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Breathlessness perception assessed by visual analogue scale and lung function in children with asthma: A real-life study

Maria A. Tosca¹, Michela Silvestri¹, Roberta Olcese¹, Angela Pistorio², Giovanni A. Rossi¹ & Giorgio Ciprandi³

¹Pediatric Pulmonology and Allergy Unit, Istituto Giannina Gaslini, Genoa, Italy; ²Clinical Epidemiology and Biostatistic Unit, Istituto Giannina Gaslini, Genoa, Italy; ³IRCCS – Azienda Ospedaliera, Universitaria San Martino, Genoa, Italy

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Correspondence

Giorgio Ciprandi, IRCCS – Azienda Ospedaliera, Universitaria San Martino, Viale Benedetto XV 6, 16132 Genoa, Italy.
Tel.: +39 10 35338120
Fax: +39 10 3538664
E-mail: gio.cip@libero.it

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Abstract

Background: In children with asthma, discrepancies between objective indicators of airway obstruction and symptom perception are often observed. Although visual analogue scale (VAS) has been proposed as a useful tool for assessing accurate symptom perception, previous studies conducted in children with asthma included only small cohorts. A study was therefore designed to investigate the usefulness of VAS in establishing a reliable relationship between breathlessness perception and lung function in a large cohort of children with clinical diagnosis of asthma.

Methods: A total of 703 children [470 boys and 233 girls, median age 10.29 (8.33–12.58) yr] with asthma were included in this cross-sectional, real-life study. Perception of breathlessness was assessed by using VAS, and lung volumes and expiratory flows were measured by spirometry.

Results: Most children had intermittent or mild persistent asthma (93.3%), and only 46 children had a significant bronchial obstruction defined by FEV₁ values <80% of predicted. Globally, VAS was significantly, even though weakly, related to lung function. Analyzing children with bronchial obstruction, a moderate relationship between both FEV₁ ($r = 0.47$) and FEF_{25–75} ($r = 0.42$) and VAS was detected. A VAS value of 6 was found to be a reliable cutoff for discriminating children with bronchial obstruction (AUC 0.83 at ROC curve; OR 9.4).

Conclusion: The present study demonstrates that VAS might be considered a useful tool to assess symptom perception, mainly in children with airflow limitation.

Asthma is the most common chronic disorder in childhood, as its prevalence may raise up to 32% in the general pediatric population. Moreover, hospitalization rates, morbidity, and mortality from asthma are increasing worldwide despite the wide spread of asthma guidelines that define the most effective approach for its management (1). Asthma control, defined as normal activity, minimal or no symptoms, no exacerbations, little use of bronchodilators, and normal lung function, is the goal of the management strategy, and the level of control achieved is the basis to classify disease severity (1). However, family pediatricians usually manage children with asthma without assessing lung function, but base treatment decisions on symptom reports and clinical

examination. Unfortunately, inaccurate perception of asthma symptoms has been often believed to be one of the main reasons for delays in diagnosis and treatment, which may increase asthma morbidity and mortality. In all age groups, fairly large discrepancies have been noted between patients' subjective ratings of the severity of pulmonary function impairment and objective measurements (2–5). Symptom perception may be measured by different tools, but the visual analogue scale (VAS) has been successfully utilized in the majority of the studies. The validity of VAS was previously demonstrated in dyspnea perception in adults and children, in experimental and clinical studies (6, 7). VAS has been also used to investigate asthma symptom perception in children as

young as 5 yr of age (8–10), being sensitive in measuring differences between the means for good, usual, and bad breathing days. VAS was considered useful in assessing symptom severity when compared with lung function testing.

In a study performed in a small cohort of 90 children to compare VAS with spirometric parameters, it was demonstrated that VAS represented the most valuable mean of obtaining best information on asthma symptoms (11). However, significant correlation between VAS and the lung function parameters was detected only in children < 10 yr of age (11). The present study was therefore designed to confirm in a large cohort of school-aged children with clinical diagnosis of asthma and the usefulness of VAS in assessing breathlessness perception in relation to lung function values, measured by spirometry.

Materials and methods

Study population

This cross-sectional study included a total of 703 children [470 boys and 233 girls, median age 10.29 (8.33–12.58) yr] with recurrent respiratory symptoms compatible with a diagnosis of asthma, who had been consecutively referred as outpatients to the Allergy Centre of the G. Gaslini Institute for further evaluation and staging in a 24-month period from December 2009 to December 2011. The Institutional Ethical Committee of the G. Gaslini Institute approved the protocol. Signed informed parental consent and the child's assent (if the child was ≥ 12 yr old) were obtained.

Data collection

Information on demography, asthma symptoms, and lung function was collected at the time of the survey. Information on current asthma-related symptoms (dyspnea, wheezing, recurrent dry cough or exercise-related symptoms) was collected.

Inclusion criteria were as follows: (i) having asthma-related symptoms and (ii) being aged between 6 and 18 yr (the minimum age of 6 yr was chosen to ensure that children were able to perform reproducible lung function tests). Exclusion criteria were as follows: (i) use of medium–high doses of inhaled corticosteroids (such as > 200 mcg of beclomethasone/daily or equivalent) or any systemic corticosteroids, (ii) current use of long-acting β_2 agonists, (iii) presence of comorbidities and/or concomitant disorders, and (iv) an insufficient knowledge of Italian language.

The diagnosis of asthma was performed by the specialist at the Allergy Centre according to the Global Initiative for Asthma (GINA) guidelines (1). In detail, asthma was diagnosed on the basis of (i) history of asthma-related symptoms (episodic breathlessness, wheezing, cough, and chest tightness), occurring after an incidental allergen exposure, seasonal symptom variability; (ii) precipitation of symptoms by non-specific irritants; and (iii) improvement of symptoms following appropriate asthma therapy. In addition, lung function was measured in all children. Severity of asthma was classified on the basis of the level of symptoms and airflow

limitation as intermittent, mild persistent, moderate persistent, and severe persistent according to the GINA guidelines (1).

As a part of sub-analysis, the asthmatic subjects with a forced expiratory volume in 1 sec (FEV₁) value (% predicted - % pred.) < 80% was defined as 'case patients' as they had bronchial obstruction (N = 46). Among children without bronchial obstruction, that is, with FEV₁ (% pred.) ≥ 80% (N = 657), an age- and sex-matched control sample (N = 92) was included in the study to obtain a case-control ratio of 1:2. Controls were also matched for drug treatment, allergic sensitization type, and diagnosis of asthma. Therefore, the final studied population consisted in 138 subjects: 46 with bronchial obstruction and 92 without bronchial obstruction.

Skin prick test

Skin prick tests were performed according to the methodology and criteria proposed by the European Academy of Allergy and Clinical Immunology (EAACI) (12). The test uses a panel of allergens extracts, including house dust mites (*Dermatophagoides farinae* and *pteronyssinus*), cat, dog, grasses mix, *Compositae* mix, *Parietaria officinalis*, birch, hazel, olive tree, *Alternaria tenuis*, *Cladosporium*, *Aspergilli* mix (Stallergenes, Milan, Italy), histamine solution (10 mg/ml) as positive control and glycerol buffer diluents of allergenic preparations as negative control. Wheals at least 3 × 3 mm greater than wheals at the site of negative control are regarded as positive.

Visual analogue scale

The VAS consisted of one ruler asking for breathlessness symptom (13). Patients indicated their actual perception of breathlessness by marking a VAS. It was hypothesized that the patient's breath perception, determined by their VAS score, could correlate with the degree of bronchial obstruction, as measured by the forced expiratory volume in 1 s (FEV₁). In this study, the VAS was a 10-cm vertical line on which 0 implied breathlessness, while 10 corresponded to no breathlessness. Initially, patients were instructed to place a mark on the line indicating their ease of breathing at that moment. It was explained that 0 represented breathlessness and 10 no problem breathing. Thus, the lower the numerical score marked by the patient, the greater their perceived breathlessness. With a movable marker, the child could mark any point on the 10-cm segment which best described his/her perception. No interval marker was visible on the line.

Measurement of lung function

Forced vital capacity (FVC), FEV₁ and forced expiratory flows at 25–75% of vital capacity (FEF_{25–75%}), and the FEV₁/FVC ratio were measured by spirometry (Med Graphics, Pulmonary Function System 1070 series 2; Med Graphics Corp., St. Paul, MN, USA), according to the guidelines provided by the *American Thoracic Society* (14). All the children were able to obtain at least three technically acceptable breathing maneuvers with the spirometer. Three forced

expiratory maneuvers were obtained, and the best values were retained. The results were compared with reference values obtained from a well-defined population, identified by the *American Thoracic Society*, of healthy subjects comparable for gender, height, and weight and then expressed in percentage (15, 16). Normal lung function was defined if spirometric parameters ranged in the normal reference intervals, such as 80–120% of predicted for FVC, FEV₁, and their ratio.

Statistical analysis

The relationship between FEV₁ (% pred.) and VAS was assessed by means of the Spearman's rank correlation coefficient. For the purpose of this analysis, correlation coefficients were considered as follows: ≥ 0.8 = very strong; 0.6 – 0.79 = strong; 0.4 – 0.59 = moderate; 0.2 – 0.39 = weak; and < 0.2 = very weak (17). Furthermore, the significance of the correlation coefficient has been evaluated by means of the t-test for the correlation, testing the null hypothesis (H_0): $\rho = 0$ against the alternative hypothesis (H_1): $\rho \neq 0$.

The sample size was calculated, assuming acceptable an expected correlation coefficient > 0.45 , with a type I error = 0.05, a power = 0.80, and a two-sided t-test on the correlation coefficient ($\rho = 0$). With these assumptions, the required sample size was 36 (18).

A receiver operating characteristic (ROC) curve analysis was performed to determine a cutoff point for VAS that optimized sensitivity and specificity and made it possible to identify patients with a bronchial obstruction. P values < 0.05 have been considered as statistically significant. 'Statistica release 8' (StatSoft Corp., Tulsa, OK, USA) has been used for all the analyses.

Results

Patients

The demographic and clinical characteristics of the patients recruited are reported in Table 1. There was a mild preponderance of male gender, but without significance. The median age was 10.29 yr, and there was a rate of 31.44% of adolescents. Atopic children were 623 (88.6%). Most of atopic children were sensitized to house dust mites (82.8%), to *Parietaria officinalis* (39.8%), or to mix of graminæ (33.7%). The mean duration of asthmatic symptoms was 5 yr. Regarding treatment prescribed by family pediatricians, 67.87% of included subjects received inhaled corticosteroids and/or antileukotrienes. Moreover, 72.54% of children had intermittent asthma, 20.12% mild persistent, 7.02% persistent moderate, and 0.31% severe persistent.

Pulmonary function

The median spirometric parameters were within normal ranges, such as the medians of predicted values were as follows: 101 for FEV₁, 96 for FVC, 96 for FEF_{25–75}, and 106 for the FEV₁/FVC ratio (Table 1). However, 46 children had FEV₁ values $< 80\%$ of predicted.

Table 1 Demographic and clinical characteristics in the whole population

Variables	
Male gender	470 (66.86)
Median age	10.29 (8.33–12.58)
Adolescence (> 12 yr old)	221 (31.44)
Atopy	623 (88.6%)
Sensitization to house dust mite in atopic subjects	516 (82.8%)
Asthma duration (yr)	5 (3–8)
FEV ₁ (% pred.)	101 (92–110)
FVC (% pred.)	96 (87–105)
FEV ₁ /FVC (% pred.)	106 (100–112)
FEF _{25–75} (% pred.)	96 (79–117)

All data are presented as No. (%) with the exception of age and pulmonary function parameters that were reported as median with lower and upper quartiles in parenthesis.

Analyzing the studied population as a whole ($N = 703$), independently from asthma duration and treatment, we found a very weak, although significant, positive correlation between VAS and FEV₁ (% pred.) ($r = 0.191$, $p < 0.0001$) or FEF_{25–75} (% pred.) ($r = 0.123$, $p = 0.0011$) (not shown). Analyzing the whole population, we found that the frequency of bronchial obstruction was almost limited being 6.54%. For this reason and to have a 'balanced' sample of patients with and without bronchial obstruction, a sub-analysis was performed including all the patients with bronchial obstruction ($N = 46$) and an age- and sex-matched sample of patients without bronchial obstruction ($N = 92$) to obtain a case-control ratio of 1:2. Analyzing these 138 patients, we found moderate positive correlations between VAS and FEV₁ (% pred.) (Fig. 1a) or FEF_{25–75} (% pred.) (Fig. 1b). On the contrary, there was no significant relationship with the other lung function parameters.

On the basis of the ROC curve analysis, we identified that the optimal cutoff value of VAS able to detect bronchial obstruction was 6 (Fig. 2a) with a sensitivity of 80.4 (66.1–90.6), a specificity of 69.6 (59.1–78.7), a diagnostic accuracy of 73.19%, and an area under the ROC curve of 0.829 (0.755–0.887). From a more practical point of view, the positive likelihood ratio (LR+) and the negative LR (LR–) were 2.71 and 0.28 giving a statistically significant diagnostic odds ratio of 9.40 (4.0–22.1). This means that the 'risk' of having bronchial obstruction is over 9-fold higher in children referring VAS ≤ 6 as compared with children reporting a VAS > 6 .

Finally, it was considered the impact of some parameters in breathlessness perception. Gender did not influence VAS results both in the whole population ($p = 0.795$) and in the subgroups. Age did not relate with VAS values ($r = 0.175$) as well as asthma duration ($r = -0.069$).

Discussion

The asthma symptom perception was investigated by several studies in children, but most of them were conducted in

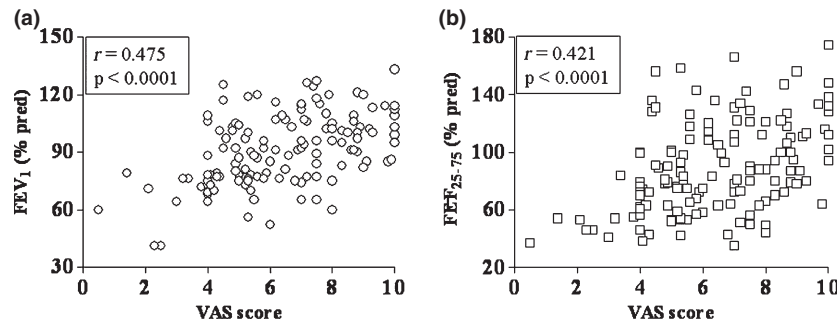


Fig 1 Correlation between forced expiratory volume in 1 s (FEV₁) (% pred.) and visual analogue scale (VAS) score in 138 patients (i.e. 46 with bronchial obstruction and 92 without bronchial obstruction) (panel a). Correlation between forced expiratory flows at 25–75% of vital capacity (FEF_{25–75}) (% pred.), and visual analogue scale (VAS) score in 138 patients (i.e. 46 with bronchial obstruction and 92 without bronchial obstruction) (panel b).

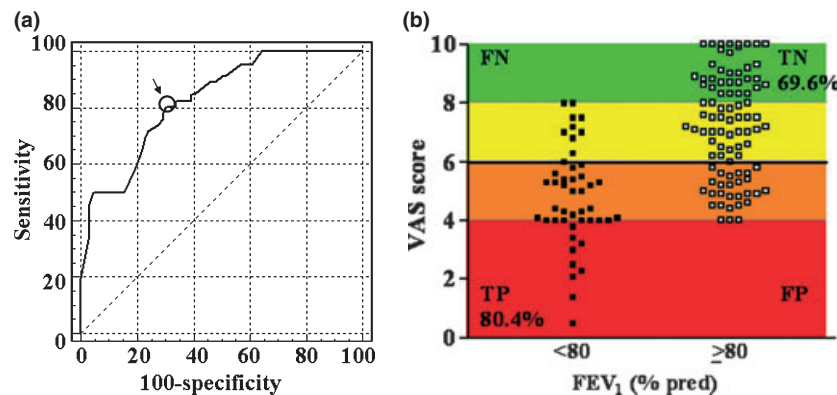


Fig 2 Receiver operator characteristic (ROC) curve analysis to determine the optimal cutoff point at which visual analogue scale (VAS) score discriminates between patients with and without bronchial obstruction (panel a). The arrow indicates the cutoff value of six associated to a sensitivity of 80.4 and a specificity of 69.6. Ability of the chosen cutoff of six to discriminate between patients with and without bronchial obstruction, defining four colored zones (panel b); FN, false negative; TN, true negative; TP, true positive; FP, false positive.

patients with symptoms experimentally induced by bronchoconstrictor stimuli (such as methacholine, histamine, or exercise) or during asthma exacerbation. Thus, these studies could be considered as in 'experimental' settings. Only one study was conducted in a real-life condition, such as considering the asthma perception during a regular consultation in an outpatient clinic, where asthmatic children were referred for the asthma diagnosis confirmation (11). However, the number of enrolled children was quite limited to draw appropriate conclusions. Therefore, the present study was designed to confirm those data in a larger real-life population of asthmatic children and adolescents.

The present findings firstly demonstrate that most of asthmatic patients had intermittent- or mild persistent asthma, and the lung function was impaired only in a restricted group of subjects. Obviously, the perception of impaired respiration should mainly depend on the severity of the disease and partially on lung function. In fact, considering the whole studied

population, there was a significant relationship between perceived respiration and lung function. Focussing the attention on the subjects with impaired lung function, that is, with bronchial airflow limitation, the relationship between the perception of impaired respiration and lung function became moderate both concerning FEV₁ and FEF_{25–75}. Particularly, a cutoff VAS value of 6 was able to accurately discriminate patients with bronchial obstruction. Therefore, the simple assessment of breathlessness by VAS could allow of obtaining raw information on bronchial airflow. This finding partially confirms previous studies, even though analyzing the literature conflicting results were reported. However, many studies had some methodological bias or limitations, mainly the number of recruited children. Ergood and colleagues investigated the perception of expiratory flow in 10 asthmatic adolescents by VAS during rest and exercise, noting that a breakdown in perception did not occur during submaximal exercise (19). Wilson and Jones further compared VAS with

Borg Scale for measuring dyspnea during exercise in 10 young adults: a good relationship between the two methods was detected (7). Boner and colleagues evaluated the perception of bronchoconstriction in chronic asthma in 30 children by a self-estimated obstruction score (SEOS) during the methacholine challenge: some children tend to underestimate their bronchospasm (20). Linna studied 65 asthmatic children measuring a symptom score by diary card comparing with spirometry: lung function correlated better than symptom score with asthma severity but concluded that both tools should be considered in the assessment of the severity of childhood asthma (21). Baker's group enrolled 35 asthmatic children to evaluate their perception of asthma symptoms by VAS: 50% of them were poor perceiver of airflow obstruction (13). Rietveld and Everaerd evaluated 30 asthmatic adolescents at home using a Likert Scale: the obstruction grade did not relate to self-reported dyspnea (22). Panditi and Silverman studied the perception of exercised-induced asthma in 43 children comparing VAS vs. Likert Scale: VAS weakly related to changes in FEV₁ after exercise, but VAS and Likert scale were highly correlated (23). Yoos and McMullen evaluated 28 children and adolescents with asthma to assess the symptom perception by VAS: adolescents were more accurate than school-aged children, and more accurate children had better morbidity outcomes (24). Horak and colleagues enrolled 90 asthmatic children to compare lung function and symptom perception by VAS: FEF₂₅₋₇₅ significantly related to VAS, but VAS assessment was more useful in children <10 yr old (11). Van Gent and colleagues conducted a study on 108 children compared children with diagnosed asthma and undiagnosed one: these last showed poor perception of dyspnea, Borg Scale, and VAS were both useful; but VAS better related with FEV₁ (25). Finally, Fritz et al. (26) evaluated 86 asthmatic children attending an asthma camp: they stated that a VAS was easily understood by children and was a useful tool in improving children's perceptual ability.

Our data demonstrate that VAS may be a useful tool to improve the information concerning asthma symptoms and bronchial obstruction, correlating significantly with both FEV₁ and FEF₂₅₋₇₅. We would like to underline that a VAS value <6 should induce to suspect the possible existence of bronchial airflow limitation. Particularly, a different step scale should be constructed defining four attention levels: (i) a green zone (VAS >8) such as we did not find any children with bronchial obstruction, (ii) a yellow zone (VAS 6–8) such as up the statistical cutoff, (iii) an orange zone (VAS 4–6) such four was the lowest VAS value referred by children without bronchial obstruction, and (iv) a red zone (VAS <4) such as only children with bronchial obstruction. This classification could be useful at home or in family pediatrician office to easily stage the asthma severity. It is to note that 10 children with overt bronchial obstruction referred a VAS value >6, but never >8 (such as the green zone). A possible explanation might be that these children may be poor perceivers: a relatively frequent situation (about 20%). On the other hand, 26 children with airflow limitation referred a VAS value <6, but

never <4: in this case, these children might be over-perceivers, likewise a well-known situation. Therefore, VAS assessment may quickly provide an approximate idea of lung function and suggest the necessary measures: (i) green zone = do not worry, (ii) yellow zone = see and wait, (iii) orange zone = refer to pediatrician and think for spirometry, and (iv) red zone = immediately treat with relievers (Fig. 2b).

Moreover, considering some confounding factors, such as age, gender, atopy, and treatment, there was no significant relationship between VAS values and each single variable both in the global cohort and in the subgroup with airflow limitation.

However, this study has two main limitations as being conducted in a real-life setting and did not include a large number of children with bronchial airflow obstruction, and the diagnosis of asthma was based on clinical ground. On the other hand, it is well known that asthma diagnosis in children is often based on clinical symptoms and response to treatment. In fact, school-aged children with mild asthma very frequently have FEV₁ values within normal range, when clinically stable (27). The Bacharier's study reported that the mean FEV₁ was 95.1% of predicted in children with mild persistent asthma, 90.2% in those with moderate persistent asthma, and 83.8% in those with severe persistent asthma (28). Therefore, significantly diminished FEV₁ values in children are the exception, not the rule, and should characterize children at risk of developing fixed airway obstruction over time or exacerbation (29). Finally, a recent study evaluating risk factors for asthma exacerbation analyzed the data of TENOR study: schoolchildren with very poorly controlled asthma had FEV₁ mean values of 88.6 (± 20.6), with not well-controlled asthma 99.3 (± 16.5), and with well-controlled asthma 102.9 (± 10.6) (30).

Anyway, the main clinical message provided by this real-life study is that a child referring a VAS value ≤6 has a relevant risk of having bronchial obstruction (such as a FEV₁ value <80% of predicted) over nine-fold higher than a child reporting a VAS >6.

In conclusion, the present study demonstrates that VAS might be considered a useful tool to assess the asthmatic symptom perception, mainly in children with bronchial obstruction. Thus, breathlessness VAS may be performed both at home and at family pediatrician office to have a quick idea of breathing.

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