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Clinical paper

Neonatal delivery room CPR: An analysis of the Get with the Guidelines[®]—Resuscitation Registry



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Abstract

Background: Cardiopulmonary resuscitation (CPR) in the delivery room (DR) after birth is rare. We hypothesized that factors related to maternal, delivery, infant and resuscitation event characteristics associated with outcomes could be identified. We also hypothesized there would be substantial variation from the Neonatal Resuscitation Program (NRP) algorithm.

Methods: Retrospective review of all neonates receiving chest compressions in the DR from the AHA Get With The Guidelines—Resuscitation registry from 2001 to 2014. The primary outcome was return of spontaneous circulation (ROSC) in the DR. Secondary outcome was survival to hospital discharge. Descriptive statistics were used to characterize data. Odds ratios with confidence intervals were calculated as appropriate to compare survivors and non-survivors.

Results: There were 1153 neonates who received chest compressions in the DR. ROSC was achieved in 968 (84%) newborns and 761 (66%) survived to hospital discharge. Fifty-one percent of the cohort received chest compressions without medications. Cardiac compressions were initiated within the first minute of life in 76% of the events, and prior to endotracheal intubation in 79% of the events. In univariate analysis, factors such as prematurity, number of endotracheal intubation attempts, increased time to first adrenaline dose, and CPR duration were associated with decreased odds of ROSC in the DR. Longer CPR duration was associated with decreased odds of ROSC in multivariate analysis.

Conclusion: In this cohort of infants receiving chest compressions following delivery, recognizable pre-birth risk factors as well as resuscitation interventions associated with increased and decreased odds of achieving ROSC were identified. Chest compressions were frequently initiated in the first minute of the event and often prior to endotracheal intubation. Further investigations should focus on methods to decrease time to critical resuscitation interventions, such as successful endotracheal intubation and administration of the first dose of adrenaline, in order to improve DR-CPR outcomes.

Keywords: Neonatal resuscitation, Delivery room resuscitation, Cardiac compressions, Adrenaline

Abbreviations: CPR, cardiopulmonary resuscitation; DR, delivery room; AHA, American Heart Association; NRP, neonatal resuscitation program; ROSC, return of spontaneous circulation; ANOVA, analysis of variance.

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Introduction

Approximately 5–7% of newborns receive resuscitative support during postnatal transition after birth.¹ Extensive resuscitation, however, is rare, with less than 1% receiving chest compressions and/or adrenaline (epinephrine).² Unlike adults, cardiovascular collapse in neonates is almost always due to perinatal asphyxia.^{3,4} Neonatal resuscitation, therefore, focuses primarily on the provision of positive pressure ventilation (PPV) to improve gas exchange via bag/mask ventilation initially, followed by endotracheal intubation preferably before performing other resuscitation measures such as chest compressions.⁵

Recognition of pre-birth risk factors can help delivery room providers anticipate and prepare for newborns who may need extensive resuscitation. For example, prematurity is associated with decreased survival following delivery room cardiopulmonary resuscitation (DR-CPR).^{1,6,7,8} Neonatal outcomes following placental abruption has also been studied,⁹ however large studies investigating multiple pre-birth factors and associations with decreased odds of achieving return of spontaneous circulation (ROSC) following DR-CPR are lacking.

In an infant requiring extensive resuscitation, delivery of appropriate and timely resuscitative interventions is essential and may impact the odds of achieving ROSC following DR-CPR. Number of endotracheal intubation attempts, adrenaline administration, and time to first adrenaline dose given are examples of resuscitation factors that may potentially impact odds of successfully achieving ROSC.

Although most North American hospitals mandate American Heart Association/Neonatal Resuscitation Program (AHA/NRP) training for pediatric DR providers, little is known about neonatal resuscitation performance. In 2000, Carbine et al. observed deviations from NRP guidelines in 54% of 100 videotaped resuscitations.¹⁰ McKinsey and Perlman also demonstrated delayed timing of many interventions during simulated neonatal resuscitations, compared with AHA/NRP guidelines.¹¹ Variation in neonatal resuscitation practices is an important concern during DR-CPR. NRP emphasizes establishing effective PPV and strongly recommends ventilation through an endotracheal tube before initiating chest compressions.⁵

Given the infrequency of DR-CPR, the current practice of neonatal resuscitation has not been well characterized in a large multi-site cohort. To address this knowledge gap, data from the Get With The Guidelines—Resuscitation (GWTG-R) registry was used to describe factors associated with infants receiving chest compressions in the DR. We hypothesized that identifiable maternal, delivery, infant and resuscitation event characteristics are associated with DR-CPR outcomes. We also hypothesized that there would be substantial variation in resuscitation practices in relation to the NRP algorithm. An improved understanding of the current clinical practice for DR-CPR in the newly born is critical for developing effective interventions to improve outcomes.

Methods

Design

This retrospective cohort study utilized the AHA's GWTG-R registry: a large, multicenter prospective database of in-hospital cardiac arrest.

Hospitals participating in the registry voluntarily submit clinical information regarding medical history, hospital care, and outcomes of consecutive patients hospitalized for cardiac arrest using an online, interactive case report form and Patient Management Tool (Quintiles, Cambridge, Massachusetts). Quintiles serves as the data collection and coordination center for the AHA/American Stroke Association GWTG[®] programs. The University of Pennsylvania serves as the data analytic center and prepares the data for research purposes. The registry uses Utstein-style¹² definitions for all patient variables and outcomes to facilitate uniform reporting across institutions. Participating hospitals may use the registry to query the database for the purposes of quality improvement and to benchmark their results for resuscitation practice and patient outcomes. Data accuracy is ensured through certification of data abstractors and uses standardized software with data checks for accuracy and completeness. Its design has been previously described in detail (www.heart.org/resuscitation). This study was exempt from review by the University of Texas Southwestern Medical Center at Dallas Institutional Review Board.

Population

The cohort included all newly born infants who received chest compressions in the DR submitted to the GWTG-R registry between 2001 and 2014. Time to chest compressions initiated, time to endotracheal tube (ET) insertion and time to first adrenaline dose was defined as the time period from the time of birth until the time the intervention was performed. The primary outcome was ROSC in the DR, defined as a sustained heart rate over 60 bpm with no further need for chest compressions for greater than 20 min. The secondary outcome was survival to hospital discharge. We compared maternal, delivery, infant, and resuscitation characteristics between survivors and non-survivors. Demographic data included birth weight, gestational age (GA), gender, race, maternal conditions, delivery complications, mode of delivery, cord blood gas pH and Apgar scores at 1, 5 and 10 min. Data collected regarding resuscitation interventions included the number of ET intubation attempts, time to ET tube insertion, time to initiation of chest compressions, time to first adrenaline dose, number of adrenaline doses, fluid bolus administration, non-drug interventions, and duration of CPR.

Statistical analysis

Descriptive statistics were used to describe infant, maternal, delivery and resuscitation event characteristics. Continuous variables were analyzed using Student's *t*-test. Categorical data were analyzed using Chi-square. Mann–Whitney *U* test was used as appropriate to compare maternal, delivery, infant and resuscitation event characteristics between survivors and non-survivors. Multivariate logistic regression was used to estimate the odds ratio (OR) with 95% confidence intervals (CI) for ROSC in the DR and survival to hospital discharge. Variables included in the multivariate logistic model were chosen from the univariate analysis based on the following criteria: *P*-value <0.10, <20% overall missing data and the number of events >1%. Admission year and hospital site were included in the model to control for year or site bias. Data were analyzed using SPSS (IBM version 19). *P* values of <0.05 were considered statistically significant.

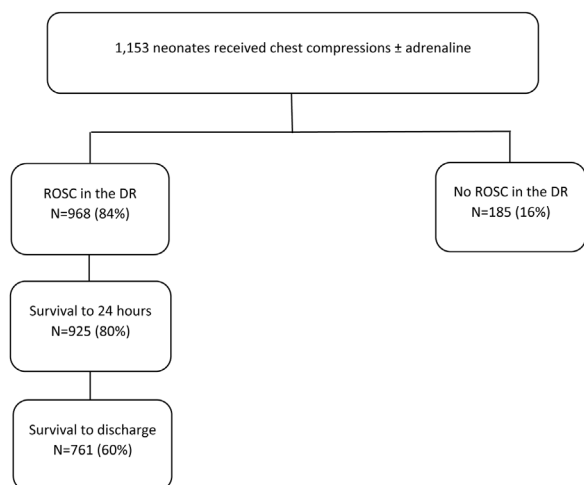


Fig. 1 – Survival outcomes for neonates following DR-CPR from the Get With The Guidelines—Resuscitation Registry from 2001 to 2014.

Results

Between January 2001 and December 2014, 1153 neonates from 129 centers who received chest compressions at birth were entered into the AHA's GWTG-R registry. ROSC was achieved in 968 (84%) neonates, 925 (80%) survived to 24 h, and 761 (66%) survived to hospital discharge (Fig. 1). Mean GA of the cohort was 33 ± 6 weeks and the mean birth weight was 2251 ± 124 g. Only 34.6% had maternal conditions such as diabetes, hypertension, chorioamnionitis and pre-eclampsia, with a significantly higher proportion of these infants achieving ROSC following DR-CPR compared to those not achieving ROSC (Table 1). Delivery complications such as placenta

previa, abruption, cord prolapse and shoulder dystocia occurred in 23.6% and emergent cesarean delivery in 10%.

Maternal and neonatal demographics of infants who achieved ROSC vs. those who died in the DR are shown in Table 1. Neonates that died in the DR were more likely to have lower GA, lower birth weight, birth via emergent cesarean delivery, cord pH less than 7, lower median Apgar scores at 1, 5 and 10 min, have a congenital malformation or be part of a multiple gestation. Maternal conditions were associated with a higher percentage of these infants achieving ROSC following DR-CPR. Gender, race, presence of prenatal care, delivery complications including cord prolapse, placental abruption, shoulder dystocia, presence of meconium stained fluid and use of fetal monitoring were all similar between neonates that achieved ROSC and those that died in the DR.

The association between resuscitation interventions and ROSC in the DR are shown in Table 2. Decreased odds of achieving ROSC in the DR was associated with an increased number of ET intubation attempts, adrenaline administration, greater number of adrenaline doses, a longer time to receive the first adrenaline dose, longer duration of CPR, delivery of a fluid bolus, and non-drug interventions such as thoracentesis, chest drain insertion or paracentesis. Chest compressions were initiated within the first minute of life for 76% of the 1153 infants who received chest compressions. Additionally, 915 infants (79%) underwent ET intubation as part of the resuscitation effort. Data on 701 neonates (77%) regarding the time of ET intubation was available, and of these, 552 neonates (79%) received chest compressions before ET intubation took place. In addition to receiving chest compressions in the DR, 561 (49%) neonates also received adrenaline. Time to 1st adrenaline administration was significantly longer in the group that died in the DR compared to those that achieved ROSC (7 min [IQR 1,11] vs. 4 min. [IQR 1,8]; $P < 0.01$).

Table 3 illustrates maternal and neonatal demographics of those neonates that survived to discharge versus those that did not. Infants

Table 1 – Maternal and infant demographics associated with ROSC for neonates receiving DR-CPR.

Variable	All neonates (n = 1153)	N	ROSC (n = 968)	N	No ROSC (n = 185)	N	P value
Gestational age (weeks)	33 ± 6	1102	33 ± 6	917	30 ± 6	185	<0.01
Weight (g)	2251 ± 124	1101	2293 ± 123	916	1682 ± 118	185	<0.01
Male	640 (55.5)	1153	541 (55.9)	968	99 (53.5)	185	0.55
Non-Hispanic white	482 (41.8)	1153	413 (42.7)	968	69 (37.3)	185	0.55
Prenatal care	988 (86.8)	1138	832 (86.8)	958	156 (86.7)	180	0.95
Maternal condition(s) ^a	399 (34.6)	1153	358 (37.0)	968	41 (22.2)	185	<0.01
Delivery complications ^b	272 (23.6)	1153	219 (22.6)	968	53 (28.6)	185	0.08
Maternal narcotics or magnesium sulfate during labor	100 (8.7)	1153	91 (9.4)	968	9 (4.9)	185	0.045
Emergent cesarean delivery	115 (10.0)	1153	82 (8.5)	968	33 (17.8)	185	<0.01
Instrumental delivery (forceps or vacuum)	56 (4.9)	1153	45 (4.6)	968	11 (5.9)	185	0.45
Meconium stained fluid	119 (10.5)	1138	106 (11.1)	957	13 (7.2)	181	0.12
Fetal monitoring (external or internal)	734 (63.7)	1153	609 (62.9)	968	125 (67.6)	185	0.23
Non-reassuring fetal heart tones	259 (22.8)	1138	226 (23.6)	957	33 (18.2)	181	0.11
Cord pH < 7.0	131 (29.2)	448	107 (27.3)	392	24 (42.9)	56	0.02
Apgar score at 1 min	1 (0, 2)	1127	1 (1, 2)	968	1 (0, 1)	159	<0.01
Apgar score at 5 min	3 (1, 6)	1125	4 (1, 6)	968	1 (0, 1)	157	<0.01
Apgar score at 10 min	4 (1, 7)	139	5 (3, 7)	112	1 (0, 1)	27	<0.01
Infant congenital malformation	5 (0.4)	1153	2 (0.2)	968	3 (1.6)	185	0.03
Multiple births	79 (6.9)	1138	60 (6.3)	957	19 (10.5)	181	0.04

Data are reported as mean \pm standard deviation, median (interquartile range), or n (%).

^a Includes maternal diabetes, hypertension, infections including chorioamnionitis, pre-eclampsia, eclampsia, or maternal drug or alcohol use.

^b Placenta previa, placental abruption, cord prolapse or shoulder dystocia.

Table 2 – Resuscitation characteristics associated with ROSC for neonates receiving DR-CPR.

Variable	All neonates (n = 1153)	N	ROSC (n = 968)	N	No ROSC (n = 185)	N	P value
Number endotracheal intubation attempts	3 ± 2	121	3 ± 1	96	4 ± 3	25	0.04
Time to endotracheal tube insertion (mins) ^a	1 (0, 4)	701	1 (0, 4)	576	2 (0, 6)	125	0.09
Time to chest compressions initiated (mins)	0 (0, 0)	328	0 (0, 1)	272	0 (0, 3)	56	0.02
Received adrenaline	561 (49)	1153	396 (41)	396	165 (89)	165	<0.01
Time to 1 st adrenaline dose (min)	4 (1, 8)	298	4 (1, 7)	211	7 (1, 11)	87	<0.01
Total number adrenaline doses	3 ± 1.9	450	2 ± 1.5	334	4 ± 2.3	116	<0.01
Duration of CPR (min)	11.9 ± 17.6	1083	8.5 ± 12.5	915	30.8 ± 26.8	168	<0.01
Fluid bolus given	64 (27.5)	233	38 (19.8)	192	26 (63.4)	41	<0.01
Non-drug interventions ^b	26 (2.3)	1153	12 (1.2)	968	14 (7.6)	185	<0.01

Data are reported as mean ± standard deviation, median (interquartile range), or n (%).

^a Time to endotracheal tube insertion known in 701 infants.

^b Thoracentesis, chest drain insertion or paracentesis.

Table 3 – Maternal and infant demographics associated with survival to discharge for neonates receiving DR-CPR.

Variable	All neonates t (n = 1153)	Survival to discharge (n = 761)	Death prior to discharge (n = 392)	P value
Gestational age (weeks)	33 ± 6	35 ± 6	30 ± 6	<0.01
Weight (g)	2251 ± 124	2291 ± 126	1690 ± 123	<0.01
Male	626 (55.8)	427 (56.1)	199 (50.8)	0.38
Non-Hispanic white	473 (42.2)	326 (42.8)	147 (37.5)	0.13
Prenatal care	963 (87.0)	652 (87.8)	311 (85.4)	0.28
Maternal condition(s) ^a	390 (34.8)	279 (37.1)	111 (30.1)	0.02
Delivery complications ^b	270 (24.1)	170 (22.6)	100 (27.1)	0.10
Maternal narcotics or magnesium sulfate during labor	96 (8.6)	73 (9.7)	23 (6.2)	0.051
Emergent cesarean delivery	109 (9.7)	60 (8.0)	49 (13.3)	<0.01
Instrumental delivery (forceps or vacuum)	56 (5.0)	39 (5.2)	17 (4.6)	0.68
Meconium stained fluid	118 (10.6)	95 (12.8)	23 (6.3)	<0.01
Fetal monitoring (external or internal)	713 (63.5)	470 (62.4)	243 (65.9)	0.26
Non-reassuring fetal heart tones	256 (23.1)	184 (24.8)	72 (19.7)	0.06
Cord pH < 7.0	128 (29.2)	71 (23.4)	57 (42.2)	<0.01
Apgar score at 1 min	1 (0, 2)	1 (1, 2)	1 (0, 2)	<0.01
Apgar score at 5 min	3 (1, 6)	4 (2, 7)	1 (0, 3)	<0.01
Apgar score at 10 min	4 (1, 7)	6 (4, 8)	1 (0, 3)	<0.01
Infant congenital malformation	5 (0.4)	2 (0.3)	3 (0.8)	0.34
Multiple births	74 (6.7)	42 (5.7)	32 (8.8)	0.051

Data are reported as mean ± standard deviation, median (interquartile range), or n (%).

^a Includes maternal diabetes, hypertension, infections including chorioamnionitis, pre-eclampsia, eclampsia, or maternal drug or alcohol use.

^b Placenta previa, placental abruption, cord prolapse or shoulder dystocia.

that died prior to discharge were more likely to have a lower GA, lower birth weight, emergent cesarean delivery, cord pH less than 7.0, and lower median Apgar scores at 1, 5 and 10 min. Presence of prenatal care, gender, race and delivery complications including cord prolapse, placental abruption or shoulder dystocia were all similar between neonates that survived to discharge and those that died.

The DR resuscitation interventions undertaken for those neonates that survived to discharge versus those that did not are shown in Table 4. Mortality prior to discharge was associated with an increased number of ET intubation attempts, adrenaline administration, increased number of adrenaline doses, longer duration of CPR, fluid bolus administration, and non-drug interventions such as thoracentesis, chest drain insertion or paracentesis.

Table 5 illustrates the multivariate logistic regression model of maternal, infant and resuscitation variables associated with ROSC of neonates receiving DR-CPR. Gestational age (aOR 1.12 [95% CI: 1.05, 1.19]; $P < 0.01$), delivery complications (placenta previa, placental abruption, cord prolapse or shoulder dystocia) (aOR 2.40 [95% CI: 1.05,

5.52]; $P = 0.04$) and higher Apgar scores at 5 min (aOR 2.46 [95% CI: 1.81, 3.34]; $P < 0.01$) were associated with ROSC in the DR. Longer duration of CPR was associated with decreased odds of ROSC (aOR 0.92 [95% CI: 0.89, 0.94]; $P < 0.01$). Early chest compressions were associated with increased odds of ROSC in univariate analysis. This variable was not included in Table 5 because missing data points exceeded 20%. Due to the potential significance of this finding, a post-hoc multivariate analysis was performed (Supplemental Table 1) which included time to chest compressions as a covariate. In this analysis, time to chest compressions was not independently associated with ROSC. Of the 129 sites that contributed to the registry, some centers entered as many as 83 events while other centers entered as few as 1 event. Despite these variations, neither specific years or sites were associated with decreased odds of achieving ROSC in infants receiving CPR in the delivery room.

A sensitivity analysis of ROSC in the DR without duration of CPR was also performed (Supplemental Table 2). In this model, GA and 5-minute Apgar scores were still associated with increased ROSC.

Table 4 – Resuscitation characteristics associated with survival to discharge for neonates receiving DR-CPR.

Variable	All neonates (n = 1153)	Survival to discharge (n = 761)	Death prior to discharge (n = 392)	P value
Number endotracheal intubation attempts	3 ± 2	3 ± 1	3 ± 2	0.04
Time to endotracheal tube insertion (mins)	1 (0, 4)	1 (0, 4)	2 (0, 4)	0.67
Time to chest compressions initiated (mins)	0 (0, 1)	0 (0, 1)	0 (0, 1)	0.11
Received adrenaline	540 (52.7)	246 (36.8)	294 (82.4)	<0.01
Time to 1st adrenaline dose (min)	4 (1, 8)	4 (2, 7)	4 (1, 8)	0.66
Total number adrenaline doses	3 ± 1.8	2 ± 1.6	3 ± 2.0	<0.01
Duration of CPR (min)	12.0 ± 17.7	8.0 ± 13.2	20.3 ± 22.4	<0.01
Fluid bolus given	64 (28.1)	23 (15.5)	41 (51.2)	<0.01
Non-drug interventions ^a	26 (2.3)	1 (0.1)	25 (6.8)	<0.01

Data are reported as mean ± standard deviation, median (interquartile range), or n (%).

^a Thoracentesis, chest drain insertion or paracentesis.

Table 5 – Multivariate regression model of maternal, neonatal, and resuscitation variables associated with ROSC in the delivery room for neonates receiving DR-CPR.

Variable for Full Model	Odds Ratio (95% Confidence Interval)	P value
Gestational age	1.12 (1.05, 1.19)	<0.01
Admission year ^a		0.33
Site ID ^a		1.00
Presence of maternal medical condition(s) ^b	2.10 (0.99, 4.48)	0.06
Delivery complications ^c	2.40 (1.05, 5.52)	0.04
Maternal narcotics or magnesium sulfate use during labor	0.62 (0.17, 2.20)	0.46
Emergent C-section delivery	0.33 (0.07, 1.61)	0.17
Apgar score at 5 min	2.46 (1.81, 3.34)	<0.01
Multiple Births	0.63 (0.18, 2.18)	0.46
Received adrenaline	0.50 (0.16, 1.59)	0.24
Duration of CPR (min)	0.92 (0.89, 0.94)	<0.01
Non-drug interventions	1.10 (0.23, 5.35)	0.90

^a Admission year is over 14 years (2001–2014) and site (N = 129). These are control variables that are not significant and odds ratio not presented.

^b Includes Maternal diabetes, hypertension, infections including chorioamnionitis, pre-eclampsia, eclampsia, or maternal drug or alcohol use.

^c Placenta previa, placental abruption, cord prolapse or shoulder dystocia.

Delivery complications were no longer associated with increased ROSC, but presence of maternal medical conditions (maternal diabetes, hypertension, infections including chorioamnionitis, pre-eclampsia) were associated with increased ROSC. In this sensitivity model, receiving adrenaline was associated with decreased odds of ROSC among infants receiving DR-CPR.

Discussion

The current retrospective study is one of the largest reports of neonatal cardiopulmonary resuscitation in the delivery room, with 1153 infants receiving chest compressions and 561 infants receiving adrenaline. Factors related to maternal, delivery, infant and resuscitation event characteristics associated with outcomes following DR-CPR were identified. The current study also highlights variation in resuscitation practice from the NRP algorithm, with a significant proportion of infants receiving chest compressions prior to endotracheal intubation.

Prematurity was associated with decreased odds of ROSC in the DR and decreased survival to hospital discharge following DR-CPR. Multiple other studies have also found that prematurity is associated with increased mortality following DR-CPR.^{1,6,7,8} Although a large resuscitation review in extremely low birth weight (ELBW) infants from

1999 demonstrated a 44% survival in infants with a birth weight of 501–750 g following DR-CPR, this survival rate was lower than in those ELBW infants not receiving CPR in the DR.¹³ Maternal conditions such as diabetes, hypertension, infections including chorioamnionitis, pre-eclampsia and maternal drug and alcohol use were actually associated with higher odds of achieving ROSC. A possible explanation for this may be closer monitoring pre-labor (in some cases in patient monitoring) and lower threshold for emergent delivery in the setting of a known high-risk pregnancy.

In multivariate analysis, prenatal risk factors associated with higher odds of ROSC included higher GA and higher 5 min Apgar scores (possibly reflecting degree of perinatal asphyxia). In 2017, Downes et al. reported that placental abruption was associated with higher neonatal mortality in the DR.⁹ Interestingly, delivery complications (placenta previa, placental abruption, cord prolapse or shoulder dystocia) were actually associated with higher adjusted odds of ROSC following DR-CPR in multivariate analysis. This suggests that identifiable acute perinatal events may lead to a better prognosis than perinatal depression without a known precipitating event. The reason for this is unknown, but one potential explanation is that recognition of these complications before or around the time of birth may lead to a more expedited delivery and/or neonatal team preparation. Unfortunately, we cannot assess this speculation with the

available data. Interestingly, delivery complications did not remain significant in the sensitivity model run without duration of CPR as a variable. In this model, maternal conditions were instead associated with higher adjusted odds of ROSC following DR-CPR.

Adrenaline administration and increasing number of adrenaline doses was associated with decreased odds of ROSC and survival to hospital discharge following DR-CPR. Previous studies have demonstrated increased mortality and morbidity in both term and preterm infants following the administration of adrenaline in the DR.^{14,15} In addition, we found that the first dose of adrenaline was administered earlier among infants who achieved ROSC compared to those who did not achieve ROSC (4 vs.7 min). This suggests that although adrenaline administration may be associated with worse outcomes, early administration of adrenaline significantly increases the infant's chance of establishing ROSC. Although neonatal studies are lacking, numerous pediatric studies have shown improved survival outcomes with adrenaline given at less than 5 min into the CPA event compared to adrenaline given later than 5 min.^{16–18} Additionally, the neonates who did not achieve ROSC were more likely to have received a greater number of adrenaline doses. It is plausible that the infants receiving adrenaline during DR-CPR were more severely asphyxiated compared to those infants that achieved ROSC without adrenaline, and that the severity of the asphyxia is what led to decreased survival in the DR. Receiving adrenaline was also associated with decreased odds of achieving ROSC following DR-CPR in the sensitivity model without duration of CPR as a variable.

Increased number of endotracheal intubation attempts was also associated with decreased odds of ROSC following DR-CPR. Multiple intubation attempts subject the neonate to additional stress and delays the next steps of the resuscitation. The premature infant is particularly vulnerable and a possible association between multiple intubation attempts and higher rates of death or neurologic developmental impairment, as well as an increase in severe intraventricular hemorrhage in infants less than 1500 g has been reported.^{19,20} In addition, the risk of inadvertent esophageal intubation will also result in poor lung ventilation and ultimately make ROSC difficult. Per NRP recommendations, the use of a laryngeal mask airway should always be considered as an alternative to intubation in larger infants.⁵

The NRP algorithm is widely used in the US. Despite this, neonatal resuscitation is “a poorly studied intervention”²¹ with a lack of studies examining how well the algorithm is followed. In 2013, Sing and Oddie²² found marked variation in delivery room management of very preterm infants. Although our study cohort was delivered prior to the 2015 NRP guidelines, which strongly emphasized the need for endotracheal intubation prior to initiation of chest compressions, effective PPV has always been the primary focus of neonatal resuscitation. If bag mask ventilation does not result in a rising heart rate, establishing an alternative airway to reverse the offending asphyxia typically results in an improvement in the heart rate, thus avoiding the need for chest compressions altogether. We found that chest compressions were initiated within the first minute of the resuscitation in 76% of cases and prior to endotracheal intubation in 79% of cases. These data are concerning, as they suggest that many episodes of CPR may have been initiated before effective ventilation was established.

The current study was a review of a large national resuscitation registry. As with any registry review, numerous limitations were present. Primarily a resuscitation database for adults and children, initial data points included were not necessarily applicable to the neonate or the neonate receiving chest compressions in the DR. In addition, certain pertinent

neonatal resuscitation data points were not initially collected in the dataset, such as dose of adrenaline administered. Modifications to the dataset have since been made, with the latest changes occurring in 2013. In addition, very few centers entered data pertaining to how chest compressions were delivered (2 thumb vs. 2 finger), if delivered chest compressions were synchronized with breaths, and if chest compressions were initiated for asystole or bradycardia. We also have no way of knowing if the heart rate was measured accurately at the time chest compressions were initiated and if chest compressions were truly warranted. Also, data points pertaining to bag mask ventilation were missing for the majority of cases and when present, there was no way of determining the quality or “effectiveness” of bag mask ventilation delivered. Information on ET intubation time was missing for 214 (23%) infants, thus we do not know at what point into the resuscitation these infants were intubated. Missing data points also limited the variables that could be included in the multivariate regression model, thus substantially limiting information obtained from multivariate analysis. Another limitation was the lack of information available regarding participating centers. No information regarding number of deliveries per year, number of level 3 or level 4 NICUs, or number of private versus academic institutions was available to compare to reported rates of DR-CPR. We, therefore, do not have population data to calculate the incidence of DR-CPR in the studied cohort.

Conclusion

In this cohort of infants receiving chest compressions following delivery, recognizable prenatal risk factors, as well as resuscitation interventions associated with increased and decreased odds of achieving ROSC were identified. Failure to achieve endotracheal intubation prior to CPR was also common, with chest compressions often initiated in the first minute of the resuscitation and often prior to endotracheal intubation. Further investigations should focus on methods to improve the timing of critical resuscitation interventions, such as successful endotracheal intubation and administration of the first dose of adrenaline in order to improve DR-CPR outcomes.

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CRedit authorship contribution statement

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Conceptualization, Writing - review & editing. **Elizabeth E. Foglia:** Conceptualization, Methodology, Writing - review & editing. **Emilie Allen:** Methodology, Writing - review & editing. **Myra H. Wyckoff:** Conceptualization, Methodology, Supervision, Writing - review & editing. **Anne-Marie Guerguerian:** . **Dianne Atkins:** . **Elizabeth E. Foglia:** . **Erica Fink:** . **Javier J. Lasa:** . **Joan Roberts:** . **Jordan Duval-Arnould:** . **Melania M. Bembea:** . **Michael Gaies:** . **Monica Kleinman:** . **Punkaj Gupta:** . **Robert M. Sutton:** . **Taylor Sawyer:** .

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Appendix A. Supplementary data

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REFERENCES

- Shah PS. Extensive cardiopulmonary resuscitation for VLBW and ELBW infants: a systemic review and meta-analysis. *J Perinatol* 2009;29:655–61.
- Wyckoff MH, Aziz K, Escobedo MB, et al. Part 13: Neonatal Resuscitation 2015 American Heart Association Guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation* 2015;132:S543–60.
- Barber CA, Wyckoff MH. Use and efficacy of endotracheal versus intravenous epinephrine during neonatal cardiopulmonary resuscitation in the delivery room. *Pediatrics* 2006;118:1028–34.
- Halling C, Sparks JE, Christie L, Wyckoff MH. Efficacy of intravenous and endotracheal epinephrine during neonatal cardiopulmonary resuscitation in the delivery room. *J Pediatr* 2017;185:232–6.
- Weiner GM. *Textbook of Neonatal Resuscitation*. 7th ed. Elk Grove Village (IL): American Academy of Pediatrics and American Heart Association; 2016.
- Soraisham AS, Lodha AK, Singhal N, et al. Neonatal outcomes following extensive cardiopulmonary resuscitation in the delivery room for infants born at less than 33 weeks gestational age. *Resuscitation* 2014;85:238–43.
- Jiang S, Lyu Y, Ye XY, Monterrosa L, Shah PS, Lee SK. Intensity of delivery room resuscitation and neonatal outcomes in infants born at 33 to 36 weeks' gestation. *J Perinat* 2016;36:100–5.
- Wyckoff MH, Salhab WA, Heyne RJ, Kendrick DE, Stoll BJ, Laptook AR. Outcome of extremely low birth weight infants who received delivery room resuscitation. *J Pediatr* 2012;160:239–44.
- Downes KL, Shenassa ED, Grantz KL. Neonatal outcomes associated with placental abruption. *Am J Epidemiol* 2017;186:1319–28.
- Carbine DN, Finer NN, Knodel E, Rich W. Video recording as a means of evaluating neonatal resuscitation performance. *Pediatrics* 2000;106:654–8.
- McKinsey S, Perlman JM. Resuscitative interventions during simulated asystole deviate from the recommended timeline. *Arch Dis Child Fetal Neonatal Ed* 2016;101:F244–247.
- Cummins RO, Chamberlain D, Hazinski MF, et al. Recommended guidelines for reviewing, reporting, and conducting research on in-hospital resuscitation: the in-hospital "Utstein style". *Circulation* 1997;95:2213–39.
- Finer NN, Horbar JD, Carpenter JH. Cardiopulmonary resuscitation in the very low birth weight infant: the Vermont Oxford Network experience. *Pediatrics* 1999;104:428–34.
- Frontanes A, Garcia-Fragoso L, Garcia I, Rivera J, Valcarcel M. Outcome of very-low-birth-weight infants who received epinephrine in the delivery room. *Resuscitation* 2011;82:427–30.
- Kapadia VS, Wyckoff MH. Epinephrine use during neonatal resuscitation. *Front Pediatr* 2017;1:97.
- Andersen LW, Berg KM, Saindon BZ, et al. Time to epinephrine and survival after pediatric in-hospital cardiac arrest. *JAMA* 2015;314:802–10.
- Lin YR, Wu MH, Chen TY, et al. Time to epinephrine treatment is associated with the risk of mortality in children who achieve sustained ROSC after traumatic out-of-hospital cardiac arrest. *Crit Care* 2019;23:101, doi:<http://dx.doi.org/10.1186/s13054-019-2391-z>.
- Fukuda T, Kundo Y, Hayashida K, Sekiguchi H, Kukita I. Time to epinephrine and survival after pediatric out-of-hospital cardiac arrest. *Eur Heart J Cardiovasc Pharmacother* 2018;4:144–51.
- Wallenstein MB, Birnie KL, Arain YH, et al. Failed endotracheal intubation and adverse outcomes among extremely low birth weight infants. *J Perinat* 2016;36:112–5.
- Sauer CW, Kong JY, Voucher YP, et al. Intubation attempts increase the risk for severe intraventricular hemorrhage in preterm infants: a retrospective cohort study. *J Pediatrics* 2016;177:108–13.
- Davis PG, Dawson JA. New concepts in neonatal resuscitation. *Curr Opin Pediatr* 2012;24:147–53.
- Sing Y, Oddie S. Marked variation in delivery room management in very preterm infants. *Resuscitation* 2013;84:1558–61.