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# **Hospital Variation in Survival After Pediatric In-Hospital Cardiac Arrest**

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# **Abstract**

**Background—**Although survival after in-hospital cardiac arrest is likely to vary among hospitals caring for children, validated methods to risk-standardize pediatric survival rates across sites do not currently exist.

**Methods and Results—**Within the American Heart Association's Get With the Guidelines-Resuscitation registry for in-hospital cardiac arrest, we identified 1,551 cardiac arrests in children (<18 years) from 2006 to 2010. Using multivariable hierarchical logistic regression, we developed and validated a model to predict survival to hospital discharge and calculated risk-standardized rates of cardiac arrest survival for hospitals with a minimum of 10 pediatric cardiac arrest cases. A total of 13 patient-level predictors were identified: age, sex, cardiac arrest rhythm, location of arrest, mechanical ventilation, acute non-stroke neurologic event, major trauma, hypotension, metabolic or electrolyte abnormalities, renal insufficiency, sepsis, illness category, and need for intravenous vasoactive agents prior to the arrest. The model had good discrimination (C-statistic of 0.71), confirmed by bootstrap validation (validation C-statistic of 0.69). Among 30 hospitals with at least 10 cardiac arrests, unadjusted hospital survival rates varied considerably (median, 37%; inter-quartile range [IQR]: 24%–42%; range: 0%–61%). After risk-standardization, the range of hospital survival rates narrowed (median, 37%; IQR: 33%–38%; range: 29%– 48%), but variation in survival persisted.

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**Conclusion—**Using a national registry, we developed and validated a model to predict survival after in-hospital cardiac arrest in children. After risk-standardization, significant variation in survival rates across hospitals remained. Leveraging these models, future studies can identify best practices at high-performing hospitals to improve survival outcomes for pediatric cardiac arrest.

#### **Keywords**

pediatrics; heart arrest; cardiopulmonary resuscitation; risk model

Although in-hospital cardiac arrest in children is associated with poor survival, the extent to which survival rates differ across hospitals is unknown.<sup>1</sup> Understanding this inter-hospital variation is important, as the presence of substantial variability would suggest an opportunity to improve pediatric outcomes after cardiac arrest. Toward that end, The Joint Commission and other national organizations, such as the American Heart Association, are developing performance measures to benchmark outcomes for in-hospital cardiac arrest and resuscitation.

Until recently, the ability to examine variation in pediatric outcomes for in-hospital cardiac arrest has been limited due to the lack of a central registry. Moreover, while standard methods have emerged to perform risk-standardization for other conditions, these have not been applied to survival after cardiac arrest in children.<sup>2</sup> Therefore, current efforts to compare hospital resuscitation outcomes for children may be premature until validated models are developed.

The emergence of the American Heart Association's Get With the Guidelines (GWTG)- Resuscitation registry—a national registry of in-hospital cardiac arrest—over the past decade provides a unique opportunity to address these current gaps in knowledge. Accordingly, we developed and validated a hierarchical regression model for survival in pediatric patients with inhospital cardiac arrest. We then applied this model to calculate riskstandardized survival rates for pediatric in-hospital cardiac arrest at each hospital and evaluated the extent of site-level variation in survival outcomes. The findings in this study will offer a methodological framework for future hospital comparisons of survival outcomes for pediatric in-hospital cardiac arrest.

#### **Methods**

#### **Study Population**

Formerly known as the National Registry of Cardiopulmonary Resuscitation, GWTG-Resuscitation is a large, prospective, national registry of in-hospital cardiac arrest sponsored by the American Heart Association. Its design has been described in detail previously.<sup>3</sup> In brief, trained hospital personnel enroll all patients without do-not-resuscitate orders with a cardiac arrest (defined as pulselessness requiring chest compressions and/or defibrillation and eliciting a hospital-wide or unit-based emergency response). Cases are identified by multiple methods, including centralized collection of cardiac arrest flow sheets, reviews of hospital paging system logs, and routine checks of code carts, pharmacy tracer drug records, and hospital billing charges for resuscitation medications.<sup>3</sup> Standardized "Utstein-style"

definitions are used for all patient variables and outcomes to facilitate uniform reporting across hospitals.<sup>4, 5</sup> In addition, data accuracy is ensured by rigorous certification of hospital staff and use of standardized software with data checks for completeness and accuracy.<sup>3</sup> Currently, the Registry incorporates data from approximately 8% of all U.S. hospitals.

From January 2000 through August 2010, data from 2,883 pediatric patients under 18 years of age with an in-hospital cardiac arrest were submitted to GWTG-Resuscitation. Since pediatric in-hospital survival rates have improved over time<sup>6</sup>, we restricted our study sample to the 1,640 patients enrolled between January 2006 and August 2010 to ensure that our risk models were based on a contemporary cohort of patients. Additionally, we excluded 89 resuscitations performed in the delivery room, as cardiac arrests in the delivery room differ physiologically and mechanistically from cardiac arrests in other hospital settings. Our final study cohort comprised 1,551 patients from 164 hospitals.

#### **Study Outcome and Variables**

The primary outcome of interest was survival to hospital discharge. A number of baseline characteristics were screened as candidate predictors for the study outcome. Variables that were considered for model inclusion were those clinical and demographic characteristics that were known to be associated with survival. These included age at the time of cardiac arrest (categorized as neonates  $\lceil 30 \text{ days} \rceil$ , infants  $\lceil 31 \text{ days} \rceil$  days to  $\lceil 1 \text{ years} \rceil$ , young children  $\lceil 1-8 \rceil$ years], and older children [>8 years of age]), sex, location of arrest (categorized as procedure areas, intensive care, monitored unit, non-monitored unit, emergency department, and other), time of arrest (day vs. night  $[11pm$  to 6:59am])<sup>7</sup>, initial cardiac arrest rhythm (ventricular fibrillation, pulseless ventricular tachycardia, asystole, pulseless electrical activity), and illness category (medical-cardiac, medical-noncardiac, surgical-cardiac, surgical-noncardiac).

In addition, the following co-morbidities or medical conditions coded as present *prior* to cardiac arrest were evaluated for the model: heart failure; renal, hepatic, or respiratory insufficiency; baseline evidence of motor, cognitive, or functional neurologic deficits (CNS depression); acute stroke; acute non-stroke neurologic event; pneumonia; hypotension; arrhythmia; sepsis; major trauma; metabolic or electrolyte abnormality; and metastatic or hematologic malignancy. Finally, we considered for model inclusion several critical care interventions (requirement for mechanical ventilation, intravenous vasoactive medications or intravenous antiarrhythmics) already in place at the time of cardiac arrest. Race was not considered for model inclusion, as prior studies have found that racial differences in survival after in-hospital cardiac arrest are partly mediated by differences in hospital care quality for blacks and whites.<sup>8, 9</sup>

#### **Model Development and Validation**

Multivariable logistic regression models were constructed to identify significant predictors of inhospital survival. Because our primary objective was to derive risk-standardized survival rates for each hospital, which would require us to account for clustering of observations within hospitals, we used hierarchical logistic regression models for our analyses.<sup>10</sup> By using hierarchical models to estimate the log-odds of in-hospital survival as a

We considered for model inclusion the candidate variables described in the previous section. Age group, sex, initial cardiac arrest rhythm, and arrest location were included in the model regardless of statistical significance. Multicollinearity between covariates was assessed for each variable prior to model inclusion.<sup>11</sup> Model discrimination was assessed with the Cstatistic, which quantifies the receiver operating characteristic curve (ROC) of the model.<sup>12</sup> To validate the model, we examined observed vs. predicted plots and performed 1000 bootstrap samples to derive a validation C-statistic that would correct for potential model over-fitting.<sup>13</sup>

#### **Hospital Risk-Standardized Survival Rates**

Using the hospital-specific estimates (i.e., random intercepts) from the hierarchical models, we then calculated risk-standardized survival rates for the 30 study hospitals with a minimum of 10 cardiac arrest cases by multiplying the registry's unadjusted survival rate by the ratio of a hospital's predicted to expected survival rate. We used the ratio of predicted to expected outcomes (described below) instead of the ratio of observed to expected outcomes to overcome analytical issues that have been described for the latter approach.<sup>14–16</sup> Specifically, our approach ensured that all hospitals, including those with smaller case volumes, would have appropriate risk-standardization and confidence intervals for their cardiac arrest survival rates.

For these calculations, the expected hospital number of cardiac arrest survivors is the number of cardiac arrest survivors expected at the hospital if the hospital's patients were treated at a "reference" hospital (i.e. the average hospital-level intercept from all hospitals in GWTG-Resuscitation). This was determined by regressing patients' risk factors and characteristics on inhospital survival with all hospitals in the sample, and then applying the subsequent estimated regression coefficients to the patient characteristics observed at a given hospital, and then summing the expected number of deaths. In effect, the expected rate is a form of indirect standardization. In contrast, the predicted hospital outcome is the number of survivors at a specific hospital. It is determined in the same way that the expected number of deaths is calculated, except that the hospital's individual random effect intercept is used. The risk-standardized survival rate was then calculated by the ratio of predicted to expected survival rate, multiplied by the unadjusted rate for the entire study sample.<sup>17</sup> The effects of risk-standardization on unadjusted hospital rates of survival were then illustrated with descriptive plots and statistics.

All study analyses were performed with SAS 9.2 (SAS Institute, Cary, NC) and R version 2.10.0.18 The hierarchical models were fitted with the use of the GLIMMIX macro in SAS. Dr. Chan had full access to the data and takes responsibility for its integrity. All authors have read and agree to the manuscript as written. The American Heart Association's GWTG-Resuscitation Committee approved the final manuscript draft.

# **Results**

Of 1,551 patients with in-hospital cardiac arrest, 481 (31.0%) were neonates, 358 (23.1%) infants, 358 (23.1%) younger children, and 354 (22.8%) older children. Fifty-eight percent of the study population was male and  $21.5%$  were black. The vast majority (n=1361, 87.7%) had a non-shockable cardiac arrest rhythm; 53.8% had a first documented rhythm of pulseless electrical activity and 33.9% with asystole. Sixty-seven percent of the arrests occurred in an intensive care unit and 21.4% in a procedure area or in the emergency department, with less than 10% occurring on a general pediatric ward. Hypotension was documented in 38.3% prior to the cardiac arrest, and respiratory insufficiency in 60.1%.

#### **Predictors of Survival**

Overall, 543 (35.0%) pediatric patients with an in-hospital cardiac arrest survived to hospital discharge. Tables 1 and 2 compare baseline demographics of the study cohort among those patients who survived and did not survive to hospital discharge. Children over 8 years of age were less likely to survive an in-hospital cardiac arrest than younger patients. In univariate analyses, the presence of hypotension, renal insufficiency, hepatic insufficiency, metabolic or electrolyte abnormalities, acute CNS non-stroke event, sepsis, major trauma, and metastatic or hematologic malignancy were also associated with a lower likelihood of survival. Finally, patients treated with mechanical ventilation and intravenous vasoactive medications at the time of cardiac arrest were less likely to survive, whereas patients treated with antiarrhythmics at the time of cardiac arrest were more likely to survive to discharge.

After multivariable adjustment, 13 variables were identified as critical factors for riskstandardization (Table 3). These included age, sex, illness category, cardiac arrest rhythm, location of arrest, mechanical ventilation, acute non-stroke neurologic event, major trauma, hypotension, metabolic or electrolyte abnormalities, renal insufficiency, sepsis, and requirement for intravenous vasoactive medications at the time of arrest. The model had good discrimination (C-statistic of 0.71). Model calibration was confirmed with observed vs. predicted plots (Figure 1). For model validation, we performed a series of 1000 bootstrap samples and found that model discrimination was similar (bootstrap-corrected validation Cstatistic of 0.69).

#### **Hospital Variation in Risk-Standardized Survival Rates**

Prior to adjustment for case-mix, survival rates for the 30 hospitals with at least 10 cardiac arrest cases varied considerably, with a median hospital rate of 37%, an inter-quartile range (IQR) of 24% to 42%, and a total range of 0% to 61% (Figure 2a). After riskstandardization, the distribution of hospital rates of survival narrowed considerably. However, some variation in hospital rates of survival persisted, with a median hospital riskstandardized rate of 37%, IQR of 33% to 38%, and a total range of 29% to 48% (Figure 2b).

# **Discussion**

Using a large national registry, we developed and validated a risk-standardized model for survival in pediatric patients with in-hospital cardiac arrest. Among a wide range of variables, our model identified 13 unique patient predictors of survival to discharge. These

variables were defined using standardized definitions and are easily obtainable from medical records. Without adjustment for patient factors, the range of survival rates across hospitals was 0% to 61%. After adjustment for patient case-mix, the range of risk-standardized hospital rates of cardiac arrest survival narrowed substantially (range= 29 to 48%), but hospital variation in survival remained. The presence of variability in risk-standardized survival rates among hospitals suggests an opportunity to save lives if hospitals in the lower range were able to achieve survival rates of higher-performing hospitals.

Most prior studies on pediatric in-hospital cardiac arrest have focused on identifying patient predictors of survival. For instance, children whose cardiac arrest is caused by an underlying cardiac etiology have been shown to have lower survival than those with a respiratory etiology.19 Likewise, those with an arrest surrounding surgery for repair or palliation of congenital heart disease are more likely to survive than those with a medical-cardiac or noncardiac diagnosis.20 Others have found that certain cardiac arrest rhythms, such as ventricular fibrillation and pulseless ventricular tachycardia, are associated with improved survival.<sup>21</sup> Despite identifying certain patient characteristics associated with survival in prior studies, there has not been, to date, a validated method to risk standardize hospital rates of survival for pediatric in-hospital cardiac arrest– a critical foundation for quality improvement. In this study, we have created and validated such a model to facilitate comparisons of pediatric outcomes for this condition between hospitals. Such a model will be of great value to benchmark hospital performance on in-hospital cardiac arrest and to guide future quality improvement efforts. Our model adhered to recommended standards for models of publicly reported outcomes, including high-quality and timely data as well as clinical coherence of the model variables.<sup>2</sup> Importantly, we utilized a hierarchical randomeffects model, which accounts for variation in sample size between hospitals to generate 'shrinkage estimates' for sites with lower case volumes.

In this study, we found that the inter-quartile range prior to risk-adjustment was 18% and narrowed to 5% following risk adjustment. This suggests that risk-standardization is critical for future benchmarking efforts, as the inter-quartile range narrowed by over 70%. It also highlights that, despite a reduction in variation of survival rates across hospitals, there remained significant variability in hospital survival rates that was not attributable to differences in patient characteristics reported in the registry. This suggests that the remaining hospital variation in pediatric cardiac arrest survival may be due to hospitalspecific factors including quality of care before, during, and after resuscitation. Such factors may include resuscitation response times (e.g., time to defibrillation), chest compression depth, frequency of interruptions in chest compressions, duration of cardiopulmonary resuscitation, and post-resuscitation care (e.g., hospital differences in intensive care expertise).<sup>1, 22–26</sup> Future studies are needed to identify "best practices" associated with higher survival rates at top-performing hospitals and whether such practices can be readily disseminated and effectively implemented to all hospitals.

The impact of having access to a risk-standardized model for survival in pediatric patients with in-hospital cardiac arrest may be profound for quality improvement initiatives. Hospitals need to be able to benchmark the effect of their improvement programs over time, and with other organizations. Similar to other conditions that are the focus of broad quality

Our study has certain limitations. GWTG-Resuscitation is a quality improvement registry, and hospital participation is voluntary. Given the fact that a minority of children's hospitals in the U.S. participate in the registry, and hospitals in a quality improvement registry are more likely to direct substantial resources to improving CPR outcomes, our findings may not be generalizable to non-registry hospitals. Second, although our model adjusted for a number of patient characteristics and had good discrimination, we did not have information on certain patient factors. For instance, we did not have information on cyanotic and acyanotic congenital heart disease in most patients, which may have improved model discrimination. Moreover, we did not have information on hospital factors, such as staffing ratios, presence of around-the-clock intensivists in critical care units, a site's annual cardiac surgery volume, and use of mock codes and other quality improvement initiatives. Additionally, our examination of variation in risk-standardized survival rates was limited to 30 hospitals with at least 10 pediatric in-hospital cardiac arrest cases; future studies with a larger hospital sample may be needed to confirm these findings. Lastly, we did not assess survival with favorable neurological outcomes – another clinically important outcome to patients – as it was missing in 26% of pediatric survivors and was outside the scope of our present study on survival.

# **Conclusion**

In a national registry of in-hospital cardiac arrest, we have developed and validated a model to risk-standardize hospital rates of survival for pediatric in-hospital cardiac arrest. After accounting for patient case-mix, we found that variation in hospital survival rates decreased but persisted. Our findings lay the methodological foundation for future efforts by national organizations to benchmark hospital survival for cardiac arrest in children and suggest the possibility that differences in hospital processes and quality of care, in part, account for the differences in survival rates across hospitals.

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# **Figure 1. Calibration of the Final Model in the Derivation Cohort**

The model showed excellent calibration, with slope of 1.1 (slope of 1.0 for perfect calibration).







Unadjusted (Fig. 2a) and Risk-Standardized (Fig. 2b) Hospital Survival Rates for In-Hospital Cardiac Arrest

## **Table 1**

Baseline Characteristics of Patients Surviving and Not Surviving to Hospital Discharge





Abbreviations: PEA, pulseless electrical activity; VF, ventricular fibrillation; VT, ventricular tachycardia; ICU, intensive care unit; ED, emergency department; CNS, central nervous system; Mon, Monday; Fri, Friday

*\** 13 patients (5 survivors, 8 non-survivors) with missing data for time of cardiac arrest

#### **Table 2**

Event Characteristics of Patients Surviving to Hospital Discharge



*\** Data available only from January 1 to August 30

<sup>†</sup><br><sup>4</sup>43 patients (20 survivors and 23 non-survivors) with missing data for teaching status and bed size

*‡* Includes institutions with residents and fellows

*§* Includes institutions with residents

#### **Table 3**

# Model Predictors for Survival to Discharge



Abbreviations: CI, confidence interval; CNS, central nervous system; ICU, intensive care unit; ED, emergency department; PEA, pulseless electrical activity; VF, ventricular fibrillation; PVT, pulseless ventricular tachycardia