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Cardiopulmonary resuscitation in hospitalized infants

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ABSTRACT

Background: Hospitalized infants requiring cardiopulmonary resuscitation (CPR) represent a high-risk group. Recent data on risk factors for mortality following CPR in this population are lacking.
Aims: We hypothesized that infant demographic characteristics, diagnoses, and levels of cardiopulmonary support at the time of CPR requirement would be associated with survival to hospital discharge following CPR.
Study design: Retrospective cohort study.
Subjects: All infants receiving CPR on day of life 2 to 120 admitted to 348 Pediatrix Medical Group neonatal intensive care units from 1997 to 2012.
Outcomes measures: We collected data on demographics, interventions, center volume, and death prior to NICU discharge. We evaluated predictors of death after CPR using multivariable logistic regression with generalized estimating equations to account for clustering of the data by center.
Results: Our cohort consisted of 2231 infants receiving CPR. Of these, 1127 (51%) survived to hospital discharge. Lower gestational age, postnatal age, 5-min APGAR, congenital anomaly, and markers of severity of illness were associated with higher mortality. Mortality after CPR did not change significantly over time (Cochran–Armitage test for trend $p = 0.35$).
Conclusions: Mortality following CPR in infants is high, particularly for less mature, younger infants with congenital anomalies and those requiring cardiopulmonary support prior to CPR. Continued focus on at risk infants may identify targets for CPR prevention and improve outcomes.

1. Introduction

Cardiopulmonary resuscitation (CPR) is life-saving for infants suffering a cardiopulmonary arrest. Although an arrest is most likely to occur immediately after birth, CPR can also be required outside of the delivery room in the neonatal intensive care unit (NICU) [1]. Data on CPR risk factors and survival in the NICU are sparse, but small, single-center studies have suggested low survival following NICU CPR [1,2]. This finding contrasts sharply with the trend in improved overall survival of infants, particularly those of very low birth weight [3,4]. The reasons for low survival rate after NICU CPR are largely unknown.

Several studies of survival following CPR in infants have focused on, or included, delivery room CPR [5–8]. Studies focusing on NICU CPR are less common, and all have been limited by their small sample size and overall high mortality [1]. Because of these limitations, risk factors and associated survival following NICU CPR are poorly understood. This lack of understanding limits the ability of providers to identify infants at risk for CPR as well as to decide which infants should undergo CPR, how extensive CPR should be, and how best to counsel parents in the setting of CPR need.

The purpose of our study was to describe the risk factors associated with survival following infant CPR in the NICU. We hypothesized that infant demographic characteristics, diagnoses, and levels of cardiopulmonary support at the time of CPR requirement would be associated with survival to hospital discharge following CPR.

Abbreviations: BW, Birth weight; CPR, Cardiopulmonary resuscitation; ECMO, Extracorporeal membrane oxygenation; FiO_2, Fraction of inspired oxygen; GA, Gestational age; NICU, Neonatal intensive care unit; PNA, Postnatal age; SGA, Small for gestational age.

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2. Material and methods

2.1. Study design and sample

We used a database derived from electronic medical records and daily progress notes generated by clinicians on all infants cared for by the Pediatrix Medical Group in 348 NICUs in North America from 1997 to 2012. Data on multiple aspects of care were entered into a shared electronic medical record to generate clinical documentation. Information on maternal history, demographics, medications, laboratory results, diagnoses, and procedures were then transferred to the Pediatrix clinical data warehouse for quality improvement and research purposes [9]. We included all infants discharged with documentation in their medical record of having received CPR between day of life 2 and 120, including those who died. We excluded infants with missing information on mortality at NICU discharge which includes infants transferred to another hospital. The study was approved by the Duke University Institutional Review Board (Fig. 1).

2.2. Study measurements

We defined CPR as any new episode of CPR that was documented in the medical record, and we counted the number of separate days during which an infant received CPR. We defined mortality as in-hospital mortality prior to discharge, maternal steroids as any steroid exposure during pregnancy regardless of number of doses, small for gestational age (SGA) as previously described, and congenital anomalies as any major anomaly as described in our study database [10]. We defined measures of cardiopulmonary support and other interventions as the presence of or exposure to any of the following on a given day: any inotrope (epinephrine, dopamine, dobutamine, amrinone, milrinone, and norepinephrine), any mechanical ventilation (conventional or high-frequency ventilation), any fraction of inspired oxygen (FiO_2) >30%, any pulmonary hypertension therapy (inhaled nitric oxide, sildenafil, bosentan, or epoprosterenol), or any central line (peripherally inserted central venous catheters, percutaneous or tunneled central venous lines, umbilical venous lines). We then evaluated cardiopulmonary support measures using 3 different methods: the use of each cardiopulmonary support measure on the day prior to CPR, the cumulative number of days each cardiopulmonary support measure was used prior to CPR, and the escalation of each cardiopulmonary support measure on the day prior to CPR. Escalation of inotropic and ventilator support, pulmonary hypertension therapy, central venous line, and FiO_2 was defined as new exposure to inotropes, initiation of mechanical ventilation or conversion from conventional to high frequency ventilation, new exposure to pulmonary hypertension therapy, insertion of central venous line, and an increase in $FiO_2 \geq 25\%$ (e.g., 25% to 50% FiO_2) on the day prior to CPR.

2.3. Statistical methods

The unit of observation for this analysis was an infant requiring CPR at least once between day of life 2 and 120. We excluded infants receiving CPR before day of life 2 to avoid CPR courses received in the delivery room or for ongoing resuscitation of birth depression, and after day of life 120 because of the small sample size and heterogeneous nature of infants hospitalized for >120 days. We used summary statistics including medians and 25th and 75th percentiles to describe continuous variables, and frequency counts and percentages to describe categorical variables. Continuous variables were categorized using clinically relevant cutoffs (gestational age [GA], birth weight [BW], and postnatal age [PNA]) or based on the distribution of our data (discharge year, center volume). We compared infant characteristics between survivors and non-survivors using chi-square tests of association and Wilcoxon rank sum tests analyzing trends over time using the Cochran–Armitage test.

We used multivariable logistic regression to evaluate the association between survival to NICU discharge following CPR and clinically relevant predictors. We used the method of generalized estimating equations to account for the clustered nature of the data by site. After performing modeling assumption diagnostics and assessments of collinearity, we included the following covariates in the final model: GA, SGA, 5-min APGAR score, inborn status, presence of any congenital anomaly, PNA on the day of CPR, discharge year, and inotropes, pulmonary hypertension therapy, mechanical ventilation, $FiO_2 > 30\%$, and presence of any central line on the day prior to CPR. We report odds ratios and 95% confidence intervals for mortality prior to NICU discharge, as well as predicted probability of death by GA group. We conducted all analyses using Stata 13.1 (College Station, Texas) and considered a $p < 0.05$ statistically significant.

3. Results

3.1. Infant characteristics

We identified 2231/887,910 (0.25%) infants who received CPR, of whom 2129/2231 (95%) received CPR on only 1 day (one event), 89/2131 (4%) received CPR on 2 days (2 events), and 13/2131 (1%) received CPR on 3 or more days (3 or more events). The overall survival to hospital discharge among all infants receiving CPR was 1127/2231 (51%). Median (25th, 75th percentile) GA, BW, and PNA on the day of first CPR was 29 weeks (25, 34), 1210 g (720, 2215), and 11 days (4, 27), respectively. Infants with CPR who survived to hospital discharge were more mature, had higher BW, and were older on the day of CPR compared to those who died (33 weeks [29, 35] vs. 26 weeks [24, 30], $p < 0.001$; 1844 g [1120, 2550] vs. 790 g [625, 1260], $p < 0.001$; and 13 days [6, 31] vs. 8 days [2, 22], $p < 0.001$; respectively). Survivors were less likely to be SGA and to suffer from a major

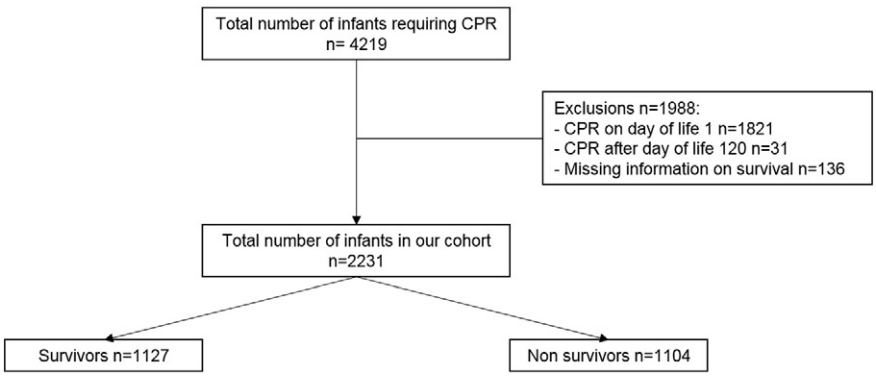

Fig. 1. Study flow diagram.