Original Article

Development and Internal Validation of a Pediatric Acute Asthma Prediction Rule for Hospitalization

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What is already known about this topic?

Clinicians have limited tools to inform asthma hospitalization decisions. The predictive validity of available acute asthma severity scores is inadequate to justify use for hospitalization decisions. An effective clinical prediction rule might facilitate hospitalization decision making.

What does this article add to our knowledge?

We have developed and internally validated an asthma prediction rule (APR) for *need for hospitalization* using predictor variables readily available before treatment. SpO_2 and expiratory prolongation were most strongly associated with *need for hospitalization*.

How does this study impact current management guidelines?

The APR might facilitate hospitalization decisions for children with acute asthma exacerbations and improve resource utilization. External validation and an impact analysis are next steps before incorporation of the APR into routine decision support.

BACKGROUND: Clinicians have difficulty predicting need for hospitalization of children with acute asthma exacerbations.

OBJECTIVE: The objective of this study was to develop and internally validate a multivariable asthma prediction rule (APR) to inform hospitalization decision making in children aged 5-17 years with acute asthma exacerbations.

METHODS: Between April 2008 and February 2013 we enrolled a prospective cohort of patients aged 5-17 years with asthma who presented to our pediatric emergency department with acute exacerbations. Predictors for APR modeling included 15 demographic characteristics, asthma chronic control measures, and pulmonary examination findings in participants at the time of triage and before treatment. The primary outcome variable for APR modeling was *need for hospitalization* (length of stay >24 h for those admitted to hospital or relapse for those discharged). A secondary outcome was the *hospitalization decision* of the clinical team. We used penalized maximum likelihood multiple logistic regression modeling to examine the adjusted association of each predictor variable with the outcome. Backward step-down variable selection techniques were used to yield reduced-form models.

RESULTS: Data from 928 of 933 participants were used for prediction rule modeling, with median [interquartile range] age 8.8 [6.9, 11.2] years, 61% male, and 59% African-American race. Both full (penalized) and reduced-form models for each outcome calibrated well, with bootstrap-corrected c-indices of 0.74 and 0.73 for *need for hospitalization* and 0.81 in each case for *hospitalization decision*.

CONCLUSION: The APR predicts the need for hospitalization of children with acute asthma exacerbations using predictor variables available at the time of presentation to an emergency department. © 2014 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2014;■:■-■)

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Abbreviations used
APR- Asthma prediction rule
BMI- Body mass index
CCS- Corticosteroid
CPR- Clinical prediction rule
df- Degrees of freedom
eNO- Exhaled nitric oxide
%FEV_1- %-predicted forced expiratory volume in 1 second
GINA- Global Initiative for Asthma
IQR- Interquartile range
PCCU- Pediatric critical care unit
PED- Pediatric emergency department
PMLE- Penalized maximum likelihood estimation
SpO_2- Oxygen saturation by pulse oximetry

Asthma is the most prevalent chronic disease of childhood and the most frequent reason for childhood hospitalization in the United States.[1,2] A challenging clinical feature of this complex environmental and genetic disease is the heterogeneity of clinical expression.[3] As such, the ability of clinicians to assess severity of acute asthma exacerbations is variable and limited in accuracy.[4]

Approximately 36 acute asthma severity scores have been proposed. The purpose of such a score is to assess severity at the bedside in order to assist clinicians in applying appropriate immediate treatment. Systematic reviews of 16 of these acute severity scores concluded that their predictive validity was inadequate to justify their use for patient hospitalization decisions.[5,6]

Further, investigators noted the difficulty that clinicians have in predicting the need for hospitalization or in predicting relapse after evaluation and treatment of exacerbations in emergency departments (EDs).[7] These features of exacerbations fulfill Steill's 5 criteria that identify the need for a clinical prediction rule (CPR).[8]

A CPR is a decision-making tool that incorporates 2 or more variables from the history, physical examination, or additional tests.[9,10] A CPR can be used in individual patients to predict the probability of an event or intervention such as hospital admission. As such, CPRs fulfill a role distinct from that of acute severity scores, assist clinicians in their clinical decision making, and potentially improve resource utilization. To our knowledge, a CPR has not been developed to predict the need for hospitalization in pediatric patients with acute asthma exacerbations.

We sought to develop and internally validate a multivariable asthma prediction rule (APR) to inform hospitalization decision making in a population of children aged 5 to 17 years with acute asthma exacerbations, in accordance with contemporary clinical and biostatistical standards established for CPR development and internal validation.[11-13]

METHODS

Study participants

Detailed methods for our study have been presented in a previous report.[13] We enrolled a prospective convenience sample aged 5 to 17 years with doctor-diagnosed asthma who presented with acute exacerbations to our academic, tertiary, urban children's hospital emergency department (PED). We excluded patients with chronic lung disease other than asthma or with other causes for pertinent signs and symptoms. We included participants with more than one enrollment for APR modeling as long as the interval between enrollments was greater than 14 days (Figure 1). The rationale for this was that patient visits having this chronologic separation were likely to represent distinct exacerbation events.

The clinical team maintained exclusive decision-making capacity regarding all management and hospitalization decisions. Study data were not made available to the clinical team, and the study protocol did not include informing clinical management. The study protocol was reviewed and approved by the Vanderbilt University IRB (protocol #080058); parents and participants provided informed written consent and assent.

Participant measurements and data acquisition

Baseline data included medical history, family asthma history, demographic and social information, medications in use, coexisting illness, asthma symptom history, and asthma characteristics that encompassed chronic disease control, environmental exposures, and prior adverse events.[13] Additional clinical variables were measured and recorded before initiating treatment. These included oxygen saturation (SpO_2) on room air, assessment for accessory muscle use (scalene, sternocleidomastoid-suprasternal, intercostal, subcostal), lung auscultation (inspiratory-to-expiratory ratio, wheezing, air entry) exhaled nitric oxide (eNO), and spirometry for %-predicted forced expiratory volume in 1 second (%FEV_1).[14,15] Using bedside physical findings and SpO_2 we calculated the Acute Asthma Intensity Research Score, a validated bedside acute severity score (though not a CPR).[16]

Candidate predictor variables

Candidate predictor variables for a CPR should be clinically and biologically plausible, ideally with some established evidence of a predictive value. For example, we have previously reported that accessory muscle group use is a physical sign readily assessed at the bedside and has a dose-response association with %FEV_1.[15,16] In addition, an APR will be more practical and widely used by clinicians if the predictor variables are available at the bedside.

We considered candidate predictor variables for APR development in accordance with these principles (Table I). These included participant demographic and asthma characteristics, pulmonary exam findings, and measures of lung function and inflammation.

A variable was excluded after data acquisition but before APR modeling if its value was subject to our hospital's local practice and not generalizable (eg, pediatric critical care unit [PCCU] admission criteria), had high measurement variability or did not calibrate well to severity (eg, respiratory rate), was rarely abnormal (eg, scalene retractions), displayed multiple colinearity with another variable (eg, air entry), had a high proportion of missing data (eg, FEV_1), or was difficult to measure or not available in clinical settings where acute asthma may be managed (eg, eNO, plethysmograph estimate of pulsus paradoxus). As a result, 7 candidate variables were excluded (see Table E1 in this article's Online Repository at www.jaci-inpractice.org),[17,18] and the final model included the 15 predictor variables in Table I.

Outcome variables

A CPR must predict an outcome that is both clearly defined and clinically important.[9,19] The primary outcome variable was *need for hospitalization*, defined as length of stay >24 h (for admitted participants) or unscheduled return for asthma care to a physician or hospital within 48 h (for discharged participants).[13] Before prediction rule modeling an expert studio panel recommended that a second pragmatic and relevant primary outcome variable would be the *hospitalization decision* of the clinical team. This outcome encompasses the multiplicity of factors that the