

ORIGINAL ARTICLE: ASTHMA

Asthma control in children: Body plethysmography in addition to spirometry

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Abstract

Background: There is a lack of agreement among measures of asthma control in children. In Central Europe, body plethysmography is additionally used for asthma monitoring. However, its value is still unclear.

Objectives: We investigated the possible additional value of body plethysmographic measures (specific resistance, RV/TLC) compared with spirometric measures forced expiratory volume in 1 second (FEV₁), forced vital capacity (FVC), FEV₁/FVC, forced expiratory flow at 25% to 75% of forced vital capacity (FEF₂₅₋₇₅), and fraction of exhaled nitric oxide (FeNO) for assessment of asthma control.

Methods: One hundred and forty-five asthmatic children aged 5 to 17 were included. All children performed measurements of FeNO, spirometry, and body plethysmography. Asthma control was assessed by the asthma control test (c-ACT/ACT) and a doctor's assessment of asthma control.

Results: Investigating single lung function parameters, FEV₁, FEV₁/FVC, FEF₂₅₋₇₅ and RV/TLC differed between controlled and partly controlled asthma. However, we found no differences between controlled and uncontrolled asthma with regard to single lung function parameters or for any parameter if investigated in a multivariable approach. This was also true if we combined obtained parameters from spirometry (comparing pathologic vs normal spirometry). Investigating the combination of body plethysmography and doctor's assessment of asthma control a significant association was found ($P = 0.02$). Furthermore, combined spirometry and body plethysmography showed a significant association with both doctor's assessed asthma control ($P = 0.009$) and the c-ACT/ACT ($P = 0.04$). The addition of FeNO did not improve the results.

Conclusions: The combination of body plethysmography and spirometry shows best agreement with asthma control in children compared with spirometry or body plethysmography alone. Further studies are needed to find out whether additional measurements of body plethysmography improve the outcome of children in asthma monitoring.

KEYWORDS

asthma, asthma control, lung function, monitoring, plethysmography

1 | BACKGROUND

Asthma is one of the most common chronic diseases in childhood and can cause hospitalizations due to severe asthma exacerbations. A reason is poor asthma control in children. This underlines the importance of optimizing asthma control in daily life, however, monitoring asthma control is known to be difficult.

National and international guidelines have defined asthma and classified it into controlled, partly controlled, or uncontrolled asthma including clinical characteristics (symptoms and exacerbations), limitations of activities and forced expiratory volume in 1 second (FEV₁)-values into the classification.^{1,2} Different questionnaires have been developed to additionally help monitor asthma control. One of the frequently used questionnaires is the asthma control test (ACT),³ for which a version for children younger than 12 years is also available (c-ACT).^{4,5} Objective methods to assess asthma control include measures of spirometry and fractional concentration of nitric oxide in exhaled air (FeNO).^{6–13} In the last years, several studies examined if the latter agree with asthma control in children. While some authors found a correlation between the parameters,^{6–8} most of the authors did not.^{9–13}

Body plethysmography provides additional parameters of lung volumes and airway resistance and thus may add information in terms of asthma control.¹⁴ It is widely used in Central Europe. Another advantage compared to spirometry is its independence of the cooperation of participants.

However, only a few studies investigated the role of body plethysmography in asthmatic children^{15–19} and to the best of our knowledge, there are no studies available investigating the relationship between asthma control and the assessment of spirometry, body plethysmography, and FeNO.

The aim of our study was, therefore, to assess the possible additional value of measurements from body plethysmography for assessment of asthma control, compared with measurements from spirometry alone. We investigated the agreement between lung function parameters from spirometry and body plethysmography and two different measures of asthma control in children, evaluated either by questionnaire or by doctor's assessment. First, we assessed the agreement between single lung function parameters and asthma control. Second, we combined the lung function parameters from spirometry only (normal vs pathologic) and from both spirometry and body plethysmography (normal vs pathologic) and investigated the association with asthma control.

2 | METHODS

2.1 | Subjects and study design

In this cross-sectional study, children and adolescents with asthma were recruited in the asthma outpatient clinic of the Children's University Hospital Halle (Saale), Germany. Asthma was diagnosed clinically by a trained pediatric asthma specialist and defined as episodic wheeze, and/or cough, and/or breathlessness responsive to bronchodilators.

Patients performed FeNO measurements and lung function testing (spirometry and body plethysmography), and thereafter the c-ACT/ACT were answered. Finally, patients underwent the doctor's assessment for asthma control performed by a trained pediatric physician. Subjects were excluded when they were smokers or had an acute respiratory infection the preceding 2 weeks. The study was approved by the local ethics committee of the Martin-Luther-University Halle-Wittenberg, Germany. Informed consent was obtained from parents and children, when it was age-appropriate.

2.2 | FeNO measurements

FeNO was measured using the NIOX MINO (Circassia Pharmaceuticals, Oxford, UK) according to the manufacturer's recommendations (flow rate of 50 mL/seconds). A FeNO value above 35 ppb was considered as pathologic.²⁰

2.3 | Lung function tests

Spirometry and body plethysmography were performed according to current guidelines as previously described (MasterLab; Jaeger, Würzburg, Germany).²¹ Assessed parameters by spirometry were FEV₁, forced vital capacity (FVC), FEV₁/FVC, and forced expiratory flow at 25% to 75% of forced vital capacity (FEF_{25–75}). Spirometry values were expressed in z-scores using the global lung initiative (GLI) reference equations.²² A z-score below –1.64 was defined as outside limits of normal. Obtained additional measurements from body plethysmography were sR_{tot} (specific airway resistance) and RV/TLC (residual volume-total lung capacity ratio). As reference values for body plethysmographic values differ in the literature and depend on equipment,²³ we used our own healthy control group to choose the cut-off values.²⁴ Pathologic body plethysmographic parameters were defined to be above 1.0 kPa-s for sRaw and above 33% for RV/TLC.

In addition, we grouped lung function parameters into the following categories: normal and pathologic spirometry, normal and pathologic body plethysmography. If FEV₁, FVC, FEV₁/FVC, FEF_{25–75} were within normal limits, "spirometry" was defined as "normal". If any of these parameter was outside normal limits, "spirometry" was defined as "pathologic". For the category "body plethysmography" the same criteria were applied including sR_{tot} and RV/TLC. For the "combination of spirometry and body plethysmography" the following parameters were included: FEV₁, FVC, FEV₁/FVC, FEF_{25–75}, sR_{tot} and RV/TLC.

2.4 | Asthma control test

The ACT was used as a questionnaire for subjects more than or equal to 12 years. Children less than 12 years and their parents completed the c-ACT.^{3,4} We coded the questionnaire's score into three groups according to a modification of Greenblatt et al²⁵ A score below 20 points was classified as "uncontrolled asthma", a score between 20 and 24 (in the ACT) or 26 (the c-ACT) points was defined as "partly controlled asthma" and a score with the maximum of points

(25 for the ACT and 27 for the c-ACT) was defined as “controlled asthma”. For additional analysis we grouped asthma control in two different ways: uncontrolled/partly controlled asthma (score below 24 or 26 points) versus controlled asthma (full score) and uncontrolled asthma (score below 20 points) versus partly controlled/controlled asthma (score above 19 points).

2.5 | Doctor's assessment of asthma control

Doctor's assessment of asthma control included a clinical examination and documentation of asthma symptoms (daytime, nighttime, exercise) and the use of bronchodilators by a trained pediatric asthma specialist. Furthermore the exacerbation rate of the preceding year was recorded. On the basis of this information and the result of FEV₁-values asthma control was classified in uncontrolled, partly controlled, or controlled asthma in accordance with National Guidelines, modified from Global Initiative for Asthma.^{1,2} In addition we grouped asthma control again as follows: uncontrolled/partly controlled asthma vs controlled asthma and uncontrolled vs partly controlled/controlled asthma.

2.6 | Statistical analysis

We performed multinomial regression analyses to investigate the association of (i) c-ACT/ACT and (ii) doctor's assessed of asthma control (as a categorical variable: uncontrolled, partly controlled, and controlled asthma) with single lung function parameters (as linear variables). After performing univariable models, we included all variables with $P \leq 0.05$ into a multivariable model. As sensitivity analyses we repeated the analyses using logistic regression selecting binary outcomes A: (i) controlled and (ii) partly/uncontrolled asthma and B: (i) controlled/partly controlled and (iii) uncontrolled asthma. The latter analyses are displayed in the supplementary material (Table SE1-SE4). In a second step, we investigated the association of (i) c-ACT/ACT and (ii) doctor's assessment of asthma control with lung function parameters as binary variables (grouped in normal and pathologic). Asthma control was divided into three categories (uncontrolled, partly controlled, and controlled asthma). In this model we also performed additional analyses with asthma control divided in only two groups: A: (i) controlled and (ii) partly/uncontrolled asthma and B: (i) controlled/partly controlled and (ii) uncontrolled asthma. The χ^2 test was used for analyses. $P \leq 0.05$ were considered statistically significant. All analyses were done using Stata (Stata Statistical Software: Release 13; Stata Corp LP, College Station, TX).

3 | RESULTS

3.1 | Study population and lung function data

In total, 145 children were enrolled in the study, aged 5 to 17 years. For detailed demographic, anthropometric and lung function

TABLE 1 Baseline demographics and lung function in study subjects

Variables (n = 145)	Mean (SD) or numbers
Age, y	11.9 (3.1)
Sex (male/female)	90/55
Height, cm	150.4 (17.9)
Atopy, n	128
ICS use, n	79
LABA use, n	16
Montelukast use, n	15
FEV ₁ (z-score)	0.03 (0.9)
FVC (z-score)	0.01 (0.9)
FEV ₁ /FVC (ratio)	0.05 (1.1)
FEF ₂₅₋₇₅ (z-score)	-0.4 (1.0)
sRtot (kPa-s)	0.7 (0.3)
RV/TLC (ratio) ^a	25.5 (7.8)
FeNO (ppb) ^b	28 (25.2)

Abbreviations: FEF₂₅₋₇₅, forced expiratory flow at 25% to 75% of forced vital capacity; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; SD, standard deviation.

^aMissing data in five patients.

^bMissing data in 10 patients.

data see Table 1. Spirometry values for FEV₁, FEV₁/FVC, FVC, and FEF_{25/75} were found outside limits of normal in 7, 7, 14, and 16 patients, respectively. In total, spirometry was abnormal in 25 of 145 children (17%). sRtot and RV/TLC were elevated above the upper limit of normal in 11 (7.5%) and 20 (13.8%) patients, respectively. In total the combination of spirometry and body plethysmography was abnormal in 39 of 145 patients (27%). Thirty-four patients had FeNO values higher than 35 ppb.

3.2 | Asthma control by questionnaire and doctor's assessment

The questionnaires median scores were 23 points (interquartile range [IQR], 20-25 points; $n = 71$) for the c-ACT and 23.5 points (IQR, 21-25, $n = 74$) for the ACT. Thirty-four patients (23%) achieved the maximal score (25 or 27 points, respectively) and were classified as having “controlled asthma”. 81 (56%) and 30 (21%) patients were classified as “partly controlled asthma” and “uncontrolled asthma”, respectively. Doctor's assessment of asthma control showed the following results: 42 (29%) were classified as having uncontrolled asthma, 62 (43%) and 41 children (28%) children met criteria for having partly controlled or controlled asthma, respectively.

3.3 | Comparison of asthma control and single lung function data

Using a multinomial regression model, investigating doctor's assessment of asthma control, we found differences between controlled asthma and partly controlled asthma for FEV₁, FEF₂₅₋₇₅,

TABLE 2 Association between doctor's assessment of asthma control and single lung function measurements

	Doctor's assessment of asthma control ^a			Doctor's assessment of asthma control ^b		
	RRR	95% CI	P value	RRR	95% CI	P value
FEV ₁						
Partly controlled	0.51	[0.31, 0.83]	0.007	0.70	[0.35, 1.43]	0.3
Uncontrolled	0.87	[0.52, 1.47]	0.6	1.3	[0.62, 2.84]	0.5
FVC						
Partly controlled	0.66	[0.41, 1.07]	0.09			
Uncontrolled	1.07	[0.63, 1.80]	0.8			
FEV ₁ /FVC						
Partly controlled	0.73	[0.50, 1.05]	0.09			
Uncontrolled	0.81	[0.55, 1.20]	0.3			
FEF ₂₅₋₇₅						
Partly controlled	0.58	[0.37, 0.90]	0.0	0.76	[0.40, 1.43]	0.4
Uncontrolled	0.73	[0.49, 1.18]	0.2	0.68	[0.34, 1.37]	0.2
sRtot (log)						
Partly controlled	2.1	[0.71, 6.26]	0.2			
Uncontrolled	1.66	[0.51, 5.37]	0.4			
RV/TLC						
Partly controlled	1.06	[1.01, 1.13]	0.03	1.05	[0.99, 1.11]	0.1
Uncontrolled	1.04	[0.98, 1.11]	0.2	1.04	[0.98, 1.11]	0.2
FeNO (log)						
Partly controlled	1.01	[0.60, 1.71]	1.0			
Uncontrolled	1.31	[0.73, 2.33]	0.35			

Abbreviations: CI, confidence interval; FEF₂₅₋₇₅, forced expiratory flow at 25% to 75% of forced vital capacity; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; RRR, relative risk ratio.

Asthma assessment was divided in three groups: controlled, partly controlled, and uncontrolled asthma. Baseline was always controlled asthma.

^aMultinomial regression models investigating the association of doctor's assessment with different lung function parameter asthma in univariable analyses.

^bMultinomial regression models investigating the association of doctor's assessment with different lung function parameter asthma in multivariable analyses.

and RV/TLC. However, no differences could be found between controlled and uncontrolled asthma (Table 2, left column) or for any parameter in the multivariable approach (Table 2, right column). Investigating asthma control using the ACT, we found differences between controlled asthma and partly controlled asthma for FEV₁/FVC and FEF₂₅₋₇₅ (Table 3, right column). Again, no differences could be found between controlled and uncontrolled asthma or for any parameters in a multivariable approach (Table 3, left column). We thus performed additional analyses grouping asthma control in only two groups A: (i) controlled compared to (ii) partly/uncontrolled asthma and B: (i) controlled/partly controlled compared to (ii) uncontrolled asthma). While results remained similar for the doctor's assessment of asthma control in analysis A (controlled vs partly/uncontrolled asthma), no associations could be found investigating doctors assessment of asthma control if comparing (B) controlled/partly controlled vs uncontrolled asthma. No association could be found for the asthma control test in either analyses. For results see Tables S1-S4 in the supplementary material.

3.4 | Comparison of asthma control and combined lung function data

We combined lung function parameters in the categorizations "spirometry" and "body plethysmography" and the "combination of body plethysmography and spirometry", using a binary outcome: normal and pathologic measurements. We investigated a possible association with the ACT and the doctor's assessment of asthma control, categorized into three groups (uncontrolled asthma, partly controlled asthma, and controlled asthma). We could not find an association with spirometry and either c-ACT/ACT ($P=0.2$) or doctor's assessment of asthma control ($P=0.1$). The body plethysmography measurements showed an association with doctor's assessment of asthma control ($P=0.02$), a trend could be seen for c-ACT/ACT ($P=0.07$). When we analyzed data from the combination of spirometry and body plethysmography, measurements showed an association with both doctor's assessments of asthma ($P=0.009$) and c-ACT/ACT ($P=0.04$). For further details see also Figure 1. In an additional model, we compared lung function measurements and

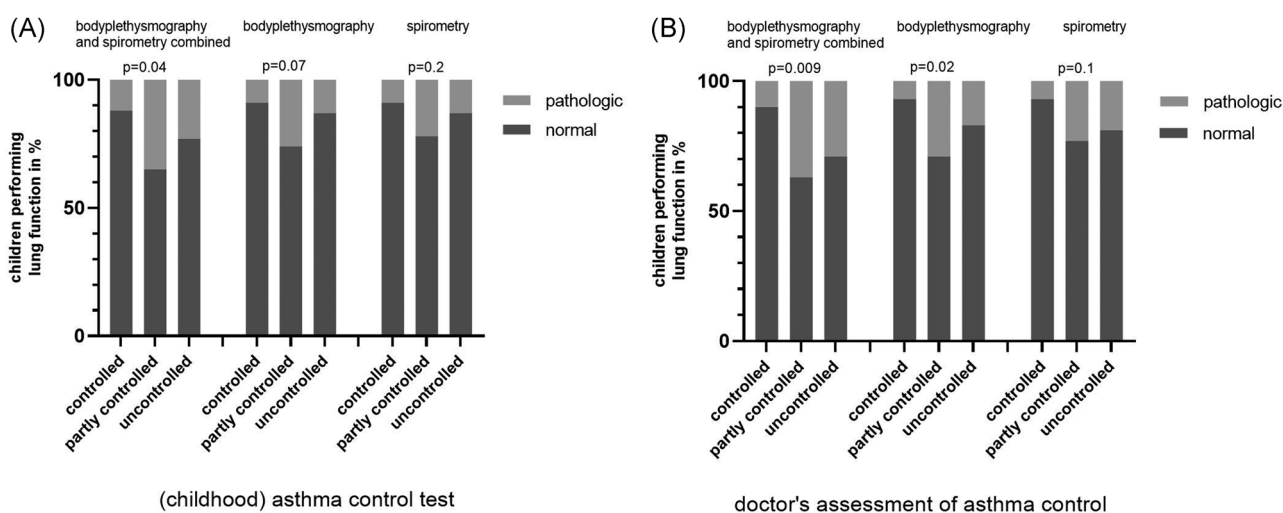
TABLE 3 Association between (childhood) asthma control test and single lung function measurements

	(Childhood) asthma control test ^a			(Childhood) asthma control test ^b		
	RRR	95% CI	P value	RRR	95% CI	P value
FEV₁						
Partly controlled	0.79	[0.50, 1.25]	0.3			
Uncontrolled	1.05	[0.60, 1.85]	0.9			
FVC						
Partly controlled	1.12	[0.70, 1.79]	0.6			
Uncontrolled	1.10	[0.62, 1.95]	0.7			
FEV₁/FVC						
Partly controlled	0.69	[0.48, 1.01]	0.056	0.93	[0.48, 1.82]	0.8
Uncontrolled	0.97	[0.62, 1.53]	0.9	0.98	[0.44, 2.19]	1.0
FEF₂₅₋₇₅						
Partly controlled	0.62	[0.39, 0.96]	0.03	0.66	[0.30, 1.44]	0.3
Uncontrolled	0.97	[0.56, 1.66]	0.9	0.99	[0.38, 2.56]	1.0
sRtot (log)						
Partly controlled	1.43	[0.49, 4.22]	0.5			
Uncontrolled	0.97	[0.26, 3.66]	1.0			
RV/TLC						
Partly controlled	1.05	[0.99, 1.11]	0.08			
Uncontrolled	1.04	[0.97, 1.12]	0.3			
FeNO (log)						
Partly controlled	0.99	[0.58, 1.69]	1.0			
Uncontrolled	1.24	[0.64, 2.39]	0.5			

Asthma assessment was divided in three groups: controlled, partly controlled, and uncontrolled asthma. Baseline was always controlled asthma. Abbreviations: CI, confidence interval; FEF₂₅₋₇₅, forced expiratory flow at 25% to 75% of forced vital capacity; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; RRR, relative risk ratio.

^aMultinomial regression models investigating the association of (childhood) asthma control test with different lung function parameter asthma in univariable analyses.

^bMultinomial regression models investigating the association of (childhood) asthma control test with different lung function parameter asthma in multivariable analyses.

**FIGURE 1** Association between combined lung function results and asthma control assessed by (A) (childhood) asthma control test and (B) doctor's assessment of asthma control

asthma control divided in two categories only. Results remained stable comparing the groups (i) uncontrolled/partly controlled asthma and (ii) controlled asthma (for the c-ACT/ACT $P = 0.02$, for doctor's assessment $P = 0.003$). No associations could be found when we compared the groups (i) uncontrolled asthma and (ii) controlled/partly controlled ($P = 0.6$ and $P = 0.8$ respectively). When FeNO measurements were also included into this analysis (using "any pathologic measurement") associations could not be seen (results not shown).

4 | DISCUSSION

To our knowledge, this is the first study investigating the association of body plethysmographic measures and the assessment of asthma control in children. We were able to show that combining results from body plethysmography and spirometry resulted in a better agreement with the c-ACT/ACT and the doctor's assessment of asthma control, compared with either spirometry or body plethysmography measures alone. The effect was mainly driven by the difference between the group of uncontrolled/partly controlled asthma and the group of controlled asthma. Between the group of uncontrolled asthma and the group of partly controlled/controlled asthma, no clear difference was seen. Children and adolescents receiving full scores in asthma control were more likely to have a normal lung function, overall. Investigating single lung function values no associations to asthma control were found in a multivariable approach, suggesting that they might be inferior to a combination of all different parameters.

The lack of asthma control leads to detrimental long term consequences. There is, however, an ongoing discussion as to which parameters are best used to monitor asthma control in children. The definition of asthma control itself is difficult to establish. Several tools have been developed, however, there is currently no gold standard of defining asthma control. A combination of subjective and objective measures is mostly recommended.^{26,27}

The c-ACT/ACT and the doctor's assessment of asthma are subjective measures of asthma control. While being the most widely used questionnaire on asthma control, the c-ACT/ACT misses exacerbation rates and FEV₁, which are important items for asthma control. Furthermore, former studies found that asthma control assessed by doctor's assessment do not give the same results as the ACT questionnaire.^{28,29} This is in agreement with our results. In the c-ACT/ACT, less patients were classified to be "controlled" or "uncontrolled" compared with the doctor's assessment. This might be explained by the fact that people tend to adjust themselves in the middle range (known as the error of central tendency). Furthermore, patients have different perceptions of their level of control than their doctor.²⁸⁻³⁰

However, the classification of asthma control is difficult to establish in general, especially when interpreting questionnaires. A score below 20 points is widely used to indicate uncontrolled asthma in the c-ACT/ACT.³¹ In contrast, the definitions for partly controlled and controlled asthma differ in the literature. Some authors distinguish between "well," "totally," or "optimal" controlled asthma and partly controlled

asthma.^{31,32} Voorend van Bergen et al³² found out that best cut-off to predict well-controlled asthma was a score of more than or equal to 22 (c-ACT) and 23 (ACT). In our study we used the presence of absence of the maximal achievable points to distinguish between controlled and partly controlled because we believe that this is the most relevant analysis for clinical management.

Objective measures of asthma control include lung function measurements. The ERS Task Force on asthma monitoring recommended spirometry once a year as an important objective tool,²⁶ although a mismatch between asthma symptoms and spirometry results in children has been described, as spirometry is mostly within normal ranges in children.³³ Although body plethysmography is widely implemented in central Europe, there is a lack of studies regarding the value of this technique and therefore body plethysmography could not be evaluated by the Task Force. The American Academy of Pediatrics published a clinical report and guidance on tools for asthma control and recommended at least the measurement of airway resistance by impulse oscillometry as a research tool.²⁷ Body plethysmography provides both measurement of specific airway resistance and lung volumes and requires less cooperation than spirometry. It is therefore especially attractive in the pediatric population, even though the technique is more expensive and time-consuming than most other lung function measurements.

In our population of asthmatic children, we found 27% of children to have a pathologic lung function (either spirometry or body plethysmography or both) overall compared with only 17% having an abnormal spirometry, suggesting the heterogeneity in lung function pathologies in asthma.

To the best of our knowledge, this is the first study investigating the association of body plethysmography and asthma control in children. A study in adults reported higher RV/TLC values in patients with low ACT scores,³⁴ while another study did not find this association.³⁵ In our study, we chose specific airway resistance (sRtot) and RV/TLC as additional body plethysmographic markers. sRtot has been described to be appropriate to detect early airway obstruction in children and potentially to be able to predict subsequent mild airflow limitations.¹⁵ RV/TLC assesses air trapping and hyperinflation. A study by Labbé et al³⁶ reported, that asthmatic children with hyperinflation (RV/TLC > 30%) had more diurnal symptoms than children without hyperinflation. Mahut et al³⁷ found a significant elevation of RV/TLC in the group of children who had an asthma exacerbation in the preceding 3 months of the study compared with children who did not. Although the studies of Mahut et al and Labbé et al did not include an assessment of asthma control they are in line with our results demonstrating that body plethysmographic parameters provide different and additional information in a considerable proportion of asthmatic children. Both specific airway resistance and RV/TLC may serve as markers of "distal" or "small airways" obstruction in early disease progression and may be important for assessing asthma control. Furthermore, we could show that children with "perfect" asthma control defined by achieving the maximal

achievable points in the ACT or c-ACT had mostly normal body plethysmography.

The doctor's assessment of asthma control showed slightly better associations with lung function measurements than the c-ACT/ACT. This may be explained to some part as FEV₁ is one item of the doctor's assessment of asthma.

Interestingly, investigating the association between single lung function measurements in a multinomial or logistic model and either c-ACT/ACT or doctor's assessment of asthma control, we found no clear association for the investigated parameters. In particular, FeNO values, either as single values or in combination, did not correlate with any other measurement. This may be explained by the generally lower FeNO values in our study population. We cannot rule out a missed signal for FeNO had we used a lower cut off for abnormal FeNO values than 35 ppb as we have done.

There are some limitations in our study. First, the study was a cross-sectional study, thus we could not investigate the prediction of asthma control in the future. Second, the numbers of children with pathologic lung function were low, although we could include almost 150 children. Larger studies might be able to discover further differences. However, the strength of our study is that our study subjects represent the "typical" population of an outpatient asthma clinic and thus we believe the observations are of clinical value.

Our results, showing differences between the partly/uncontrolled and the controlled asthma groups, but not between the uncontrolled and the partly controlled/controlled asthma groups, suggest the following: Both partly and uncontrolled asthma reflect clinical situations which are not acceptable in patient management and need to be improved. Anything less than "complete" asthma control needs better management, monitoring and treatment adjustment. Measurement of "small airways disease" by body plethysmography may help to characterize this special group of partly controlled/uncontrolled asthmatic children.

In summary, our study shows best agreement of lung function indices with asthma control when using a combination of body plethysmography and spirometry in asthmatic children. This suggests that measuring potential markers of small airways disease may provide additional information during asthma monitoring. However, further studies are needed to find out if additional measurements of body plethysmography during asthma monitoring potentially improve the outcome of asthmatic children in future.

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AUTHOR CONTRIBUTIONS

CL conceived and coordinated the study and revised the manuscript. IK participated in data acquisition, carried out the interpretation and

analysis of the data and drafted the manuscript. AH participated in the analysis of the data. AZ and NB revised the manuscript.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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Asthma control in children: Body plethysmography in addition to spirometry

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Online Supplement

Table E1: Association between doctor's assessed asthma control (comparing controlled and partly/ uncontrolled asthma) and single lung function measurements.

	doctor's assessed asthma control ^a			doctor's assessed asthma control ^b		
	OR	95% CI	p-value	OR	95% CI	p-value
FEV ₁	0.64	[0.41,0.99]	0.04	0.92	[0.48, 1.73]	0.8
FVC	0.8	[0.52,1.24]	0.32			
FEV ₁ /FVC	0.76	[0.54,1.06]	0.1			
FEF25/75	0.64	[0.43,0.96]	0.03	0.72	[0.42, 1.29]	0.3
sR _{tot} (log)	1.91	[0.71, 5.20]	0.2			
RV/TLC	1.06	[1.00,1.11]	0.04	f	[0.99, 2.97]	0.1
FeNO (log)	1.12	[0.64,1.81]	0.6			

Logistic regression models investigating the association of doctor's assessed asthma control with different lung function parameters in ^aunivariable analyses and ^bmultivariable analyses. Asthma assessment was divided in 2 groups: controlled and partly controlled/uncontrolled asthma. Baseline was always controlled asthma. OR: odds ratio, CI: Confidence Interval

Table E2: Association between (childhood) asthma control test (comparing controlled and partly/uncontrolled asthma) and single lung function measurements.

	(childhood) asthma control test		
	OR	95% CI	p-value
FEV ₁	0.85	[0.55,1.32]	0.5
FVC	1.12	[0.71,1.75]	0.6
FEV ₁ /FVC	0.76	[0.53,1.09]	0.1
FEF25/75	0.7	[0.46,1.06]	0.09
sR _{tot}	1.3	[0.46,3.63]	0.6
RV/TLC	1.05	[0.99,1.11]	0.09
FeNO	1.05	[0.63,1.75]	0.8

Logistic regression models investigating the association of (childhood) asthma control test with different lung function parameters in univariable analyses. Asthma assessment was divided in 2 groups: controlled and partly controlled/uncontrolled asthma. Baseline was always controlled asthma. OR: odds ratio, CI: Confidence Interval

Table E3: Association between doctor's assessed asthma control (comparing controlled/partly controlled and uncontrolled asthma) and single lung function measurements.

	doctor's assessed asthma control		
	OR	95% CI	p-value
FEV ₁	1.31	[0.87, 1.99]	0.2
FVC	1.37	[0.89, 2.11]	0.2
FEV ₁ /FVC	0.99	[0.71, 1.36]	0.9
FEF25/75	1.02	[0.71, 1.49]	0.9
sR _{tot}	1.05	[0.40, 2.72]	0.9
RV/TLC	1.00	[0.96, 1.05]	0.9
FeNO	1.03	[0.80, 2.11]	0.3

Logistic regression models investigating the association of doctor's assessed asthma control with different lung function parameters in univariable analyses. Asthma assessment was divided in 2 groups: controlled/partly controlled and uncontrolled asthma. Baseline was always controlled/partly controlled asthma. OR: odds ratio, CI: Confidence Interval

Table E 4: Association between (childhood) asthma control test (comparing controlled/partly controlled and uncontrolled asthma) and single lung function measurements.

	(childhood) asthma control test		
	Coef	95% CI	p-value
FEV ₁	1.24	[0.79, 1.97]	0.4
FVC	1.02	[0.63, 1.62]	1.0
FEV ₁ /FVC	1.25	[0.87, 1.81]	1.8
FEF25/75	1.36	[0.88, 2.1.0]	0.2
sR _{tot}	0.75	[0.25, 2.22]	0.6
RV/TLC	1.00	[0.95, 1.06]	0.9
FeNO	1.23	[0.72, 2.14]	0.4

Logistic regression models investigating the association of (childhood) asthma control test with different lung function parameters in univariable analyses. Asthma assessment was divided in 2 groups: controlled/partly controlled and uncontrolled asthma. Baseline was always controlled/partly controlled asthma. OR: odds ratio, CI:

Confidence Interval