An Empirically Derived Pediatric Cardiac Inotrope Score Associated With Pediatric Heart Surgery

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We aimed to empirically derive an inotrope score to predict real-time outcomes using the doses of inotropes after pediatric cardiac surgery. The outcomes evaluated included in-hospital mortality, prolonged hospital length of stay, and composite poor outcome (mortality or prolonged hospital length of stay). The study population included patients <18 years of age undergoing heart operations (with or without cardiopulmonary bypass) of varying complexity. To create this novel pediatric cardiac inotrope score (PCIS), we collected the data on the highest doses of 4 commonly used inotropes (epinephrine, norepinephrine, dopamine, and milrinone) in the first 24 hours after heart operation. We employed a hierarchical framework by representing discrete probability models with continuous latent variables that depended on the dosage of drugs for a particular patient. We used Bayesian conditional probit regression to model the effects of the inotropes on the mean of the latent variables. We then used Markov chain Monte Carlo simulations for simulating posterior samples to create a score function for each of the study outcomes. The training dataset utilized 1030 patients to make the scientific model. An online calculator for the tool can be accessed at https://soipredictiontool.shinyapps.io/InotropeScoreApp. The newly proposed empiric PCIS demonstrated a high degree of discrimination for predicting study outcomes in children undergoing heart operations. The newly proposed empiric PCIS provides a novel measure to predict real-time outcomes using the doses of inotropes among children undergoing heart operations of varying complexity.

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A critically ill patient receiving multiple inotropes after complex congenital heart operation at the Arkansas Children's Hospital.

Central Message

The newly proposed empiric score provides a scientific measure to calculate outcomes using the doses of inotropes in children undergoing heart operations.

Perspective Statement

We sought to create an inotrope score using advanced statistical methods, such as Bayesian conditional probit regression models and Markov chain Monte Carlo (MCMC) simulations. The newly proposed empiric pediatric cardiac inotrope score has a high degree of discrimination for predicting poor outcomes in children undergoing heart operations.

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INTRODUCTION

In children undergoing heart operations, inotropic and vasoactive agents are routinely employed after cardiac surgery to decrease the incidence of low cardiac output. In 1995, Wernovsky and colleagues initially described the concept of inotrope score to quantify the amount of cardiovascular support received by neonates after the arterial switch operation.[1] Since the invention of this inotrope score, this score has been modified and validated multiple times as a severity of illness marker among children undergoing heart operations.[2-8] The original inotrope score proposed by Wernovsky et al included 3 inotropes, namely, epinephrine, dopamine, and dobutamine.[1] With subsequent modifications, more drugs such as milrinone, vasopressin, and norepinephrine were added to the already existing scores.[2-8]

Previous investigators have used expert opinion and clinical judgment to create and alter inotrope scores (Table 1). Ostensibly, the coefficients for varied inotropes in the previous inotrope scores were chosen in a manner so as to convert dosages in each drug to an integer value and to give each medication equal weight in the calculation. To address these knowledge gaps, we sought to create an inotrope score using advanced statistical methods, such as Bayesian conditional probit regression models and MCMC simulations among children undergoing heart operations. The outcomes evaluated included mortality at hospital discharge, prolonged hospital length of stay (LOS), and composite poor outcome (defined as mortality at hospital discharge or prolonged hospital LOS).

MATERIALS AND METHODS

We performed a single-center retrospective observational study in an 18-bed pediatric cardiovascular ICU (CVICU) at a tertiary academic children's hospital. The study population included all patients <18 years of age undergoing heart operations (with or without cardiopulmonary bypass [CPB]) during the period July 2012 to July 2015. We also included patients undergoing procedures in the STS-EACTS category 5 (Society of Thoracic Surgeons-European Association for Cardiothoracic Surgery) for the period January 2009 to July 2012. Patients operated upon in outside institutions and subsequently transferred to our institution were excluded from the study. The Institutional Review Board of the University of Arkansas Medical Sciences approved the study and the need for informed consent was waived.

We collected data on demographics, heart operation, inotropes, and study outcomes. To create this novel tool, we collected the data on the highest doses of 4 commonly used inotropes in our CVICU (epinephrine, norepinephrine, dopamine, and milrinone) in the first 24 hours after heart operation. At our institution, inotropic and vasoactive medications are initiated in the operating room at the discretion of the cardiac surgical team. After arrival in CVICU, the medications are initiated or adjusted by the medical team managing the patient, based on physiological status, fluid balance, clinical condition, age, anatomical diagnosis, and surgery performed. In our operating room and CVICU, decisions regarding ongoing titration of inotropic medications are made without any preestablished protocol.

Statistical Methods

We summarized patient demographics, cardiac surgery type, laboratory values, existing inotrope scores, and study outcomes among patients with and without composite poor outcomes. Continuous variables were summarized using median and interquartile ranges (IQRs), whereas categorical variables were summarized using frequency and percentages. Two group univariate comparisons among variables were done using Wilcoxon rank sum test or chi-squared test for continuous and categorical variables, respectively.

Statistical Model

The primary goal of this study was to create an inotrope score as a marker of severity of illness after pediatric cardiac surgery. We aimed to create a score that predicts composite poor outcome (y) defined as either mortality or prolonged LOS. We used 2 different cutoffs for prolonged LOS, 1 for patients undergoing high complexity operations (STS-EACTS categories 4 and 5), and 1 for patients undergoing low complexity operations (STS-EACTS categories 1, 2 and 3) (Figures S1 and S2). The distribution of length of stay within each complexity category was investigated and the 75th percentile was determined to be an appropriate threshold to define prolonged hospital LOS. This definition uses the same approach as used by other authors in published literature.[1,7] We created the inotrope score using a Bayesian probit regression model. We used dosage information within the first 24 hours on the following 4 inotropes: dopamine, epinephrine, norepinephrine, and milrinone to create a score. To ensure that the inotrope score will be an independent predictor of composite poor outcome, we included the following covariates as well in the model used to create the inotrope score: age (months), gender, weight (kg), and total CPB time (minutes).

Table 1. Inotrope Scores in Existing Literature

Agrawal et al	Dopamine + dobutamine + 100 (epinephrine) + 100 (norepinephrine) + 10 (milrinone)
Algra et al	Dopamine + dobutamine + 100 (epinephrine) + 100 (norepinephrine) + 15 (milrinone)
Alten et al	Dopamine + 10 (phenylephrine) + 100 (epinephrine) + 100 (norepinephrine)
Bradley et al	Dopamine + 10 (milrinone) + 100 (epinephrine)
Fenton et al	(Dopamine + dobutamine + amrinone) × 1 + (milrinone) × 20) + (epinephrine + norepinephrine + isoproterenol) × 100]
Gaies et al	Dopamine + dobutamine + 100 (epinephrine) + 100 (norepinephrine) + 10,000 (vasopressin) + 10 (milrinone)
Ko et al	Dopamine + dobutamine + 100 (epinephrine) + 100 (norepinephrine) + 100 (isoproterenol) + 15 (milrinone)
Wernovsky et al	Dopamine + dobutamine + 100 (epinephrine)

Note: Dosages for all drugs are in μg/kg/min, except vasopressin where the units are in units/kg/min.