Allergy Asthma Immunol Res. 2025 Nov;17(6):787-796
https://doi.org/10.4168/aair.2025.17.6.787
pISSN 2092-7355·eISSN 2092-7363

Allergy, Asthma & Immunology Research AAIR

Brief Communication

Check for updates

Bronchodilator Response of TEV/FEV3 and Its Implications in Pediatric Asthma

Hamin Kim [1], **Yoon Hee Kim** [2], **Jae Hwa Jung** [1], **Mireu Park** [1], **Yun Young Roh** [3], **Jong Deok Kim** [1], **Min Jung Kim** [4], **Yong Ju Lee** [4], **Kyung Won Kim** [1], **Myung Hyun Sohn** [1], **Soo Yeon Kim** [1*]

[1]Department of Pediatrics, Severance Hospital, Institute of Allergy, Institute for Innovation in Digital Healthcare, Yonsei University College of Medicine, Seoul, Korea
[2]Department of Pediatrics, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea
[3]Department of Pediatrics, Kangdong Sacred Heart Hospital, Hallym University College of Medicine, Seoul, Korea
[4]Department of Pediatrics, Yongin Severance Hospital, Yonsei University College of Medicine, Yongin, Korea

OPEN ACCESS

Received: Jan 1, 2025
Revised: Jun 10, 2025
Accepted: Jun 23, 2025
Published online: Sep 18, 2025

Correspondence to
Soo Yeon Kim, MD
Department of Pediatrics, Severance Hospital, Institute of Allergy, Institute for Innovation in Digital Healthcare, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea.
Tel: +82-2-2228-2058
Fax: +82-2-393-9118
Email: sophi1@yuhs.ac

ORCID iDs
Hamin Kim
https://orcid.org/0000-0002-0601-7300
Yoon Hee Kim
https://orcid.org/0000-0002-2149-8501
Jae Hwa Jung
https://orcid.org/0000-0001-7443-9073

ABSTRACT

The diagnosis of asthma in children is challenging due to limitations of conventional spirometry, which primarily assesses large airway function and requires considerable patient effort. Terminal expiration volume (TEV)/forced expiratory volume in 3 seconds (FEV3) has been proposed as a new metric that may help assess small airway dysfunction, where TEV represents the volume difference between FEV3 and forced expiratory volume in 1 seconds (FEV1) and reflects terminal expiratory airflow. We aimed to evaluate the bronchodilator response (BDR) of TEV/FEV3 (BDR-TEV/FEV3) as an index reflecting variable small airway obstruction in children. This retrospective study included 1,199 children who underwent both spirometry and bronchial provocation testing for asthma at a tertiary hospital between January 2017 and December 2019. BDR-TEV/FEV3 was compared according to asthma status and severity. The findings were verified using an external validation group (n = 105). We also explored the association between BDR-TEV/FEV3 and established indices of airway inflammation. BDR-TEV/FEV3 was significantly higher in children with asthma than in those without asthma (3.74% vs. 1.81%, $P < 0.001$) and showed a stepwise increment with asthma severity (P for trend < 0.001). Moreover, BDR-TEV/FEV3 showed a positive correlation with changes in airflow limitation markers, impulse oscillometry parameters, and inflammatory markers such as eosinophil count and fractional exhaled nitric oxide. The change in TEV/FEV3 after bronchodilator inhalation significantly differed between asthmatic and non-asthmatic children and across asthma severity groups. BDR-TEV/FEV3 may be used as a parameter to assess the reversibility of small airway obstruction in children with asthma.

Keywords: Asthma; airway obstruction; children; forced expiratory volume; respiratory hypersensitivity; spirometry

Allergy, Asthma & Immunology Research AAIR

Mireu Park
https://orcid.org/0000-0003-4342-6143
Yun Young Roh
https://orcid.org/0000-0002-8751-6784
Jong Deok Kim
https://orcid.org/0000-0002-4266-5655
Min Jung Kim
https://orcid.org/0000-0002-5634-9709
Yong Ju Lee
https://orcid.org/0000-0002-0796-2558
Kyung Won Kim
https://orcid.org/0000-0003-4529-6135
Myung Hyun Sohn
https://orcid.org/0000-0002-2478-487X
Soo Yeon Kim
https://orcid.org/0000-0003-4965-6193

Disclosure
There are no financial or other issues that might lead to conflict of interest.

INTRODUCTION

Asthma is a disease characterized by chronic airway inflammation and reversible airway obstruction.[1] Its early diagnosis is paramount to facilitate timely intervention, alleviate symptoms, and potentially alter the disease course. Conventional spirometry, while widely used, has limitations in pediatric populations due to its effort-dependent nature and relative insensitivity in detecting early-stage asthma, as it primarily measures large airway function.[2]

Small airway dysfunction (SAD) assessment has gained increasing attention in asthma research.[3] SAD occurs early in the disease progression, often before symptom onset and detectable changes in conventional spirometry parameters such as forced expiratory volume in 1 second (FEV1).[4] While forced expiratory flow at 25%–75% of the forced vital capacity (FVC) (FEF_{25-75}) is believed to reflect SAD, it very likely represents both central and peripheral airway dysfunction and is highly volume dependent with considerable variability.[3,5-7]

Recently, Jung et al.[8] suggested the terminal expiration volume (TEV)-forced expiratory volume in 3 seconds (FEV3) ratio (TEV/FEV3) as a new volume-based metric for assessing small airway obstruction. TEV is calculated as the difference between FEV3 and FEV1, representing the latter fraction of forced exhalation. TEV/FEV3 was significantly elevated in children with asthma and increased with asthma severity. Similarly, in a study by Bao et al.,[9] (FEV3-FEV1)/FVC was proposed as a terminal airflow variable demonstrating sensitivity to airway hyperresponsiveness and inflammation in symptomatic patients with preserved spirometry measurements.

Current asthma diagnosis relies on confirming bronchodilator response (BDR), typically defined as an increase in FEV1 of > 12% from baseline.[1] However, this criterion may not be sufficiently sensitive for diagnosing asthma in children, as factors such as height, age, and sex can affect results, and the unified cutoff of 12% may not be universally appropriate.[10]

In this study, we aimed to determine the level of BDR-TEV/FEV3, a volume-based metric reflecting variable small airway obstruction, in pediatric asthma. We investigated whether BDR-TEV/FEV3 differs between children with and without asthma, examined variations across different levels of asthma severity, and assessed associations between BDR-TEV/FEV3 and other parameters of SAD and airway inflammation.

MATERIALS AND METHODS

Study design and population

This retrospective study included children aged 4–18 years referred to the Pediatric Pulmonology and Allergy Outpatient Clinic of Severance Children's Hospital for symptoms suggestive of asthma between January 2017 and December 2019. We identified 1,199 children without prior asthma medications who underwent clinical evaluations including spirometry with BDR, impulse oscillometry (IOS), and methacholine challenge test (MCT). Children with a prior diagnosis of chronic respiratory conditions or recent respiratory infections (within 4 weeks) were excluded.

Asthma was diagnosed based on clinical symptoms with evidence of variable expiratory airflow limitation using the following criteria: FEV1/FVC < 0.9 when FEV1 is below the lower

https://doi.org/10.4168/aair.2025.17.6.787

limit of normal value (z-score < –1.64); positive BDR (increase in FEV1 > 12% or 200 mL from baseline after bronchodilator inhalation); or positive bronchial hyperresponsiveness (methacholine concentration causing 20% decline in FEV1 ≤ 16 mg/mL).[1,11] Asthma severity was assessed according to the Global Initiative for Asthma guidelines.[1] The non-asthma group was composed of children without evidence of variable airflow limitation, whose history and examinations did not support asthma diagnosis, and whose symptoms could be explained by alternative diagnosis.

For external validation, we used a separate dataset from Gangnam Severance Hospital (Seoul, Korea) applying the same inclusion criteria for the period between January and December 2019. This study was approved by the Institutional Review Board of Severance Hospital (No. 4-2023-1650), with the requirement for informed consent waived due to the retrospective design.

Diagnostic tests

Spirometry and MCT were conducted with a Jaeger MasterScreen PFT system (Jaeger Co., Würzburg, Germany) using standard techniques.[5,12] FVC, FEV1, peak expiratory flow, and FEF_{25-75} were measured before and after bronchodilator inhalation. FEV3 was measured as FEV in 3 seconds, and TEV/FEV3 was expressed as a percentage. Post-bronchodilator measures were obtained 10 minutes after inhaling 200 μg of salbutamol, and BDR-TEV/FEV3 was calculated as follows: − [(Post-bronchodilator TEV/Post-bronchodilator FEV3) − (Pre-bronchodilator TEV/Pre-bronchodilator FEV3)] × 100 (%). For MCT, children inhaled increasing concentrations of methacholine by a dosimeter (MB3; Mefar, Brescia, Italy) until FEV1 was reduced by 20%, and the provocative concentration causing this response was determined.

IOS was performed with a Jaeger MasterScreen IOS system (Jaeger Co.).[13] The following parameters were recorded: mean respiratory resistance at 5 Hz (R5) and 10 Hz (R10), difference between respiratory resistance at 5 and 20 Hz (R5–R20), reactance value at 5 Hz (X5), and reactance area (AX).

Fractional exhaled nitric oxide (FeNO) was measured using a CLD 88 analyzer (Eco Medics, Durnten, Switzerland) at a constant expiratory flow rate of 50 mL/s according to standard guidelines in children over 8 years of age.[14]

Statistical analysis

Statistical analyses were conducted using IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA) and R version 4.3.0 (The R Foundation for Statistical Computing, Vienna, Austria). Comparisons between groups were performed using Student's *t*-test or Mann-Whitney *U* test for continuous variables, and the χ^2 test or Fisher's exact test for categorical variables. The Kruskal-Wallis and Jonckheere-Terpstra tests were employed to compare BDR-TEV/FEV3 according to asthma severity. Spearman's correlation analysis was used to analyze relationships between BDR-TEV/FEV3 and parameters of airway dysfunction and inflammation. The performance of BDR-TEV/FEV3 for asthma diagnosis was evaluated using receiver operating characteristic (ROC) analysis. Values of $P < 0.05$ were considered statistically significant.

https://doi.org/10.4168/aair.2025.17.6.787

RESULTS

Patients' characteristics

Among the 1,199 children screened, 447 (37.2%) were diagnosed with asthma, 550 (45.8%) were classified in the non-asthma group, and the remaining 202 children had lung function test results that did not meet the objective criteria of variable airflow limitation and were excluded from the analysis. Consequently, 997 children were included. Compared with children in the non-asthma group, those with asthma showed higher prevalence of allergic disease comorbidity and higher blood eosinophil counts and FeNO levels (**Table**).

FVC, FEV1, post-bronchodilator FEV1, FEV1/FVC, and FEF_{25-75} values were significantly lower in the asthma group than in the non-asthma group. Conversely, all IOS parameters except for resistance at 20 Hz (R20) demonstrated significantly higher values in the asthma group than in the non-asthma group. Pre- and post-bronchodilator FEV3 values were available for 850 (85.3%) and 763 (76.5%) children, respectively. Compared with children without asthma, those with asthma had significantly lower FEV3 values and significantly higher TEV/FEV3 and post-bronchodilator TEV/FEV3 values.

Table. Patients' characteristics (n = 997)

Characteristics	Non-asthma (n = 550)	Asthma (n = 447)	*P* value
Age (yr)	8.74 (6.72, 11.24)	7.16 (5.86, 9.06)	< 0.001
Sex, % male	333 (60.5)	303 (67.8)	0.018
BMI (kg/m^2)	17.42 (15.57, 20.46)	16.65 (15.34, 18.94)	0.001
Allergic disease comorbidity	294 (53.6)	320 (71.7)	< 0.001
Blood eosinophils (/μL, n = 831)	16.0 (9.0, 31.0)	36.0 (16.0, 57.75)	< 0.001
Spirometry			
FVC (L)	2.11 (1.62, 2.77)	1.68 (1.38, 2.16)	< 0.001
FVC (% predicted)	104.38 ± 12.28	101.73 ± 14.95	0.003
FEV1 (L)	1.81 (1.42, 2.39)	1.38 (1.13, 1.71)	< 0.001
FEV1 (% predicted)	106.90 (97.78, 116.20)	97.70 (86.0, 109.20)	< 0.001
Post-BD FEV1 (L)	1.86 (1.48, 2.43)	1.46 (1.22, 1.82)	< 0.001
Post-BD FEV1 (% predicted)	110.81 ± 13.17	104.72 ± 17.11	< 0.001
Change in FEV1 (%)	3.00 (0.90, 5.30)	7.00 (2.90, 12.60)	< 0.001
FEV1/FVC (%)	98.0 (90.47, 104.35)	86.77 (80.39, 95.0)	< 0.001
FEF_{25-75} (% predicted)	94.35 (78.80, 109.40)	67.60 (54.00, 84.00)	< 0.001
FEF_{25-75} (L/s)	2.02 (1.61, 2.68)	1.29 (1.02, 1.71)	< 0.001
Post-BD FEF_{25-75} (L/s)	2.29 (1.81, 2.99)	1.68 (1.33, 2.12)	< 0.001
Change in FEF_{25-75} (%)	12.65 (4.1, 20.3)	28.7 (12.5, 46.6)	< 0.001
FEV3 (L, n = 850)	2.12 (1.65, 2.83)	1.68 (1.38, 2.11)	< 0.001
TEV/FEV3 (%, n = 850)	11.95 ± 4.44	17.11 ± 5.45	< 0.001
Post-BD TEV/FEV3 (%, n = 763)	10.37 (7.65, 12.50)	13.46 (10.48, 16.08)	< 0.001
Impulse oscillometry			
X5 (% predicted, n = 992)	77.10 (53.80, 102.80)	103.50 (76.65, 143.25)	< 0.001
Change in X5 (% predicted, n = 990)	−27.80 (−41.90, −5.95)	−32.40 (−44.85, −15.25)	< 0.001
AX (kPa/L, n = 988)	1.86 (0.93, 2.96)	3.05 (1.97, 4.37)	< 0.001
Post-BD AX (kPa/L, n = 994)	1.15 (0.53, 2.03)	1.75 (1.00, 2.75)	< 0.001
Change in AX (% predicted, n = 986)	−38.10 (−55.90, −13.50)	−41.60 (−57.80, −24.60)	0.014
R5 (% predicted, n = 992)	103.30 (89.50, 117.90)	114.10 (99.35, 130.0)	< 0.001
R20 (% predicted, n = 992)	87.80 (76.30, 101.70)	90.10 (76.80, 102.0)	0.330
R5–R20 (kPA(L/s), n = 992)	0.59 ± 0.17	0.70 ± 0.18	< 0.001
Post-BD R5–R20 (kPa(L/s), n = 995)	0.51 (0.40, 0.62)	0.59 (0.48, 0.69)	< 0.001
Change in R5–R20 (% predicted, n = 995)	−13.00 (−19.98, −4.90)	−15.80 (−23.20, −9.00)	< 0.001
FeNO (ppb, n = 667)	9.60 (5.90, 16.48)	17.60 (8.56, 30.95)	< 0.001

Data are presented as number (%), mean ± standard deviation for normally distributed variables, and median (interquartile range) for non-normally distributed variables.

BMI, body mass index; FVC, forced vital capacity; FEV1, forced expiratory volume in the 1 second; BD, bronchodilator; FEF_{25-75}, forced expiratory flow at 25%–75% of forced vital capacity; FEV_3, forced expiratory volume in 3 seconds; TEV, terminal expiration volume; X5, reactance at 5 Hz; AX, area of reactance; R5, resistance at 5 Hz; R20, resistance at 20 Hz; FeNO, fractional exhaled nitric oxide.

https://doi.org/10.4168/aair.2025.17.6.787

BDR-TEV/FEV3 according to asthma status and severity

BDR-TEV/FEV3 was significantly higher in the asthma group than in the non-asthma group (3.74% vs. 1.81%, $P < 0.001$) (**Fig. 1**). Furthermore, it showed a significant stepwise increment according to asthma severity (P for trend < 0.001), with values of 3.70% (1.73%–6.12%) in mild, 3.72% (1.35%–7.05%) in moderate, and 5.41% (2.91%–7.96%) in severe asthma (**Fig. 2**).

Correlation of BDR-TEV/FEV3 with markers of airflow limitation and atopy

In the asthma group, BDR-TEV/FEV3 showed a positive correlation with the changes in FEV1 (r = 0.579, $P < 0.001$) and $FEF_{25–75}$ (r = 0.759, $P < 0.001$) before and after bronchodilator inhalation (**Fig. 3**). BDR-TEV/FEV3 was negatively correlated with the changes in R5–R20 (r = −0.247, $P < 0.001$), X5 (r = −0.284, $P < 0.001$), and AX (r = −0.247, $P < 0.001$), which are considered parameters of peripheral airflow limitation. These associations were consistently observed across all asthma severity groups, whereas weaker associations were noted in the non-asthma group (**Supplementary Table S1**). Moreover, in the entire population, BDR-TEV/FEV3 demonstrated a positive correlation with blood eosinophil (r = 0.182, $P < 0.001$) and FeNO levels (r = 0.186, $P < 0.001$), which are associated with atopy.

External validation of BDR-TEV/FEV3

Of the 105 children screened in the external validation cohort, 80 were included (47 in the asthma and 33 in the non-asthma groups). Among them, both pre- and post-bronchodilator FEV3 values were available for 57 (71.3%) children. In this cohort as well,

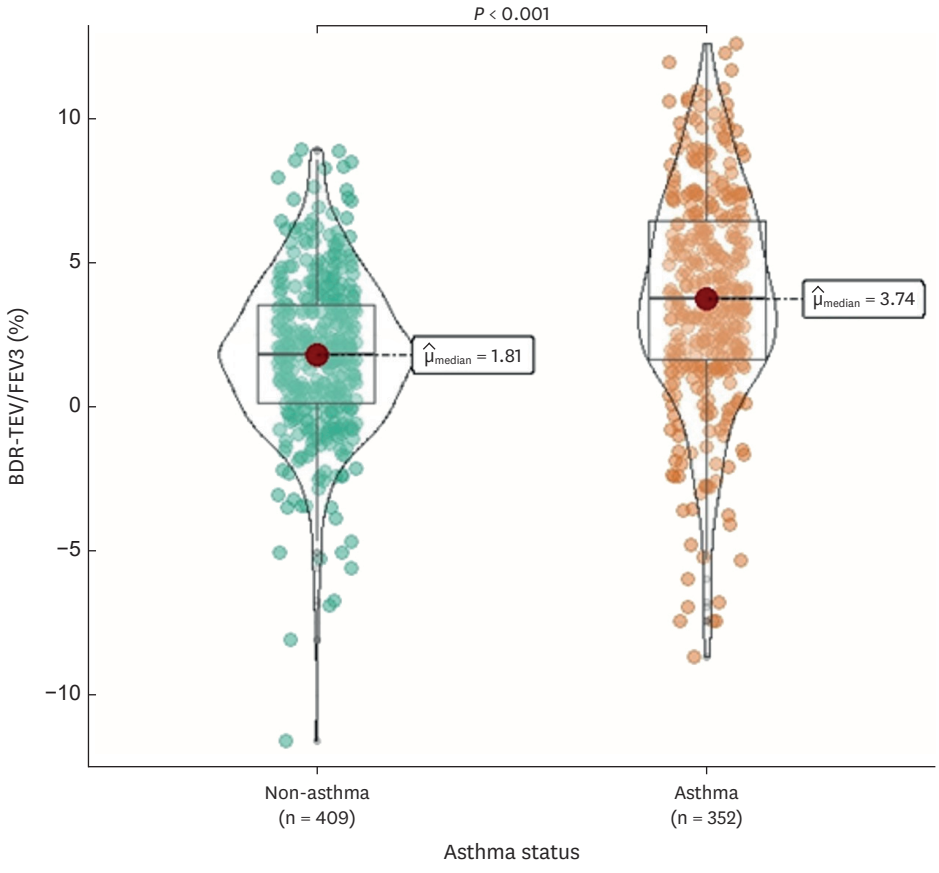

Fig. 1. BDR-TEV/FEV3 according to asthma status (n = 761).
BDR, bronchodilator response; TEV/FEV3, terminal expiration volume/forced expiratory volume in 3 seconds.

https://doi.org/10.4168/aair.2025.17.6.787

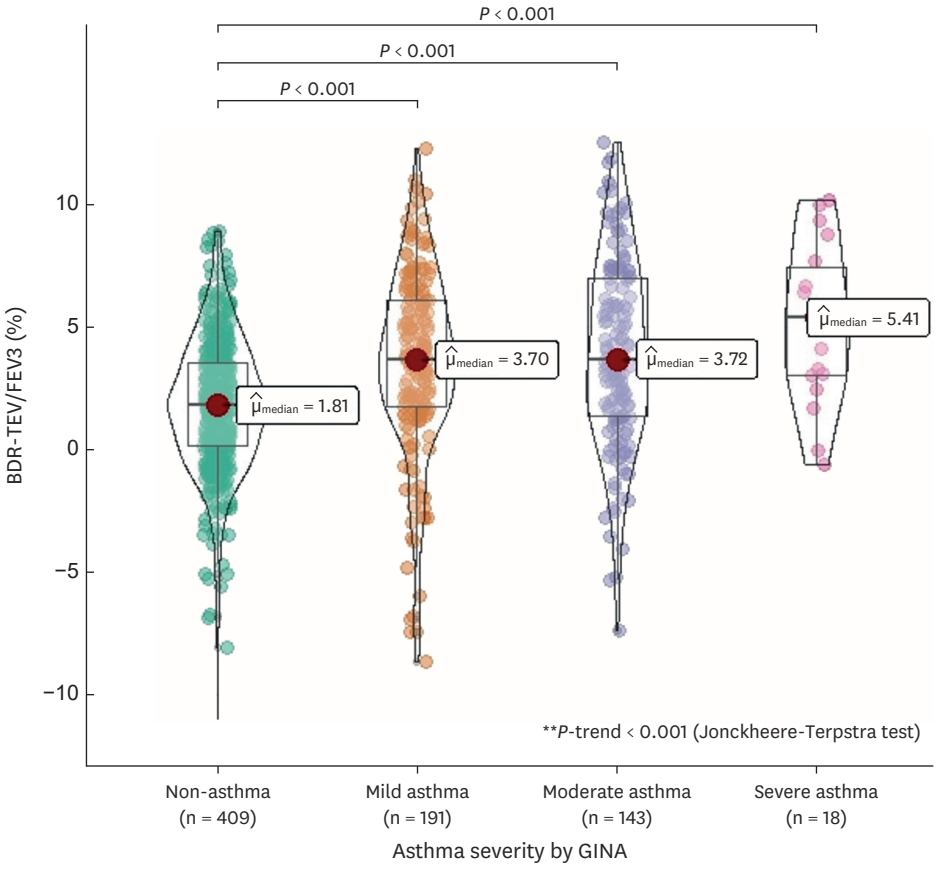

Fig. 2. Difference in BDR-TEV/FEV3 according to asthma severity (n = 761).
BDR, bronchodilator response; TEV/FEV3, terminal expiration volume/forced expiratory volume in 3 seconds; GINA, Global Initiative for Asthma.

BDR-TEV/FEV3 was significantly higher in the asthma than in the non-asthma group (3.28% vs. 2.60%, $P = 0.046$) (**Supplementary Fig. S1**), and demonstrated a positive correlation with the pre-post bronchodilator changes in FEV1 (r = 0.796, $P < 0.001$) and $FEF_{25–75}$ (r = 0.865, $P < 0.001$) among children with asthma (**Supplementary Fig. S2**).

Performance of BDR-TEV/FEV3 in asthma diagnosis

ROC analysis in asthma diagnosis according to BDR-TEV/FEV3 values resulted in AUC (95% confidence interval) of 0.678 (0.639–0.717). With the calculated optimal cutoff of 3.03, performance in the external validation group was 0.596 (0.462–0.729) in terms of area under the curve (AUC).

DISCUSSION

Our study demonstrated that BDR-TEV/FEV3 was higher in children with asthma than in those without asthma and showed a stepwise increment as asthma severity increased. Additionally, BDR-TEV/FEV3 significantly correlated with known spirometry and IOS parameters of airway dysfunction, as well as with markers of airway inflammation.

https://doi.org/10.4168/aair.2025.17.6.787

Allergy, Asthma & Immunology Research AAIR

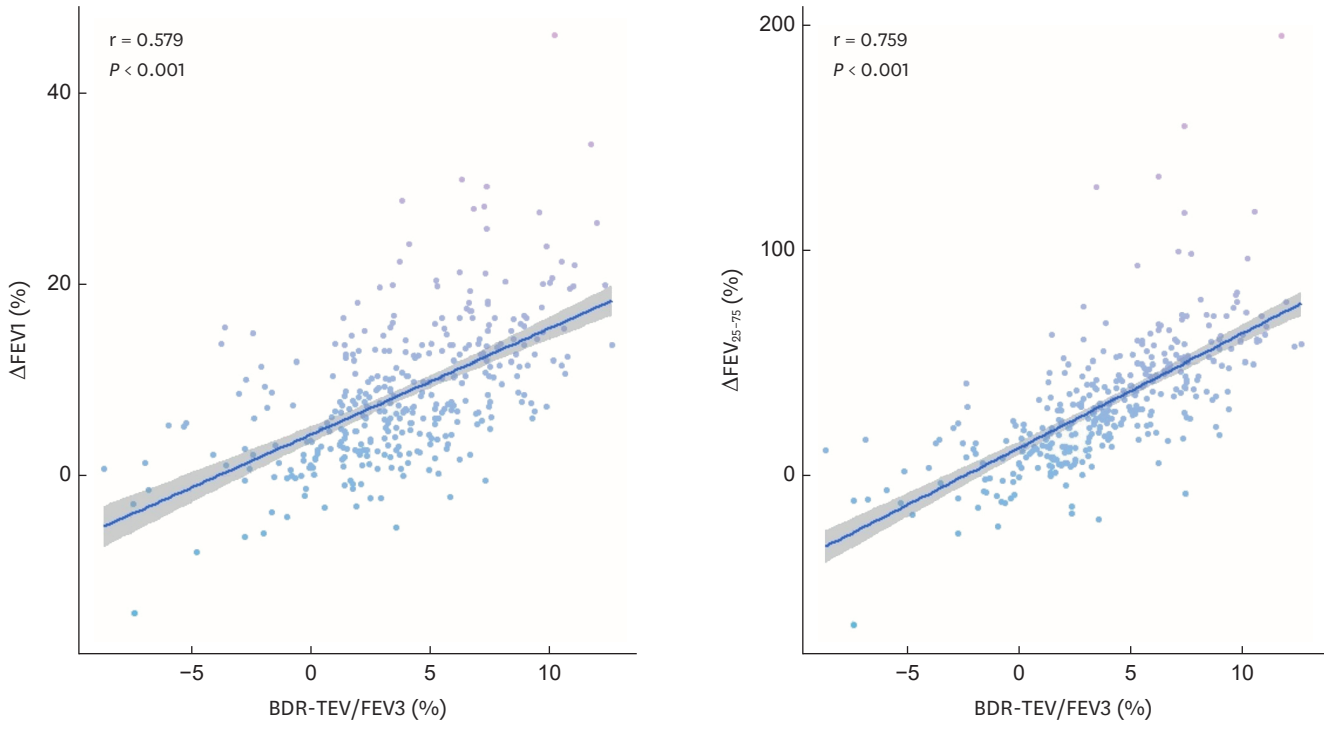

Fig. 3. Correlation with parameters of airway dysfunction in the asthma group (n = 352).
FEV1, forced expiratory volume in the first second; FEF_{25-75}, forced expiratory flow at 25%–75% of forced vital capacity; r, Spearman's rho correlation coefficient; BDR, bronchodilator response; TEV/FEV3, terminal expiration volume/forced expiratory volume in 3 seconds.

The importance of measuring small airway flows in pediatric asthma has been underestimated. Although asthma affects the entire respiratory tract, current diagnostic methods and guidelines primarily focus on large airway function.[15] This may be due to the lack of established methods for measuring small airway flows and limited understanding of the clinical implications of SAD. However, evidence suggests that SAD is present across all severity levels of asthma, with the highest prevalence in severe cases.[16]

While FEV1 is widely used for evaluating airway obstruction due to its reproducibility, its application in pediatric asthma is controversial.[17,18] In a study that compared different spirometry parameters, including FEV1, peak expiratory flow rate, $FEF_{25–75}$, FEF_{50}, and FEF_{75}, small airway parameters were more sensitive than large airway parameters for detecting airway obstruction.[19] In addition, small airway indices have the advantage of being less effort dependent than FEV1.[19]

The BDR in pediatric asthma is associated with reduced lung function, higher FeNO levels, higher eosinophil count, and longer disease duration.[20] However, the sensitivity of the currently used BDR of FEV1 cutoff of 12% is questionable in children, as it is established primarily based on adult data.[21,22] Moreover, although BDR tends to increase with lower baseline lung function, lung function is relatively preserved in children, even in severe asthma.[17,18,23,24] While post-bronchodilator FEV1/FVC and $FEF_{25–75}$ values were significantly lower in children with severe asthma than in those with lower disease severity levels, FEV1 values were not, suggesting limited sensitivity of current standards using FEV1.[25] In our study, BDR-TEV/FEV3, which showed significant differences according to asthma severity, may overcome these limitations in current spirometry measures.

https://doi.org/10.4168/aair.2025.17.6.787

$FEF_{25–75}$ has been suggested as a parameter with greater sensitivity than that of FEV1 for assessing small airway obstruction in children.[26] In children with asthma with normal FEV1 values, % predicted $FEF_{25–75}$ correlated better with BDR-FEV1 than % predicted FEV_1, indicating potential usefulness of $FEF_{25–75}$ in predicting clinically relevant reversible airflow obstruction.[27] However, BDR of $FEF_{25–75}$ alone is not sufficient to confirm asthma diagnosis and has been suggested as an adjunctive index.[28] Compared with $FEF_{25–75}$, which is a flow-based metric susceptible to high variability due to its dependence on the measured volume, BDR-TEV/FEV3 is a volume-based metric with theoretical strength in terms of reproducibility. Our study demonstrated that BDR-TEV/FEV3 was significantly correlated with BDR of FEV1, BDR of $FEF_{25–75}$, and changes in IOS indices of small airway obstruction.

Our study has several limitations. First, the number of children with severe asthma was relatively small compared with those with mild and moderate asthma. Second, FEV3 data were not available for all children, particularly younger ones, limiting the applicability of our proposed metric in this subgroup. Thirdly, some IOS parameters and FeNO values were not available in the validation cohort, which further limited validation efforts.

We propose BDR-TEV/FEV3 as a parameter to assess the reversibility of small airway obstruction in children with asthma by using conventional spirometry maneuvers. Our study demonstrated that BDR-TEV/FEV3 shows significant differences between asthmatic and non-asthmatic groups, as well as across varying degrees of asthma severity. While a change in FEV1 after bronchodilator inhalation is the current standard for asthma diagnosis, many children with asthma do not meet this criterion. BDR-TEV/FEV3 may serve as a complementary tool for detecting reversible SAD in pediatric asthma patients. Further validation studies are needed to determine its clinical utility in assessing small airway obstruction reversibility in children with suspected asthma.

ACKNOWLEDGMENTS

This study was supported by Technology Innovation Program from the Ministry of Trade, Industry and Energy (MOTIE, Korea) (Project No. 20018111).

SUPPLEMENTARY MATERIALS

Supplementary Table S1
Correlation of BDR-TEV/FEV3 with markers of airflow limitation according to asthma severity

Supplementary Fig. S1
BDR-TEV/FEV3 according to asthma status in the external validation cohort (n = 57).

Supplementary Fig. S2
Correlation with parameters of airway dysfunction in the external validation cohort (n = 35).

https://doi.org/10.4168/aair.2025.17.6.787

REFERENCES

1. Global Initiative for Asthma. Global strategy for asthma management and prevention, 2023 [Internet]. Fontana (WI): Global Initiative for Asthma; 2023 [cited 2023 Sep 11]. Available from: www.ginasthma.org.
2. Zimmermann SC, Tonga KO, Thamrin C. Dismantling airway disease with the use of new pulmonary function indices. Eur Respir Rev 2019;28:180122. PUBMED | CROSSREF
3. Cottini M, Lombardi C, Berti A, Comberiati P. Small-airway dysfunction in paediatric asthma. Curr Opin Allergy Clin Immunol 2021;21:128-34. PUBMED | CROSSREF
4. Komarow HD, Skinner J, Young M, Gaskins D, Nelson C, Gergen PJ, et al. A study of the use of impulse oscillometry in the evaluation of children with asthma: analysis of lung parameters, order effect, and utility compared with spirometry. Pediatr Pulmonol 2012;47:18-26. PUBMED | CROSSREF
5. Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R, et al. Interpretative strategies for lung function tests. Eur Respir J 2005;26:948-68. PUBMED | CROSSREF
6. Stanojevic S, Wade A, Stocks J, Hankinson J, Coates AL, Pan H, et al. Reference ranges for spirometry across all ages: a new approach. Am J Respir Crit Care Med 2008;177:253-60. PUBMED | CROSSREF
7. Galant SP, Komarow HD, Shin HW, Siddiqui S, Lipworth BJ. The case for impulse oscillometry in the management of asthma in children and adults. Ann Allergy Asthma Immunol 2017;118:664-71. PUBMED | CROSSREF
8. Jung JH, Park M, Kim GE, Kim JD, Kim MJ, Choi SH, et al. TEV/FEV3 as a coherent metric of small airway dysfunction in childhood asthma. Allergy Asthma Proc 2023;44:171-8. PUBMED | CROSSREF
9. Bao W, Lin Y, Zhao L, Zhang Y, Lin J, Yin J, et al. (FEV3-FEV1)/FVC: a terminal-airflow variable for airway hyperresponsiveness and inflammation prediction in patients with symptoms despite preserved spirometry. J Allergy Clin Immunol Pract 2025;13:107-118.e8. PUBMED | CROSSREF
10. Tuomisto LE, Ilmarinen P, Lehtimäki L, Tommola M, Kankaanranta H. Immediate bronchodilator response in FEV1 as a diagnostic criterion for adult asthma. Eur Respir J 2019;53:1800904. PUBMED | CROSSREF
11. Cooper BG, Stocks J, Hall GL, Culver B, Steenbruggen I, Carter KW, et al. The Global Lung Function Initiative (GLI) Network: bringing the world's respiratory reference values together. Breathe (Sheff) 2017;13:e56-64. PUBMED | CROSSREF
12. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al. Standardisation of spirometry. Eur Respir J 2005;26:319-38. PUBMED | CROSSREF
13. Oostveen E, MacLeod D, Lorino H, Farré R, Hantos Z, Desager K, et al. The forced oscillation technique in clinical practice: methodology, recommendations and future developments. Eur Respir J 2003;22:1026-41. PUBMED | CROSSREF
14. Dweik RA, Boggs PB, Erzurum SC, Irvin CG, Leigh MW, Lundberg JO, et al. An official ATS clinical practice guideline: interpretation of exhaled nitric oxide levels (FENO) for clinical applications. Am J Respir Crit Care Med 2011;184:602-15. PUBMED | CROSSREF
15. Hopp RJ, Wilson MC, Pasha MA. Small airway disease in pediatric asthma: the who, what, when, where, why, and how to remediate. A review and commentary. Clin Rev Allergy Immunol 2022;62:145-59. PUBMED | CROSSREF
16. Postma DS, Brightling C, Baldi S, Van den Berge M, Fabbri LM, Gagnatelli A, et al. Exploring the relevance and extent of small airways dysfunction in asthma (ATLANTIS): baseline data from a prospective cohort study. Lancet Respir Med 2019;7:402-16. PUBMED | CROSSREF
17. Bacharier LB, Strunk RC, Mauger D, White D, Lemanske RF Jr, Sorkness CA. Classifying asthma severity in children: mismatch between symptoms, medication use, and lung function. Am J Respir Crit Care Med 2004;170:426-32. PUBMED | CROSSREF
18. Paull K, Covar R, Jain N, Gelfand EW, Spahn JD. Do NHLBI lung function criteria apply to children? A cross-sectional evaluation of childhood asthma at National Jewish Medical and Research Center, 1999-2002. Pediatr Pulmonol 2005;39:311-7. PUBMED | CROSSREF
19. Francisco B, Ner Z, Ge B, Hewett J, König P. Sensitivity of different spirometric tests for detecting airway obstruction in childhood asthma. J Asthma 2015;52:505-11. PUBMED | CROSSREF
20. Coverstone AM, Bacharier LB, Wilson BS, Fitzpatrick AM, Teague WG, Phipatanakul W, et al. Clinical significance of the bronchodilator response in children with severe asthma. Pediatr Pulmonol 2019;54:1694-703. PUBMED | CROSSREF
21. Lorber DB, Kaltenborn W, Burrows B. Responses to isoproterenol in a general population sample. Am Rev Respir Dis 1978;118:855-61. PUBMED | CROSSREF

22. Tse SM, Gold DR, Sordillo JE, Hoffman EB, Gillman MW, Rifas-Shiman SL, et al. Diagnostic accuracy of the bronchodilator response in children. J Allergy Clin Immunol 2013;132:554-559.e5. PUBMED | CROSSREF

23. Weir DC, Sherwood Burge P. Measures of reversibility in response to bronchodilators in chronic airflow obstruction: relation to airway calibre. Thorax 1991;46:43-5. PUBMED | CROSSREF

24. Fitzpatrick AM, Teague WG, Meyers DA, Peters SP, Li X, Li H, et al. Heterogeneity of severe asthma in childhood: confirmation by cluster analysis of children in the National Institutes of Health/National Heart, Lung, and Blood Institute Severe Asthma Research Program. J Allergy Clin Immunol 2011;127:382-389.e1-13. PUBMED | CROSSREF

25. Lang AM, Konradsen J, Carlsen KH, Sachs-Olsen C, Mowinckel P, Hedlin G, et al. Identifying problematic severe asthma in the individual child--does lung function matter? Acta Paediatr 2010;99:404-10. PUBMED | CROSSREF

26. Lebecque P, Kiakulanda P, Coates AL. Spirometry in the asthmatic child: is FEF_{25-75} a more sensitive test than FEV1/FVC? Pediatr Pulmonol 1993;16:19-22. PUBMED | CROSSREF

27. Simon MR, Chinchilli VM, Phillips BR, Sorkness CA, Lemanske RF Jr, Szefler SJ, et al. Forced expiratory flow between 25% and 75% of vital capacity and FEV1/forced vital capacity ratio in relation to clinical and physiological parameters in asthmatic children with normal FEV1 values. J Allergy Clin Immunol 2010;126:527-534.e1-8. PUBMED | CROSSREF

28. Linares MB, Rodríguez MA, Icarte DM, Martínez BA, Milla VP, Zygier NF, et al. Bronchodilator response in FEF_{25-75} for the diagnosis of asthma in children. Respir Care 2023;68:505-10. PUBMED | CROSSREF