Validation of Ramathibodi's Acute Asthma Predictive Score

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Background: *The authors have recently developed Ramathibodi's acute asthma predictive score to help the attending physician decide on a safe discharge of an acute asthmatic patient from the emergency room (ER). However, the authors did not validate it in the previous study.*
Objective: *To validate the predictive score with a new different population.*
Material and Method: *The authors conducted a study on acute asthmatic patients, in continuation from our previous study, between September 2005 and September 2007 in the ER of Ramathibodi Hospital. Vital signs, oxygen saturation, and severity factors were recorded. All patients were treated with nebulized salbutamol initially and repeatedly if the peak expiratory flow rates were < 70% predicted or if unfavorable physical signs were seen. The patients who had any of the severity factors were given systemic steroids. Patients were assessed for admission if further treatments were needed after the fourth nebulization. An unfavorable outcome was defined as either hospital admission or relapse within 48 hours of the ER discharge. Then, the authors' predictive score was calculated to give a total score for each patient. Using a cutoff score of 2, the authors calculated sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). The area under the receiver operating characteristic (ROC) curve (AUC) was also calculated and compared with that of the development cohort.*
Results: *There were 863 visits from 546 patients and 66.6% had a score of ≤ 1 while 33.4% had a score of ≥ 2. Using a cutoff score of 2, the acute asthma score exhibited a sensitivity of 60.0%, a specificity of 67.4%, a PPV of 5.7%, and a NPV of 98.1%. The validation group's AUC did not differ from that of the development group.*
Conclusion: *Ramathibodi's acute asthma predictive score was found as a valid useful tool for a proper ER discharge of acute asthmatic patients.*

Keywords: *Acute asthma, Predictive score, Emergency*

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Asthma is often associated with exacerbations of symptoms, especially when it is partly controlled or uncontrolled[1]. In Ramathibodi Hospital institute, acute asthma is the most leading cause that brings the patient to the emergency room (ER) for treatment, estimated at more than 500 episodes per year. The severity of exacerbations may range from mild to life threatening. The physician in the ER has great difficulty in predicting when hospitalization is indicated. It would be helpful if patients with asthma who require admission to hospital for an acute attack could be identified. Unfortunately, in spite of a variety of clinical and laboratory measures currently used to assess acute asthma severity, no single finding has been found to reliably predict the outcomes[2,3]. Previously, the authors have demonstrated three clinical parameters that were independently associated with treatment outcome and developed Ramathibodi's acute asthma predictive score as a reliable guide for a proper emergency room discharge of acute asthmatic patient (Table 1)[4].

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Nevertheless, it has not been validated for its precision of prediction when applied to patients of different populations. Thus, the authors conducted the present study with the objective to validate of the acute asthma predictive score to demonstrate its usefulness in clinical practice.

Material and Method

Subjects

A cohort study was conducted continually from the authors previous study[4] between September 2005 and September 2007 in the ER of Ramathibodi Hospital. All patients who appeared for treatment of acute asthma at the ER were recruited. The diagnosis of acute asthma was based on the criteria proposed by the National Heart, Lung, and Blood Institute (NHLBI)[1]. Patients were excluded from the present study if they were unable to perform peak expiratory flow rate (PEFR) measurement, or were having respiratory arrest imminent of immediate intubations and admissions. The present study protocol was approved by the Ethics Committee on Human Experimentation of Ramathibodi Hospital, Faculty of Medicine, Mahidol University.

Acute asthma treatment protocol and data collection

The acute asthma treatment protocol was run in the same manner as used in the authors previous study (development cohort)[4]. Briefly, on arrival to the ER, all patients were initially evaluated for severity factors that included factors obtained from history (previous intubation or admission, excessive use of inhaled β_2-agonists, current use of steroid), and unfavorable physical examinations (inability to lie down on general physical examination, inability to complete a sentence, active use of accessory muscles, and presence of respiratory paradox). All patients were then treated with 2.5 mg salbutamol by continuous flow nebulization, followed by assessments of vital signs, oxygenation, wheezing, physical signs indicative of severity and PEFR. Repeated doses of nebulized salbutamol (15 min interval) would be needed only if the assessed PEFR were < 70% predicted (based on age, sex, height, and race) and/or presence of unfavorable physical findings. When the arterial oxygen saturation as assessed by pulse oximetry was less than 92%, 1-2 l/min of supplemental oxygen was administered through a nasal cannula. The patients whose severity factors were identified also initially received systemic steroid (intravenous dexamethasone or oral prednisolone). Patients were assessed for admission if further treatments were needed after the fourth nebulization, as judged by the treating physician. Oral steroids were prescribed (a 5-7 day course of 30 mg. prednisone daily) for all patients who were discharged from the ER. Hospitalized patients received treatments according to the discretion of individual physicians.

Collected data included patients' demographic variables, vital signs, severity factors, arterial oxygen saturations at presentation, frequency of nebulization, physical signs, and PEFRs after last nebulization or before discharge. Patients were designated as showing favorable outcomes were those who were successfully discharged from the ER and did not require a visit to a hospital's ER or hospital admission for acute asthma treatment within the next 48 hours. Patients designated as unfavorable outcomes were those who were admitted to the hospital or those discharged from the ER but required a visit to a hospital's ER or hospital admission for acute asthma treatment within the next 48 hours.

Statistical analysis

All values were expressed as the mean $\pm$ standard deviation (SD) for continuous variables and percent for categorical variables. When data were non-normally distributed, median values and ranges were reported instead.

The authors compared baseline characteristics of the patients in the present study (validation cohort) with the development cohort[4]. Between-group comparisons for continuous variables were performed using the Student's two-tailed t-test or nonparametric Mann-Whitney-U test, whatever appropriated. Chi-square and Fisher's exact tests were used to analyze differences among categorical variables.

The predictive score was composed of three bedside parameters (inability to lie down at presentation, presence of wheeze and PEFR after last nebulization) (Table 1). A score of 0, 1 or 2 was assigned to each of the three independent predictors. These numerical values were summed to give a total score for each patient. The minimal score was 0 and the maximal score was 4. From the development cohort, the authors found that a cutoff score of 2 yielded the more power distinction between a favorable or unfavorable outcome. Using this cutoff score, the authors calculated sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). Additionally, the area under the receiver operating characteristic (ROC) curve (AUC) was calculated and compared with that of the development cohort.

All statistical tests were 2-sided, and $p < 0.05$ was considered statistically significant. All data were analyzed with a statistical software package (SPSS, version 11.5 for windows; SPSS Inc; Chicago IL).

Results

There were 863 consecutive visits from 546 patients who appeared for treatment of acute asthma at the ER of Ramathibodi Hospital and met the criteria during the study period. Of these, 25.3% were male and the mean age was 45.9 years. Table 2 lists the characteristics of the 863 patients studied and the development cohort from a previous study[4]. Compared with the development cohort, age, history of acute asthma admission in the past year, and presence of wheeze at presentation were significantly lower in the validation cohort. Furthermore, in the validation cohort, acute asthma seemed to be more responsive to treatment than

Table 1. Ramathibodi's acute asthma predictive score

Predictive score	0	1	2
Inability to lie down at presentation	absent	present	
Wheezing after last nebulization	absent	present	
PEFR (% predicted) after last dose of bronchodilator	>60	35-60	<35

Table 2. Characteristics of development cohort[4] and validation cohort

	Development cohort (n = 905)	Validation cohort (n = 863)	p-value
Age, yrs*	57.6 (12.7)	45.9 (16.1)	<0.001
Sex, male**	30.7	25.3	0.62
Severity factors by history			
Previous intubation**	12.7	10.4	0.14
Current steroid use**	64.3	61.0	0.16
Admission within 1 yr**	17.9	10.3	<0.001
Use of β_2-agonists > 1 canister/mo**	21.6	19.5	0.31
Initial examination			
Wheezing**	99.0	96.4	<0.001
Inability to complete a sentence**	13.1	13.9	0.61
Use of accessory muscles**	58.6	55.2	0.17
Paradoxical respiration**	3.7	5.4	0.09
Inability to lie down**	14.1	14.7	0.73
Pulse, beats/min*	100.6 (30.1)	98.4 (17.7)	0.07
RR, breaths/min*	27.1 (10.9)	27.3 (14.4)	0.67
O_2 saturation, percent*	96.2 (31.5)	93.9 (14.0)	0.06
Systolic BP, mmHg*	134.0 (25.1)	135.2 (23.3)	0.31
Diastolic BP, mmHg*	81.7 (29.7)	80.1 (19.3)	0.23
After last nebulization			
Wheezing**	26.5	7.5	<0.001
PR > 130 beats/min**	4.1	4.6	0.68
RR > 30 breaths/min**	3.1	2.0	0.10
Duration of treatment in ER, median (range)	2.0 (0.2-21.3)	1.7 (0.2-13.9)	<0.001
No. doses of bronchodilators*	2.9 (1.0)	2.7 (1.0)	<0.001
PEFR < 35% predicted**	10.7	3.2	<0.001
PEFR 35-60% predicted**	31.4	26.9	
PEFR > 60% predicted	57.9	69.9	

* Mean (SD)
** Percent of cases

in the development cohort. Median ER length of stay was also significantly shorter in the validation group. The incidence of unfavorable outcomes in the validation sample was significantly lower than that in the development group (4.4% vs. 10.7%; $p < 0.001$).

The authors then applied Ramathibodi's acute asthma predictive score to the validation sample. Table 3 shows the percent of development and validation cohort patients in each score. In the validation cohort, 66.6% had a score of ≤ 1 and 33.4% had a score of ≥ 2. Using a cutoff score of 2, the acute asthma score exhibited a sensitivity of 60.0%, a specificity of 67.4%, a positive predictive value of 5.7%, and a negative predictive value of 98.1%. The validation group's area under the ROC curve did not differ from that of the development group ($p = 0.13$) (Table 4).

Discussion

In the ER setting, the most critical issue facing the attending physician is deciding when outpatient therapy of acute asthma is adequate, or when hospitalization is indicated. Investigators have tried to identify the signs or symptoms that predict the outcomes of patients with acute asthma. However, the literature relevant to this issue is confusing with respect to the relative importance of the various components of patient assessment. This results from the fact that no single finding has been found to reliably predict outcomes[5].

Table 3. Distribution of acute asthma scores in patients in the development[4] and validation cohorts

	Acute asthma score				
	0	1	2	3	4
Development cohort, %	41.7	33.4	17.4	5.9	1.6
Validation cohort, %	6.2	60.4	26.4	6.0	1.0

Using multivariate logistic regression analysis, significant variables associated with the outcome could be determined and point values could be assigned to each risk factor by using the β-coefficients from the logistic model. From these concepts, several predictive scores were developed for ER physicians in helping decision judgment of safe home discharge or hospital admission[3,6-9]. Unfortunately, differences in characteristics of population, definition, and treatment protocol might influence lessening of the validity of each predictive score[10].

Previously, the authors developed Ramathibodi's acute asthma predictive score as a reliable guide for a proper emergency room discharge of acute asthmatic patients. It is composed of three bedside variables that are easily and commonly measured during the assessment of acute asthma treatment[4]. The authors' treatment protocol was run closely with The Global Initiative for Asthma (GINA)[1] and Thoracic Society of Thailand Treatment Guideline[11] that were applied throughout the country. Therefore, the authors' predictive score would be applicable in every ER setting in Thailand. In the present study, the authors performed external validation studies in independent population. Surprisingly, the pattern of characteristics of patients had some changes. The incidence of acute asthma receiving treatment at Ramathibodi Hospital ER during the present study period was lower than that in the past. Furthermore, the validation sample seemed to be less severe than that in the development sample. In addition, acute asthma appeared to be more responsive to treatment in the present study than in the development sample. This might be due the result of appropriate asthma treatment in the ambulatory care. Inhaled corticosteroid was demonstrated to reduce frequency, severity of acute asthma[12-14] and prevent further relapse[15]. With the available and widespread use of asthma guideline[11], the authors believe that the rate of inhaled corticosteroid use will increase. Unfortunately, the

Table 4. Sensitivity, specificity, predictive values, and area under ROC curve by a cutoff score of 2 for the development and validation cohorts

	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Area under ROC curve
Development cohort	69.0 (65.0-73.1)	79.1 (75.5-82.6)	23.0 (19.3-26.7)	96.6 (95.0-98.2)	0.74 (0.66-0.82)
Validation cohort	60.0 (56.2-63.8)	67.4 (63.7-71.1)	5.7 (3.9-7.5)	98.1 (97.0-99.2)	0.64 (0.52-0.76)

Data are presented as values (95% confidence interval)

differences in asthma control in both samples were not investigated in the present study.

Because the prevalence of the unfavorable outcomes was very low in the present study, it was inevitable that many patients with positive test results will be false positives[16]. Moreover, some changes in characteristics of population resulted in less sensitivity and specificity of the authors' predictive score. Nevertheless, AUC, a better but more sophisticated indication of accuracy of the test, was not different from the development sample. Furthermore, the authors' predictive score was demonstrated to have strength in its high NPV that could exclude the low risk asthmatic patient having a predictive score ≤ 1. However, it should be noted that this predictive score could change in the future with more prescriptions in controller medication.

Conclusion

The present study has shown Ramathibodi's acute asthma predictive score as a reliable guide for a proper emergency room discharge of acute asthmatic patients.

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Conflict of interest statement

All of us declare that we do not have a conflict of interest and that we do not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript.

Abbreviations

ER = emergency room
NHLBI = National Heart, Lung, and Blood Institute
PEFR = peak expiratory flow rate
SD = standard deviation
PPV = positive predictive value
NPV = negative predictive value
ROC = receiver operating characteristic
AUC = area under the receiver operating characteristic curve
GINA, The Global Initiative for Asthma

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การประเมินความเที่ยงตรงของคะแนนในการทำนายการไม่ตอบสนองต่อการรักษาในผู้ป่วยหอบหืดเฉียบพลันที่เข้ารับการรักษาที่ห้องฉุกเฉิน

วิบูลย์ บุญสร้างสุข, ณัษฐา พิภพไชยาสิทธิ์, สุมาลี เกียรติบุญศรี

ภูมิหลัง: *ผู้ทำการศึกษาได้สร้างคะแนนในการทำนายการไม่ตอบสนองต่อการรักษาในผู้ป่วยหอบหืดในการช่วยให้แพทย์มีความมั่นใจว่าจะสามารถให้ผู้ป่วยกลับบ้านได้โดยปลอดภัย*

วัตถุประสงค์: *เพื่อทำการประเมินความเที่ยงตรงของคะแนนในผู้ป่วยหอบหืดเฉียบพลันกลุ่มใหม่*

วิธีการศึกษา: *ทำการศึกษาในผู้ป่วยหอบหืดเฉียบพลันที่เข้ารับการรักษาที่ห้องฉุกเฉินของโรงพยาบาลรามาธิบดี ต่อเนื่องจากการศึกษาก่อน โดยเริ่มตั้งแต่เดือนกันยายน พ.ศ. 2548 ถึงเดือนกันยายน พ.ศ. 2550 ข้อมูลทางด้านสัญญาณชีพ, ความอิ่มตัวของออกซิเจนในเลือด และปัจจัยที่บ่งถึงความรุนแรงของหอบหืดเฉียบพลันจะถูกบันทึก หลังจากนั้นให้การรักษาผู้ป่วยโดยการใช้ salbutamol โดยวิธีการพ่นเป็นฝอยละออง และให้ซ้ำถ้าค่าความเร็วลมหายใจออกสูงสุดยังน้อยกว่าร้อยละ 70 ของค่าปกติ หรือมีการตรวจพบ ที่บ่งถึงภาวะหายใจล้มเหลว นอกจากนั้นในรายที่มีปัจจัย ที่บ่งถึงหอบหืดรุนแรงจะได้รับ systemic steroid ภายหลังการพ่นยาครั้งที่ 4 ถ้าอาการยังไม่ดีขึ้นผู้ป่วยจะได้รับการรักษาต่อในโรงพยาบาล การไม่ตอบสนองต่อการรักษา หมายถึง การที่ผู้ป่วยต้องถูกรับเข้ารักษาในโรงพยาบาล หรือ เกิดการกำเริบภายใน 48 ชั่วโมง ภายหลังจำหน่ายจากห้องฉุกเฉิน หลังจากนั้นได้คำนวณคะแนนในการทำนายการไม่ตอบสนองต่อการรักษาแก่ผู้ป่วยทุกราย ที่เกณฑ์คะแนนที่ $\geq$ 2 นำมาคำนวณหาความเที่ยงตรงของคะแนน ในการทำนายผลลัพธ์ของการรักษา*

ผลการศึกษา: *มีภาวะหอบหืดเฉียบพลัน 863 ครั้งจากผู้ป่วย 546 ราย 66.6% คำนวณคะแนนได้ $\leq$ 1 และ 33.4% คำนวณคะแนนได้ $\geq$ 2 ที่เกณฑ์คะแนนที่ $\geq$ 2 พบความไว 60.0%, ความจำเพาะ 67.4% ค่า AUC ในผู้ป่วยที่ทำการศึกษาไม่ต่างกับกลุ่มที่นำมาสร้างคะแนน*

สรุป: *คะแนนในการทำนายการไม่ตอบสนองต่อการรักษาในผู้ป่วยหอบหืดมีความเที่ยงตรงในการช่วยให้แพทย์ผู้ดูแลมีความมั่นใจว่าจะสามารถให้ผู้ป่วยหอบหืดที่ห้องฉุกเฉินกลับบ้านได้โดยปลอดภัย*