteristic	Finding (N = 43)
Age, mean (SD), y	45.02 (12.30)
Male, No. (%)	21 (51.2)
Body mass index, mean (SD)	24.85 (2.91)
VAS score, mean (SD)	7.61 (1.69)
ACT score, mean (SD)	21.48 (3.54)
QLQAKA score, mean (SD)	68.77 (9.86)
WBC count, mean (SD), / μ L	6,794.84 (1,593.19)
Blood eosinophil count, mean (SD), / μ L	394.16 (312.24)
Sputum eosinophil, mean (SD), %	12.33 (11.33)
Serum total IgE, mean (SD)	545.90 (831.06)
PC ₂₀ , mean (SD)	5.45 (12.16)
FEV ₁ , mean (SD), % predicted	84.21 (16.83)
FVC, mean (SD), % predicted	89.17 (14.18)
FEV ₁ /FVC ratio, mean (SD), %	78.25 (8.42)
Initial treatment after xenon CT, No. (%) (n = 22)	
ICS	3 (13.6)
ICS and LABA	16 (72.7)
Oral corticosteroid	1 (4.5)
Leukotriene modifier	10 (45.5)
Theophylline	1 (4.5)

Abbreviations: ACT, Asthma Control Test; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; ICS, inhaled corticosteroid; LABA, long-acting β_2 -agonist; PC₂₀, a provocative concentration of methacholine causing a 20% decrease in FEV₁; QLQAKA, Quality of Life Questionnaire for Adult Korean Asthmatics; VAS, the visual analog scale; WBC, white blood cell.

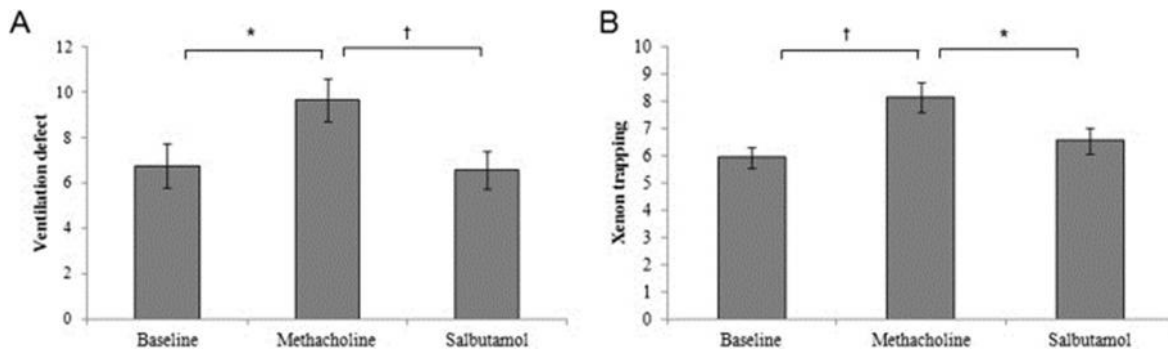


Figure 1. Change according to methacholine and salbutamol inhalation. A, Ventilation defect; B, Xenon trapping. Ventilation defects and xenon trapping were significantly increased and decreased after methacholine challenge and salbutamol inhalation. * $P < .001$, † $P < .005$.

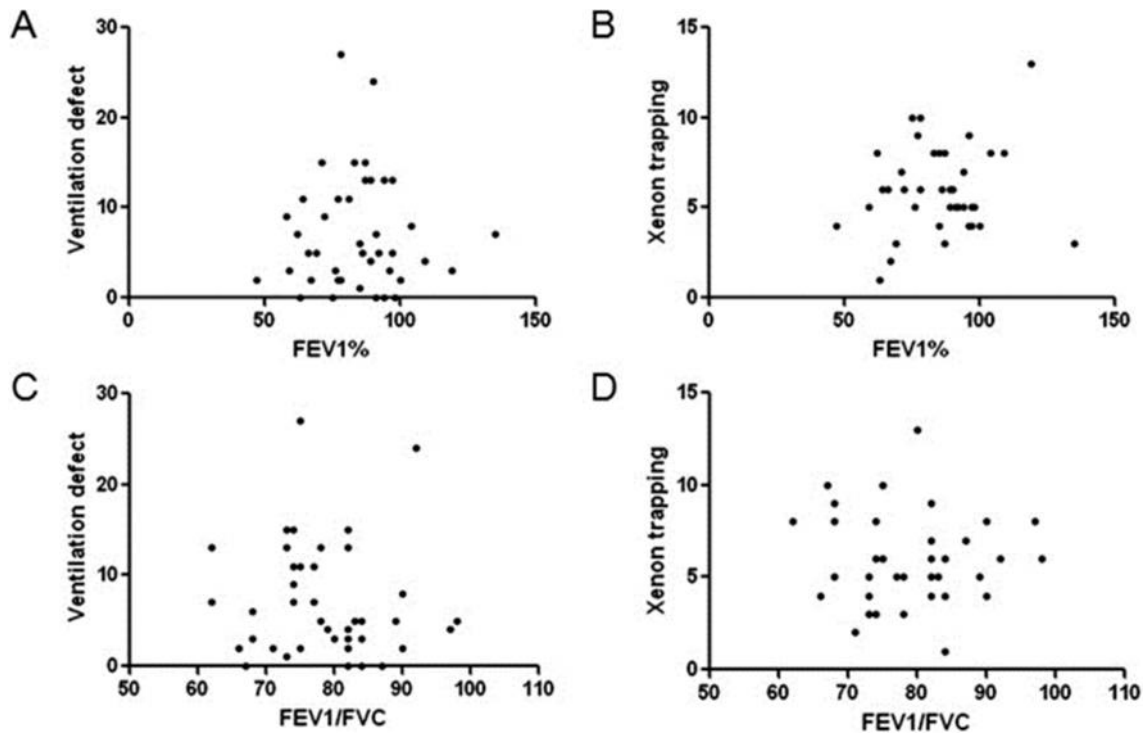


Figure 2. Discordance between ventilation abnormality and forced expiratory volume in 1 second (FEV1) percentage or ratio of FEV1 to forced vital capacity (FVC). A, FEV1 and ventilation defect; B, FEV1 and xenon trapping; C, FEV1/FVC ratio and ventilation defect; D, FEV1/FVC ratio and xenon trapping. The ventilation abnormalities were not significantly related to FEV1 percentage or the FEV1/FVC ratio.