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Vital signs should be maintained as continuous variables when predicting bacterial infections in febrile children

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Abstract

Objective: To determine how vital signs such as heart and respiratory rates should be included in prediction models for serious bacterial infections (SBIs) in febrile children.

Study Design and Setting: Prospective observational study of 1,750 febrile children aged <16 years, visiting the emergency department of a university hospital; of them 13% (n = 222) had SBI. Common age-specific thresholds of heart and respiratory rates were used to define tachycardia and tachypnea. We compared seven strategies to handle vital signs as predictors of SBI (dichotomized or continuously in various ways).

Results: The dichotomous predictors, namely tachycardia and tachypnea, containing information on the vital sign and age showed limited value to predict the presence of SBI (area under the receiver operating characteristic curve [AUC (ROC)]: 0.53 for heart rate and 0.55 for respiratory rate). In comparison, a model with age as a single continuous predictor resulted in an AUC of 0.58. Models with age and one of the vital signs included continuously showed the highest AUC (heart rate: 0.60 and respiratory rate: 0.63).

Conclusion: Heart and respiratory rates should be maintained as continuous variables in model development to predict SBI in febrile children, as dichotomization results in information loss and lower predictive ability.

Keywords: Child; Fever; Vital signs; Bacterial infections; Acute disease; Clinical prediction rule

1. Introduction

Children visiting the emergency departments with fever can present with a wide spectrum of disease. In the clinical evaluation of a febrile child, clinicians use general features, vital signs, and disease-specific characteristics often complemented by laboratory tests to discriminate those at high risk for serious infections from those with minor disease [1,2]. Measurement of vital signs is a key part of triage in pediatric emergency departments [3]. Several prediction models for serious bacterial infection (SBI) have been developed to support clinicians and guide diagnostic and therapeutic decisions [4,5]. The vital signs, namely heart and respiratory rates, are often used in the prediction of serious infections, although their diagnostic value remains a debate [6,7].

Diagnostic research in this area has used different approaches to handle heart and respiratory rates in prediction models [8]. The rates are continuous measures, but their use in children is complicated as normal ranges vary with age, and in some cases with other characteristics [9]. To simplify the interpretation of heart and respiratory rates, clinicians typically use age-specific threshold values to define abnormality [10]. Diagnostic studies on febrile children (n = 25) identified by a systematic literature search converted the continuous variables mostly to dichotomous or categorical variables (n = 20), whereas the variables were kept continuous in five articles (See Appendix at www.jclinepi.com). Statistical arguments

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What is new?

Key findings

- The vital signs, namely the heart and respiratory rates, showed more predictive information for serious bacterial infections (SBIs) in febrile children when treated as continuous variables together with age compared with the dichotomous variables tachycardia and tachypnea.

What this adds to what was known?

- The commonly used dichotomization of heart and respiratory rates leads to suboptimally performing prediction models.

What is the implication and what should change now?

- Heart and respiratory rates should be treated as continuous variables in the prediction modeling of SBI in febrile children. Formats other than regression models, such as the score charts or nomograms, may help the user to apply the model.

against dichotomization include the loss of considerable information, which can lead to less discriminative models and reduction of statistical power [11]. Furthermore, the thresholds used to dichotomize may not be related to the presence of SBI [12].

We aimed to compare several strategies for handling heart and respiratory rates in predictive models and the effects of these on diagnostic performance for identifying children with SBI.

2. Methods

2.1. Patients

Data were used from a prospective study of children (aged 1 month to 16 years) visiting the emergency department of the Erasmus MC–Sophia Children's Hospital, Rotterdam, The Netherlands, with fever (temperature ≥38.0°C) between July 2003 and December 2005 [13]. Patients with a significant medical history and children who used antibiotics within 1 week of presentation to the emergency department were excluded.

Data were obtained from a computerized triage system and standardized electronic patient records in which nurses prospectively documented patients' characteristics and vital signs, including heart rate (beats/min), respiratory rate (breaths/min), and temperature (°C).

Presence of SBI was defined as a positive culture from a normally sterile site (e.g., urinary tract infection, bacterial meningitis, and sepsis), radiographically proven (e.g., pneumonia), or by consensus diagnosis reached by the investigators, as previously described [14]. Telephonic follow-up after 1 week was used to rule out missed diagnoses of SBI.

2.2. Data analyses

Analyses focused on heart and respiratory rates in combination with age [9,12]. Logistic regression was used to study the association of heart and respiratory rates with SBIs. Missing values were imputed once (single imputation) to accommodate the analysis of all included children [15]. Analyses were performed using R software, version 2.12.0 (R Development Core team, Vienna, Austria; 2006) [16].

We evaluated seven modeling strategies (Table 1). The first model reflects the typical approach in clinical practice with the rates dichotomized using age-specific thresholds [9]. Model 2 includes the normalized values for the rates. The associations of the rates with SBI was further studied linearly (model 3), with nonlinear terms (model 4), in interaction with age (model 5) and with models defining the deviation of heart and respiratory rates from median values, adjusted for age (model 6) or adjusted for age and temperature (model 7), so called centiles [9,12,17].

Nonlinearity was assessed with restricted cubic splines (RCS) with a maximum of four knots. The RCS are very flexible, but are restricted to be linear in the tails and have been proposed for a stable approach for prediction models [18]. Age was included as a linear term (similar to model 3) as splines did not outperform the linear term.

The diagnostic performance of the models was assessed in terms of model fit (model χ^2), explained variation (R^2), and area under the receiver operating characteristic curve [AUC (ROC)]. The continuous Net Reclassification Index (cNRI) was calculated for each model compared with a model containing only age [19].

3. Results

The demographic and clinical characteristics and final diagnoses of 1,750 included children are presented in Table 2. An SBI was present in 222 (12.7%) of the children. Tachypnea was significantly more frequent in the SBI group compared with the non-SBI group (57% vs. 48%, respectively). A similar trend, although smaller, was observed for tachycardia (SBI: 40% vs. non-SBI: 35%).

The model containing only age (linear term) is considered as a reference and showed a model χ^2 of 23.8, R^2 of 2.5%, and AUC of 0.58 (Table 1). Dichotomizing the rates with the age-specific APLS thresholds (Acute Pediatric Life Support group; www.aplsonline.com), which are often considered as variables that include information on both the rate and age, showed less predictive information than the continuous age variable only. Addition of continuous predictors of heart or respiratory rates improved the model performance compared with only age. The way the rates were