Resuscitation 133 (2018) 25–32

Contents lists available at ScienceDirect

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Clinical paper

Predicting cardiac arrests in pediatric intensive care units☆

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ARTICLE INFO

Keywords:
Pediatric intensive care unit
Cardiac arrest
Cardiopulmonary resuscitation
Critical care
Severity of illness
Predictive analytics

ABSTRACT

Background: Early identification of children at risk for cardiac arrest would allow for skill training associated with improved outcomes and provides a prevention opportunity.
Objective: Develop and assess a predictive model for cardiopulmonary arrest using data available in the first 4 h.
Methods: Data from PICU patients from 8 institutions included descriptive, severity of illness, cardiac arrest, and outcomes.
Results: Of the 10074 patients, 120 satisfying inclusion criteria sustained a cardiac arrest and 67 (55.9%) died. In univariate analysis, patients with cardiac arrest prior to admission were over 6 times and those with cardiac arrests during the first 4 h were over 50 times more likely to have a subsequent arrest. The multivariate logistic regression model performance was excellent (area under the ROC curve = 0.85 and Hosmer-Lemeshow statistic, p = 0.35). The variables with the highest odds ratio's for sustaining a cardiac arrest in the multivariable model were admission from an inpatient unit (8.23 (CI: 4.35–15.54)), and cardiac arrest in the first 4 h (6.48 (CI: 2.07–20.36). The average risk predicted by the model was highest (11.6%) among children sustaining an arrest during hours > 4–12 and continued to be high even for days after the risk assessment period; the average predicted risk was 9.5% for arrests that occurred after 8 PICU days.
Conclusions: Patients at high risk of cardiac arrest can be identified with routinely available data after 4 h. The cardiac arrest may occur relatively close to the risk assessment period or days later.

Introduction

Cardiac arrests occur in approximately six thousands hospitalized children yearly [1–5]. Increasingly, these cardiac arrests predominantly occur in the pediatric intensive care unit (PICU) [6] as a result of physiological decompensation in spite of critical care monitoring and therapies [2,6,7]. Notably, hospital survival rates following cardiac arrest are improving from rates of about 15% in the 1990's to current hospital survival rates of approximately 50% [1,3,4,6,8–10].

Improvements in cardiopulmonary resuscitation outcomes have been associated with both better organization and training of resuscitation teams, and improved resuscitation techniques [4,11,12]. Recently, clinical identification of high risk patients and point-of-care, just-in-time bedside skill training focused on these high-risk patients

☆ A Spanish translated version of the abstract of this article appears as Appendix in the final online version at https://doi.org/10.1016/j.resuscitation.2018.09.019.

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https://doi.org/10.1016/j.resuscitation.2018.09.019
Received 16 May 2018; Received in revised form 22 August 2018; Accepted 19 September 2018

demonstrated improved outcomes. Thus, identification of patients at risk for cardiac arrest has the practical importance of improved outcomes through focused skill training and situational awareness allowing pro-active team preparedness [13–15].

Despite this potentially important clinical impact, there are few objective, early warning methods to assess cardiac arrest risk for children admitted to the PICU. Early warning scores have been used with variable success to identify patients at risk for clinical deterioration [16,17] and a checklist has been developed in a single PICU to identify daily those patients at increased proximate risk [7,13]. High risk events antecedent to cardiac arrests have also been identified in adults [18–21]. Our aims were to identify clinical data available within the first 4 h of PICU admission that are associated with pediatric cardiac arrest and to use these data to develop and assess a predictive model for assigning objective risks to suffer a cardiopulmonary arrest.

Methods

Data and patients

The data for this analysis originated in the Trichotomous Outcome Prediction in Critical Care (TOPICC) study conducted by the Collaborative Pediatric Critical Care Research Network (CPCCRN) of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development. Data collection methods and the institutional characteristics have been previously described [22]. There were seven sites and one was composed of two institutions. In brief, patients from newborn to less than 18 years were randomly selected and stratified by hospital from December 4, 2011 to April 7, 2013. Patients from both general/medical and cardiac/cardiovascular PICUs were included. Moribund patients (vital signs incompatible with life for the first two hours after PICU admission) were excluded. Only the first PICU admission during a hospitalization was included. In this analysis, we excluded all patients dying within the first 4 h of PICU stay because we focused on predicting cardiac arrest after the first 4 h (see below). The protocol was approved by all participating Institutional Review Boards. Other analyses utilizing this database have been published [1,22–26]. In particular, a previous publication detailed the descriptive characteristics of those patients with cardiac arrest as well as the characteristics of those arrests and outcomes [1].

Data included descriptive and demographic information (Tables 1 and 2). A cardiac arrest was defined as chest compression for at least 1 min and/or defibrillation [1]. Admission source was classified as emergency department, inpatient unit, post intervention unit, or admission from another institution. Diagnosis was classified by system of primary dysfunction based on the reason for PICU admission; cardiovascular conditions were classified as congenital or acquired. Interventions included both surgery and interventional catheterization. Pre-ICU cardiac arrest included closed chest massage within 24 h prior to hospitalization or after hospital admission, but prior to PICU admission. The Functional Status Scale (FSS) was used to describe baseline (prehospital admission) functional status as good (FSS 6, 7), mild dysfunction (FSS 8, 9), moderate dysfunction (FSS 10–15), severe dysfunction (FSS 16–21) and very severe dysfunction (FSS > 21) [27].

Physiological profiles were measured using the Pediatric Risk of Mortality (PRISM) score [28] with a shortened time interval (2 h prior to PICU admission to 4 h after admission for laboratory data and the first 4 h of PICU care for other physiological variables). For this analysis, we also partitioned the PRISM score into cardiovascular (heart rate, systolic blood pressure, temperature), neurological (pupillary reactivity, mental status), respiratory (arterial PO2, pH, PCO2, total bicarbonate), chemical (glucose, potassium, blood urea nitrogen, creatinine), and hematological (white blood cell count, platelet count, prothrombin and partial thromboplastin time) components. We computed the risk of mortality with a previously developed algorithm [26] and assessed the association of mortality risk with the risk of cardiac arrest (see below) with the Pearson correlation coefficient.

The timing interval for assigning the admission time and assessing data was modified for cardiac patients under 91 days of age because some institutions admit infants to the PICU prior to a cardiac intervention to “optimize” the clinical status but not for intensive care; in these cases, the post-intervention period more accurately reflects intensive care. However, in other infants for whom the cardiac intervention is delayed after PICU admission or the intervention is a therapy required due to failed medical management of the acute condition, the first vital sign is the most appropriate initial time for admission and PRISM data collection time interval since it is the start of the ICU critical illness [22].

Model development

Our approach for modeling focused on the data available in the first 4 h of care to estimate the subsequent risk of cardiac arrest. We did not attempt to predict cardiac arrests in the first 4 h of PICU care because these events are generally associated with pre-ICU factors. We did include cardiac arrests occurring in the first 4 h of care as a predictor variable for risk of subsequent arrests. The four hour modeling period was chosen because physiological profiles are important predictors of death, and this data set utilized physiological profiles measured with the PRISM score obtained from the first 4 h of admission [24,26].

Statistical analyses utilized SAS 9.4® (SAS Institute Inc. Cary, NC 27513-2414, USA) for descriptive statistics, model development, and fit assessment, and R 3.1.1 (R Foundation for Statistical Computing, https://www.r-project.org/) for evaluation of predictive ability. Patient characteristics were descriptively compared and evaluated across sites using the Kruskal-Wallis test for continuous variables, and the Pearson chi-squared test for categorical variables. The statistical analysis was under the direction of R.H.

Our primary outcome was the first cardiac arrest occurring after the first 4 h of PICU care. Since this outcome was relatively rare, we did not split the sample into development and validation sets, in order to maximize the sample size available for model development. Univariate mortality odds ratios were computed and variables with a significance level < 0.1 were considered candidate predictors for the final model. Variables were not included if there was a large percentage of unknowns/missing. A non-automated (examined by biostatistician and clinician at each step) backward stepwise selection approach was used to select factors. Multi-categorical factors (e.g., categorized age) had levels or factors combined when appropriate per statistical and clinical criteria. We also tested the total PRISM score and its partitioned scores, and the association of these partitioned scores with their “natural” diagnostic group (e.g. cardiac PRISM with patients with cardiac conditions versus non-cardiac conditions). Construction of a clinically relevant, sufficiently predictive model using information readily available to the clinician took precedence over inclusion based solely on statistical significance. Final candidate models were evaluated based on receiver operating characteristic (ROC) (discrimination), and the Hosmer-Lemeshow goodness of fit (calibration). To augment the potential utility of the ROC curve, we also assessed the relationship between the true positive rate (sensitivity, recall) and positive predictive value (precision, PPV) with the precision-recall curve and a plot illustrating the relationship between the number needed to evaluate (NNTE, 1/PPV) and the true positive rate [29,30]. The NNTE is the number of patients classified as “high risk” using a particular cutpoint to identify one actual cardiac arrest.

Results

Overall, there were 10,078 patients in the TOPICC database. Four patients died in the first 4 h after PICU admission, resulting in 10074 patients used for this analysis. A total of 132 patients sustained cardiac arrests after PICU admission. Nineteen arrests occurring during the first