

Original Article

Early prognosis of acute asthma in the emergency room*

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ABSTRACT

Objective: To evaluate clinical and pulmonary function measurements taken in the first fifteen minutes of the assessment of acute asthma in the emergency room and used for prognostic purposes. **Methods:** A prospective cohort study involving consecutive patients with acute asthma. Only patients who were between the ages of 12 and 55 and presented peak expiratory flow rates $<$ or $=$ 50% of predicted were included. Evaluations were performed upon admission, then again at 15 minutes and 4 hours after the initiation of treatment. Treatment included albuterol and ipratropium delivered by metered-dose inhaler with a spacer, together with 100 mg of intravenous hydrocortisone. Favorable outcomes were defined as peak expiratory flow $>$ or $=$ 50% of predicted after 4 hours of treatment, and unfavorable outcomes were defined as peak expiratory flow $<$ 50% after 4 hours of treatment. **Results:** Favorable outcomes were seen in 27 patients, and unfavorable outcomes were seen in 24 patients. In the multivariate analysis, peak expiratory flow as percentage of predicted was identified as the variable with the highest predictive value. A peak expiratory flow $>$ or $=$ 40% after 15 minutes of treatment showed significant power in predicting a favorable outcome (sensitivity = 0.74, specificity = 1.00, and positive predictive value = 1.00). A peak expiratory flow $<$ 30% after 15 minutes of treatment was predictive of a poor outcome (sensitivity = 0.54, specificity = 0.93, and positive predictive value = 0.87). **Conclusion:** Our results suggest that measuring peak expiratory flow after 15 minutes of management in the emergency room is a useful tool for predicting outcomes in cases of acute asthma.

Keywords: Asthma; Acute disease; Respiratory mechanics; Prognosis; Emergency Service, Hospital; Cohort studies

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INTRODUCTION

Acute asthma is a quite common medical emergency,⁽¹⁻²⁾ accounting for a significant portion of the resources expended in the emergency sector and presenting high hospitalization rates.⁽³⁾ Patients with acute asthma are typically hospitalized only after initial treatment in the emergency room.⁽⁴⁾ Consequently, a great number of patients remain under treatment in, often overcrowded, emergency rooms before a decision to hospitalize or discharge them is made. Early differentiation between patients who require hospitalization and those who can be discharged and treated at home may help improve the quality of the treatment of asthma attacks and optimize the allocation of health resources.⁽⁵⁾

It has been demonstrated that the severity of asthma attacks is defined by the outcome rather than by the initial clinical presentation. Therefore, immediate functional response to inhaled bronchodilators constitutes a prognostic parameter. Patients who do not attain 45% of predicted peak expiratory flow (PEF) after the administration of 5 to 10 mg of albuterol delivered via nebulization constitute a worse prognosis group and typically require hospitalization.⁽¹⁾

Various studies have analyzed the variables associated with the outcomes of acute asthma attacks treated in emergency rooms.⁽⁶⁻¹⁵⁾ It has recently been demonstrated that subjective and objective measures used in the evaluation of asthma attacks represent different dimensions that could be used in conjunction in order to evaluate the outcomes of such attacks.⁽¹²⁾ In another study,⁽¹⁴⁾ a predictive index was developed based on two variables of practical gauging: PEF measured at 30 minutes after the initiation of treatment, and the difference between that measurement and the PEF measured at baseline.

Despite these studies, additional prospective studies have been called for in order to confirm the utility of prognostic indicators of asthma severity based on the outcome of an asthma attack.⁽¹⁾

The objective of this study was to identify an early prognostic indicator (at 15 minutes after initiation of treatment) for the management of acute asthma in emergency rooms, predicting the outcome of an asthma attack at 4 hours of evolution.

METHODS

This was a prospective cohort study, carried out in the Emergency Room of the Hospital de Clínicas of Porto Alegre. Clinical and functional pulmonary measurements taken in the first 15 minutes of the assessment of acute asthma in the emergency room were analyzed. The results of this analysis were used for making prognoses regarding the outcomes of asthma attacks at 4 hours of evolution.

The study was approved by the Ethics and Research Committee of the Hospital de Clínicas of Porto Alegre. All patients or their legal guardians gave written informed consent.

The sample comprised patients with acute asthma treated in the adult sector of the hospital emergency room. Inclusion criteria were previous diagnosis of bronchial asthma, requiring treatment for asthma exacerbation (cough, wheezing or dyspnea), being between the ages of 12 and 55, and presenting PEF = 50% of predicted. Exclusion criteria were asthma attacks that were severe enough to prevent the patient from completing the study protocol, pregnancy, chronic pulmonary diseases, congestive cardiac insufficiency, pneumonia, previous participation in the study, undergoing treatment that did not follow the study standards, refusal to give written informed consent, incomplete evaluation, or withdrawal of consent during the course of the study.

All the patients were evaluated by an emergency room physician and a member of the research team. Patient history and physical examination data were recorded on a standardized data collection form. Data regarding age, gender, dyspnea, cough, chest tightness, duration of current attack and smoking (active or passive) were recorded. The physical examination was conducted with the patient sitting upright and included determination of heart rate, respiratory rate, pulsus paradoxus, central cyanosis, respiratory accessory muscle use, supraclavicular or intercostal retractions, inability to speak, clipped speech and wheezing. Accessory muscle use was defined as visible and palpable contraction of the sternocleidomastoid muscles during inspiration. The height and weight of each patient were recorded.

With the patient sitting, a portable peak flow monitor (Vitalograph; Boehringer Ingelheim,

Ingelheim am Rhein, Germany) was used to measure PEF. Three successive expiratory maneuvers were performed, and the one with the highest value was recorded. The result is expressed as the percentage of the predicted value based on gender, age and height.⁽¹⁶⁾ Arterial oxygen saturation was measured using a pulse oximeter with a digital sensor (Oxypleth Dx 2405; Dixtal, São Paulo, Brazil), with the patient stabilized and breathing room air.

Standard treatment (defined by the protocol) was then started.

The evaluation of symptoms and the physical examination, as well as the measurement of PEF and oxygen saturation, were repeated at 15 minutes and at 4 hours after the first administration of the inhaled bronchodilator.

The decision to hospitalize or discharge the patient was made by the emergency room physician, without any interference from the research team members.

After the initial assessment, all patients were treated with eight inhalations of albuterol sulfate (120 mcg/inhalation) and ipratropium bromide (20 mcg/inhalation) every 20 minutes during the first hour and then once an hour throughout the period of treatment in the emergency room. The aerosol bronchodilator was delivered with an inhaler into a spacer device with a volume of 650 mL (Flumax spacer, Flumax Equipamentos Médicos Ltda., Belo Horizonte, Brazil).

All patients received 100 mg of intravenous hydrocortisone together with the first administration of the aerosol bronchodilator,

followed by 100 mg i.v. every 4 hours, if necessary. When oxygen saturation was lower than 92%, oxygen therapy was administered through a nasal cannula at a flow rate of 1-3 L/min.

The outcome was evaluated by measuring PEF at hour 4 of treatment in the emergency room. A favorable outcome (FO) was defined as a PEF = 50% of predicted, whereas a PEF < 50% of predicted was considered an unfavorable outcome (UO). It was also noted whether the patient was discharged from the emergency room or was hospitalized.

The data were entered into a Microsoft Excel (version 2000) database, and the Statistical Package for the Social Sciences (version 10.0) program was used to process and analyze the data. Data related to FO patients were compared with those related to UO patients. A descriptive analysis was performed in each group using the mean \pm standard deviation or the number of cases (proportion). Continuous variables presenting normal distribution were compared using the Student's t-test, continuous variables presenting normal distribution were compared using Mann-Whitney U test, and the chi-square was used for categorical variables.

The variables in which the descriptive level of significance was $p < 0.1$ in the univariate analysis were submitted to a multivariate analysis using stepwise logistic regression, adjusted for gender and age. The most significant variables identified in this multivariate analysis were selected. Each selected variable or combination of selected variables was correlated with the outcome and submitted to the

TABLE 1
Distribution of patients by gender, age, smoking habits and outcome

Variables	Total (n = 51)	Favorable Outcome (n = 27)	Unfavorable Outcome (n = 24)	p
Gender, n (%)				
Male	16 (31.4)	7 (13.7)	9 (17.6)	0.557
Female	35 (68.6)	20 (39.2)	15 (29.4)	
Age, mean \pm SD	31.5 \pm 12.6	29.6 \pm 12.8	33.7 \pm 12.3	0.244
Smoking, n (%)				
Current	15 (29.4)	8 (15.7)	7 (13.7)	0.545
Former	7 (13.7)	5 (9.8)	2 (3.9)	
Never	29 (56.9)	14 (27.5)	15 (29.4)	
Passive smoking, n (%)	16 (31.4)	9 (17.6)	7 (13.7)	0.986

SD: standard deviation; chi-square test for categorical variables and Student's t-test for independent samples for continuous variables

receiver operating characteristic (ROC) curve, to determine the cut-off point that maximized the predictive value. Sensitivity, specificity, positive predictive value and negative predictive value were calculated. To ensure statistical significance, 95% confidence intervals were determined, and the level of statistical significance was set at $p < 0.05$. All tests were two-tailed.

RESULTS

From July to November of 2003, 203 patients with acute asthma were treated. Of those 203, 152 were excluded: 49 for being over 55 years of age; 10 for presenting a PEF $> 50\%$ of predicted; 5 for being treated in the emergency room for primary ailments other than acute exacerbation of asthma; 2 for not having previously been diagnosed with bronchial asthma; 19 for presenting concomitant

chronic pulmonary diseases; 19 for having pneumonia; 19 for being under treatment that did not meet the standards of the study; 13 for not completing the evaluation or for withdrawing their consent before the end of the study; 12 for presenting overly severe asthma attacks; 3 for having already participated in the study; and 1 for refusing to give written informed consent. Therefore, 51 patients were included in the study.

Table 1 shows the general characteristics of the study sample. Of the 51 patients studied, 35 (68.6%) were female, and 16 (31.4%) were male. Mean age was 31.5 years (standard deviation, 12.6 years). There were 15 smokers (29.4%), 7 former smokers (13.7%) and 29 nonsmokers (56.9%). There were 16 patients (31.4%) who reported being passive smokers. There was no statistically significant difference between the FO group and the UO group regarding these variables.

TABLE 2

Clinical evaluation of the asthma attack and outcome

Variables	DF (n = 27)	DD (n = 24)	RR	IC 95%	p
Wheezing, n (%)					
Initial	22 (81.5)	24 (100.0)	-	-	0.034
15 min	18 (66.7)	23 (95.8)	5.61	0.86 - 36.73	0.012
Cough, n (%)					
Initial	21 (77.8)	21 (87.5)	1.50	0.57 - 3.97	0.473
15 min	18 (66.7)	19 (79.2)	1.44	0.67 - 3.10	0.494
Dyspnea, n (%)					
Initial	26 (96.3)	21 (87.5)	0.60	0.31 - 1.14	0.261
15 min	20 (74.1)	19 (79.2)	1.17	0.56 - 2.46	0.923
Thoracic constriction, n (%)					
Initial	12 (44.4)	14 (58.3)	1.35	0.74 - 2.45	0.478
15 min	8 (29.6)	8 (33.3)	1.09	0.60 - 2.01	1.000
Silent chest, n (%)					
Initial	1 (3.7)	0	-	-	1.000
15 min	0	0	-	-	-
Cyanosis, n (%)					
Initial	2 (7.4)	2 (8.3)	1.07	0.38 - 2.98	1.000
15 min	0	1 (4.2)	2.17	1.61 - 2.94	0.471
Retraction, n (%)					
Initial	6 (22.2)	6 (25.0)	1.08	0.56 - 2.10	1.000
15 min	3 (11.1)	3 (12.5)	1.07	0.45 - 2.53	1.000
Monosyllabic, n (%)					
Initial	3 (11.1)	1 (4.2)	0.51	0.09 - 2.86	0.612
15 min	0	0	-	-	-
Accessory musc, n (%)					
Initial	6 (22.2)	11 (45.8)	1.69	0.97 - 2.94	0.137
15 min	3 (11.1)	9 (37.5)	1.95	1.17 - 3.26	0.059

Accessory musc.: respiratory accessory muscle use; FO: favorable outcome; UO: unfavorable outcome; RR: relative risk of UO; 95% CI: 95% confidence interval; chi-square test

TABLE 3
Objective evaluation of the severity and outcome of the asthma attack

Variables	Favorable outcome (n = 27)	Unfavorable outcome (n = 24)	p
PEF, liters			
Initial	163.4 ± 53.0	131.3 ± 24.4	0.009
15 min	230.6 ± 70.7	146.9 ± 32.3	< 0.001
PEF, % of predicted			
Initial	32.9 ± 8.8	25.5 ± 5.0	0.001
15 min	46.6 ± 12.5	28.65 ± 6.8	< 0.001
Saturation O ₂ , %			
Initial	96.3 ± 2.6	95.83 ± 1.9	0.518
15 min	95.9 ± 3.0	95.8 ± 2.4	0.818
PEF Variation, liters	67.19 ± 53.36	15.63 ± 29.17	< 0.001

PEF = Peak expiratory flow, O₂ = oxygen; Student's t-test for independent samples

Table 2 presents the result of the clinical evaluation of the asthma attacks. When comparing the FO group with the UO group, a statistically significant difference was observed for the variables initial wheezing (p = 0.034) and wheezing at 15 minutes (p = 0.012).

Table 3 shows the result of the objective evaluation of the severity of the asthma attacks. A statistically significant difference was observed between the FO group and the UO group regarding the variables initial PEF in liters (p = 0.009), PEF in liters at 15 minutes (p < 0.001), initial PEF in percentage of predicted (p = 0.001), PEF in percentage of predicted at 15 minutes (p < 0.001) and PEF variation at 15 minutes (p < 0.001).

The multivariate analysis identified PEF in percentage of predicted at 15 minutes (p < 0.001) as the most significant variable. Among the significant variables, no combination had better predictive performance than did PEF in percentage of predicted at 15 minutes in isolation. The area under the ROC curve was calculated as 0.90 for both groups.

Using the cut-off point of PEF at 15 minutes = 40% of predicted to identify an FO, sensitivity was 74%, specificity was 100%, the positive predictive value was 100%, and the negative predictive value was 0.77. Using the cut-off point of PEF at 15 minutes < 30% of predicted to identify a UO, sensitivity was 54%, specificity was 93%, the positive predictive

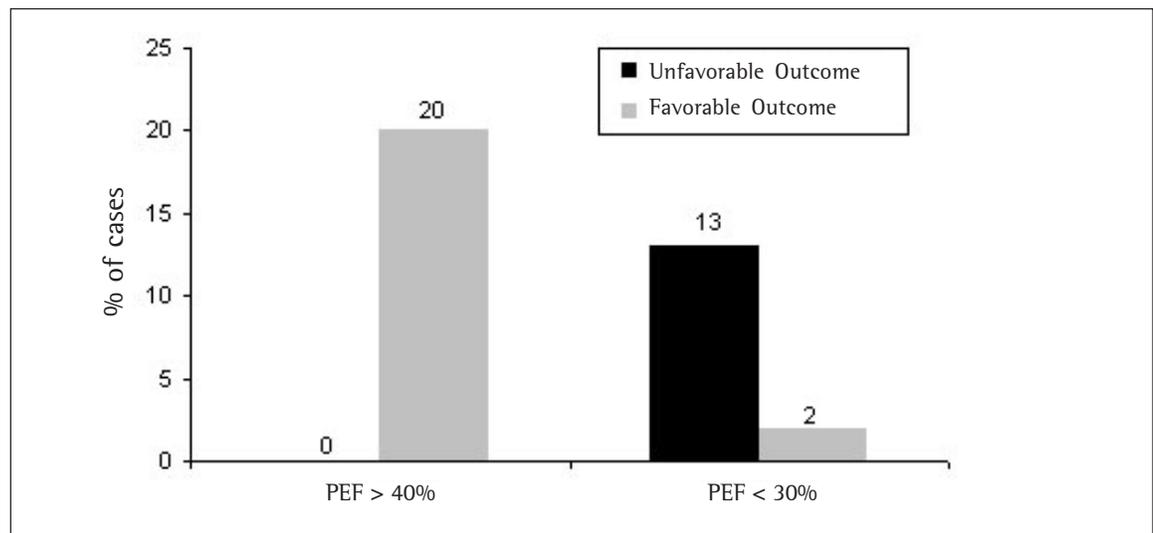


Figure 1 - Distribution of outcomes by cut-off points

value was 87%, and the negative predictive value was 0.69. Figure 1 shows the distribution of the outcomes for the PEF cut-off points.

Considering the decision of the emergency room physician regarding whether to discharge or hospitalize the patient as a clinical outcome, we observed that: of the 20 patients with a PEF = 40% at 15 minutes, 18 were discharged from the emergency room, and 2 required hospitalization (a positive predictive value of 90% and a negative predictive value of 23%); of the 15 patients with a PEF < 30% at 15 minutes, 10 were discharged, and 5 were hospitalized (a positive predictive value of 66% and a negative predictive value of 11%).

DISCUSSION

The objective of the present study was to identify an early prognostic indicator of the outcome of an acute asthma attack treated in an emergency room. The patients were evaluated upon admission and at 15 minutes after administration of a bronchodilator, delivered using a metered-dose inhaler with a spacer. The outcome of the asthma attacks was defined according to the pulmonary functional response at hour 4 of treatment. Among the clinical and pulmonary function variables studied, PEF in percentage of predicted at 15 minutes of treatment was identified as the most accurate prognostic indicator. Two cut-off points were determined for this variable: = 40% of predicted (to identify an FO); and < 30% (to identify a UO). Our results suggest that early measurement of PEF after the first dose of inhaled bronchodilator constitutes a useful tool for early prognosis of outcomes in cases of acute asthma attacks treated in emergency rooms.

The current guidelines for the management of acute asthma recommend giving short-acting β_2 -agonist inhaled bronchodilators as the first-line treatment.⁽¹⁷⁻¹⁹⁾ Nevertheless, approximately one-fifth to one-third of all asthmatic patients treated in emergency rooms respond poorly to inhaled bronchodilators, failing to attain 45% of predicted FEV₁ or PEF after receiving 5 to 10 mg of nebulized albuterol.⁽¹⁾ Therefore, part of the spectrum of acute asthma exacerbations corresponds to those patients who fail to present an immediate response to β_2 -agonist inhaled bronchodilators, which shows that severity is better defined in terms of

outcome than in terms of initial presentation. It is fundamental that these patients with poor bronchodilator response be identified objectively (through monitoring of their pulmonary function).^(1,3)

Airflow limitation in acute asthma can be determined in the emergency room through the determination of FEV₁ by spirometry or by measuring PEF.⁽⁵⁾ The results of these tests are generally expressed in relation to predicted values based on gender, age and height.^(5,20) However, some patients with more severe asthma can present a component of fixed airflow obstruction, even when asymptomatic. Knowledge of the degree of fixed airflow obstruction during asymptomatic periods and of the best FEV₁ or PEF values for a given patient is useful in interpreting pulmonary function measurements made during the acute exacerbation period. Unfortunately, information regarding the best individual FEV₁ or PEF value is not typically available or is unknown in the emergency room setting.^(1,5)

In our study, for technical reasons, only PEF was used as a pulmonary function variable. Even though spirometry is the gold standard for the evaluation of airflow in asthma cases, in the emergency room, measurement of PEF can be performed more easily than can spirometry. In addition, the equipment used to measure PEF is more affordable and more readily available in this sector.⁽²¹⁾

Corresponding to approximately 20% of the forced vital capacity, PEF is an instantaneous flow that is mainly composed of bronchial airflow, with little contribution from the small airways. Including a considerable effort-dependent component, PEF is determined by the volume and elasticity of the lungs, by the dimension and compliance of the intrathoracic central airways and by the force and speed of expiratory muscle contraction.⁽²²⁾ Early PEF improvement in asthma, in addition to being a sensitive indicator of improvement of various parameters involved in the provocation and physiopathology of asthma attacks, can be interpreted as a marker of the tendency of the physiological evolution resulting from the treatment instituted.^(1,5)

Although the guidelines for asthma management recommend that the ideal pulmonary function criterion for discharge from the emergency room in cases of asthma attacks is FEV₁ or PEF = 70% of predicted,⁽¹⁷⁻¹⁹⁾ there is evidence

that FEV1 > 45% after initial treatment with an inhaled bronchodilator constitutes an indicator of an FO in an acute asthma attack.(2-3,5) There is a reasonable correlation between PEF and FEV1 measurements in asthma patients. However, when these parameters are expressed as percentages, PEF values are, on average, 10% higher.(20) Based on that premise, in the present study, outcomes were considered favorable if the PEF measured at hour 4 of treatment were = 50% of predicted or unfavorable if this value were < 50% of predicted.

Previous studies have demonstrated that the lack of improvement in expiratory flow after initial bronchodilator treatment constitutes a prognostic indicator of exacerbation of acute asthma in the emergency room and of the need for hospitalization.^(6-8,10,13-14,23)

In a study conducted in 1976,⁽⁶⁾ 67 episodes of acute asthma attack treated in an emergency room were analyzed, and the results suggest that patients with severe airflow obstruction (PEF < 16% of predicted) whose PEF remains < 60 L/min, or who present improvement of less than 16% after receiving 0.3 mL of adrenaline, should be hospitalized immediately.

In another study, conducted in 1979,⁽¹⁰⁾ 82 patients experiencing acute asthma attacks were evaluated before and after emergency treatment with s.c. terbutaline and i.v. aminophylline. The authors of that study observed that FEV₁ = 0.6l before treatment, or FEV₁ = 1.6l after treatment, was associated with unfavorable progression of the asthma attack. They concluded that spirometry can identify the asthma patients who require hospitalization or who might present significant airway obstruction within 48 hours of discharge from the emergency room.

In 1981, a study⁽⁸⁾ was conducted in which 205 patients under emergency room treatment for acute asthma attacks were evaluated. The treatment protocol included s.c. adrenaline or s.c. terbutaline, together with inhaled isoetharine, i.v. aminophylline and i.v. hydrocortisone. The authors developed a predictive index using a combination of the following factors: pulse rate > 120/min, respiratory rate = 30 breaths/min, pulsus paradoxus = 18 mmHg, PEF = 120 L/min, moderate to severe dyspnea, accessory muscle use and wheezing. The index ranged from zero to seven, increasing with the severity of the symptoms. An index equal to or

higher than four was 95% accurate in predicting a recurrence of the attack and 96% accurate in predicting the need for hospitalization.

A study evaluating 52 patients with acute asthma attacks and under treatment in an emergency room was carried out in 1992.⁽⁷⁾ The patients were treated with inhaled fenoterol, i.v. aminophylline and i.v. hydrocortisone. The analysis of the clinical and functional pulmonary data did not allow the long-term outcomes of the attacks to be reliably predicted, with or without the use of a predictive index. In the patients studied, the Fischl index⁽⁸⁾ was less useful than the measurement of PEF in isolation. This was due to the overlapping of the results.

In a 1997 study,⁽¹³⁾ 184 adult patients who sought emergency room treatment for acute asthma attacks were examined. The patients were treated with albuterol (delivered by metered-dose inhaler with a spacer) and i.v. hydrocortisone. Three independent variables were identified as providing the greatest contribution to discriminating between patients who would be discharged from the emergency room and those who would be hospitalized: PEF variation in relation to the baseline value; PEF in percentage of predicted; and respiratory accessory muscle use (all measured after 30 minutes of treatment). The index presented a sensitivity of 0.86, specificity of 0.96, positive predictive value of 0.75 and negative predictive value of 0.98.

In 1998, in another study⁽¹³⁾ conducted by the authors of the 1997 study, an index with only two variables (PEF in percentage of predicted and variation of PEF in relation to the baseline, both evaluated after 30 minutes of treatment) was developed. The treatment included albuterol (delivered by metered-dose inhaler with a spacer) and i.v. hydrocortisone. The index score ranged from zero to four points, according to the severity of the attack. A score of four was the most predictive, with a sensitivity of 0.79, specificity of 0.96, positive predictive value of 0.94 and negative predictive value of 0.86.

In 2002, yet another predictive index was developed⁽²³⁾ using PEF in percentage of predicted and respiratory accessory muscle use after the first hour of treatment for an acute asthma attack treated in the emergency room. The patients were treated with albuterol (administered via nebulization) and i.v. hydrocortisone. The score

ranged from zero to two, increasing according to the severity of the attack. The scores zero and two had predictive value for the outcome of the attack in ten days.

The present study evaluated patients with acute asthma who were between 18 and 55 years old and presented no comorbidities. There were 49 patients who were excluded because they were over 55 years of age and 10 who were excluded because they presented PEF values > 50% of predicted. Another 50 patients were also excluded from the study: 19 because they were diagnosed with concomitant chronic pulmonary diseases; 19 because they had pneumonia; and 12 patients presented severe asthma attacks. The exclusion of these particular patients from the study might have limited the clinical usefulness of the early prognosis of acute asthma in the emergency room, thereby impairing the external validity of the study. Nevertheless, we consider this method of functional evaluation simple, practical and able to discriminate between two groups of patients requiring distinctly different management in the emergency room. Some of these inclusion and exclusion criteria might be modified so that, in validation samples, the usefulness of the early PEF measurement can be broadened.

It is important to emphasize that, in our study, PEF variation was included in the multivariate analysis. However, the PEF in percentage of predicted better discriminated the outcome. In addition, the index based on the combination of PEF in percentage of predicted at 15 minutes of treatment and PEF variation from the baseline value did not add discriminatory power in comparison to PEF in percentage of predicted at 15 minutes evaluated in isolation.

In this study, we did not evaluate the duration of asthma attacks prior to the arrival of the patient in the emergency room, the previous use of inhaled β_2 -agonists at home or the regular use of inhaled corticosteroids between attacks. Nor did we classify the severity of asthma between attacks. Although this information might have been useful, we prioritized the simplification of the questionnaire so it could be applied in the emergency room.

Our study contributes to the theme by showing that very early evaluation (15 minutes after the first bronchodilator dose) can permit a prognostic estimate of the short-term (4-hour) outcome of the asthma attack. Our findings also provide the

additional information that no combination of the variables studied results in a better predictive performance. However, as there was significant overlapping of the FOs and UOs for the patients with PEF = 30% and < 40% of predicted (31% of the patients studied presented PEF values within this range), we suggest that there is a real need for further studies evaluating clinical and pulmonary function data obtained from such patients as well as from other asthma attack victims whose stays in the emergency room exceed 4 hours.

In conclusion, measuring PEF in percentage of predicted at 15 minutes after the first dose of an inhaled bronchodilator was found to constitute a useful prognostic indicator of the outcomes of acute asthma attacks treated in emergency rooms.

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