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Survival after delivery room cardiopulmonary resuscitation: A national registry study

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Abstract

Aims: Survival after delivery room cardiopulmonary resuscitation (DR-CPR) is not well characterized in full-term infants, and survival outcomes after DR-CPR have not been defined across the spectrum of gestation. The study objectives were to define gestational age (GA) specific survival following DR-CPR and to assess the association between GA and DR-CPR characteristics and survival outcomes.

Methods: Retrospective cohort study of prospectively collected data in the American Heart Association Get With the Guidelines-Resuscitation registry. Newborn infants without congenital abnormalities who received greater than 1 min of chest compressions for DR-CPR were included. GA was stratified by categorical subgroups: ≥ 36 weeks; 33–35^{6/7} weeks; 29–32^{6/7} weeks; 25–28^{6/7} weeks; 22–24^{6/7} weeks. The primary outcome was survival to hospital discharge; the secondary outcome was return of circulation (ROC).

Results: Among 1022 infants who received DR-CPR, 83% experienced ROC and 64% survived to hospital discharge. GA-stratified hospital survival rates were 83% (≥ 36 weeks), 66% (33–35 weeks), 60% (29–32 weeks), 52% (25–28 weeks), and 25% (22–24 weeks). Compared with GA ≥ 36 weeks, lower GA was independently associated with decreasing odds of survival (33–35 weeks: adjusted Odds Ratio [aOR] 0.46, 95% Confidence Interval [CI] 0.26–0.81; 29–32 weeks: aOR 0.40, 95% CI 0.23–0.69; 25–28 weeks: aOR 0.21, 95% CI 0.11–0.41; 22–24 weeks: aOR 0.06, 95% CI 0.03–0.10).

Conclusions: In this national registry of infants who received delivery room cardiopulmonary resuscitation (DR-CPR), 83% survived the event and two-thirds survived to hospital discharge. These results contribute to defining survival outcomes following DR-CPR across the continuum of gestation.

Keywords: Newborn, Cardiopulmonary resuscitation, Delivery room, Survival

Introduction

Cardiopulmonary resuscitation (CPR) is performed after birth in less than 1% of all infants,^{1,2} with a higher incidence among preterm infants.^{3–9} Because cardiac resuscitation at birth is an unpredictable event, limited information on characteristics and outcomes of delivery

room CPR (DR-CPR) exist. Bradycardia or asystole during neonatal transition typically arises from progressive acidosis and hypoxemia due to failed placental gas exchange antenatally or inadequate respiratory function immediately after birth.¹⁰ Thus, the underlying pathophysiology leading to CPR at birth differs from cardiac arrest that occurs after successful newborn transition, and characteristics of CPR in other settings may not apply to DR-CPR.

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DR-CPR in full-term infants is poorly described; most data come from single-center studies,^{1,2,11,12} with small sample sizes and limited generalizability. Multi-site neonatal networks have reported outcomes after DR-CPR within specific populations of preterm infants,^{3–9} but these focused studies do not allow for characterization of DR-CPR outcomes across the continuum of gestation within a single dataset. In addition, many analyses only assessed mortality prior to hospital discharge. This prevents an accurate characterization of how frequently DR-CPR is successful but followed by subsequent in-hospital mortality. Finally, other studies did not include infants who died prior to neonatal intensive care unit (NICU) admission,^{5,13} introducing the risk of selection bias.

The American Heart Association Get With the Guidelines Resuscitation (GWTG-R) registry is a North American, multi-site registry of in-hospital cardiac arrests. Delivery room events are captured in the registry but have not been reported to date. We undertook this study to define gestational age (GA)-specific survival outcomes following DR-CPR and to investigate the impact of GA on the characteristics and outcomes of DR-CPR.

Methods

This was a retrospective cohort study of data collected prospectively for the American Heart Association GWTG-R registry.¹⁴ GWTG-R is the only national registry of in-hospital cardiac arrests in North America. Participating hospitals voluntarily submit standardized de-identified clinical information regarding the medical history, hospital care, and outcomes of consecutive patients with in-hospital cardiac arrest using an online, interactive case report form and Patient Management Tool™ (IQVIA, Parsippany, New Jersey), in accordance with the Health Insurance Portability and Accountability Act. IQVIA is the data collection coordination center for the American Heart Association/American Stroke Association Get With The Guidelines programs.

Previous publications have described details of hospital certification, data collection and reporting, and data integrity verification for the GWTG-R registry.¹⁵ The GWTG-R program provides detailed coding instructions and requires all abstractors to pass a certifying exam prior to using the Patient Management tool. In addition, field staff work directly with sites to answer questions and provide ongoing education. Standardized software data checks assure data accuracy and completeness. GWTG-R reporting is based on the Utstein template, which was developed in older populations as a structured framework to report resuscitation practice and patient outcomes of cardiac arrest.¹⁶

Variables collected for delivery room events in the GWTG-Resuscitation registry include demographic data, maternal data, delivery details, resuscitation characteristics, and discharge status. The variables included in the case report forms have changed throughout the study period; only variables that were consistently collected in >80% of the cohort were included in this analysis. All participating institutions were required to comply with local regulatory and privacy guidelines and to secure institutional review board (IRB) approval, if required. Because local sites used the data primarily for quality improvement, sites were granted a waiver of informed consent under the common rule. The Children's Hospital of Philadelphia IRB determined that oversight of this study was not required for the analysis of deidentified data.

Inclusion and exclusion criteria

Eligible patients were newly born infants who received >1 min of chest compressions in the delivery room or delivery operating room setting from August 1, 2004 to December 31, 2016. We excluded infants with major congenital anomalies, infants with a gestational age <22 weeks at birth, and infants with missing data related to the exposure of interest (GA) or the primary outcome (survival to hospital discharge). The study dates were selected in order to generate the largest possible cohort from the initiation of consistent DR-CPR event capture in the registry.

Exposures

The primary exposure of interest was GA, stratified according to the following subgroups: ≥ 36 weeks; 33–35^{6/7} weeks; 29–32^{6/7} weeks; 25–28^{6/7} weeks; 22–24^{6/7} weeks. These groupings were chosen to be consistent with GA ranges of many studies of therapeutic hypothermia for the most mature group,^{17,18} an ongoing trial of therapeutic hypothermia for preterm infants 33–35^{6/7} weeks GA,¹⁹ and to encompass the limits of viability for the least mature group, which evolved during the study period.²⁰

The evaluated resuscitation characteristics were defined as per the GWTG-R registry. The duration of CPR was defined as the interval in minutes between the recognition of cardiac arrest and discontinuation of resuscitative efforts, either because the patient died or experienced a sustained return of circulation (ROC) without need for further chest compressions for 20 min. For infants who survived the resuscitation event, the time the chest compressions ended was documented as the *beginning* of sustained ROC. Because data for the cardiac rhythm at the initiation of CPR were not consistently captured, we utilized a 1-minute Apgar score of 0 to indicate the absence of a detectable heart rate as a dichotomous indicator of initial assessment (ie: Apgar score = 0, indicating no clinically detectable heart rate).

Outcomes

The primary outcome was survival to hospital discharge. The secondary outcome was sustained ROC, defined as return of cardiac function following cardiopulmonary arrest that lasted for a duration of at least 20 min, consistent with GWTG-R definitions.

Statistical analysis

Using Stata 15.1 (StataCorp, College Station, TX), we assessed for trends in demographic and delivery characteristics and survival outcomes across GA subgroups and across calendar years using linear regression. We examined the association between infant demographics, delivery characteristics, and resuscitation interventions on the primary outcome using chi-squared tests or Wilcoxon rank sum tests as appropriate.

We developed a multivariable logistic regression model to assess the independent association between GA and survival to hospital discharge. The model included factors that were associated with in-hospital survival with a p-value <0.2 in the bivariable analysis. Association estimates were calculated using a generalized estimating equation (GEE) model, which accounted for clustering by site. We did not include Apgar scores at 5 and 10 min in the model, as these are indicative of the infant's response to CPR. Because the duration of CPR may be associated with survival in complex ways, we performed

a sensitivity analysis utilizing the same model but excluding duration of CPR to determine whether removing this covariate substantially altered the associations of interest.

To graphically assess the GA-stratified relationship between the duration of CPR and survival to hospital discharge, fractional polynomials were fitted and the chi-squared test for deviance differences determined the shape that best fit the relationship between duration of CPR and survival.²¹ A polynomial model with an interaction term between GA stratum and the duration of CPR was fitted, adjusting for other key covariates identified in the multivariable logistic regression model. All p-values were 2-sided, with $p < 0.05$ considered statistically significant. We did not adjust for multiple comparisons in this exploratory analysis.

Results

During the study period, 1022 eligible infants in 129 contributing centers received DR-CPR (eFig. 1). There was no evidence of a significant change over time in the proportion of infants within the individual GA subgroups ($p=0.46$) or rates of survival to hospital discharge by year among DR-CPR events contributed to the registry during the study period ($p=0.97$).

Significantly more black and fewer white infants were represented in the lower GA subgroups. Infants at lower GA were also more likely to be part of multiple gestations and to be born on the weekend.

Compared with more mature infants, fewer infants in the lower GA subgroups were assigned a 1-minute Apgar score of 0 (Table 1). Vital sign monitoring prior to CPR included pulse oximetry in 189 (18%) events and electrocardiogram in 86 (8%) events.

Among all infants in this study, 844/1022 (83%) experienced ROC and 659/1022 (64%) survived to hospital discharge. Survival outcomes according to week of gestation at birth are provided in eTable 1 and eFig. 2. Lower gestational age, lower birthweight, multiple gestations, Hispanic ethnicity, weekend delivery, cesarean delivery, lower Apgar scores, adrenaline (epinephrine) administration, and longer CPR duration were associated with lower rates of survival to hospital discharge in univariable analysis (Table 2).

Decreasing GA subgroup was associated with lower rates of ROC and survival to discharge, $p < 0.001$ (Fig. 1). Gestational age-stratified rates of survival to hospital discharge were 83% (≥ 36 weeks), 66% (33–35 weeks), 60% (29–32 weeks), 52% (25–28 weeks), and 25% (22–24 weeks). After controlling for potential confounders, factors independently associated with decreased odds of survival to hospital discharge were lower GA subgroup, cesarean delivery, 1-minute Apgar score of 0, adrenaline administration during CPR, and duration of CPR. (Table 3). Removing duration of CPR from the GEE model did not substantially change most associations of interest (eTable 2).

We determined that duration of CPR had a non-linear (quadratic or U-shaped) effect on the primary outcome survival to hospital discharge. The GA-stratified predicted probabilities of survival to discharge based on duration of CPR are shown in Fig. 2.

Table 1 – Demographic and resuscitation characteristics according to gestational age subgroups.

Characteristic	≥ 36 weeks gestation (n = 439)	33–35 ^{6/7} weeks gestation (n = 103)	29–32 ^{6/7} weeks gestation (n = 142)	25–28 ^{6/7} weeks gestation (n = 207)	22–24 ^{6/7} weeks gestation (n = 131)	p Value (trend)
Birth weight, g; mean (SD)	3318 (670) [n = 424]	2522 (660) [n = 95]	1597 (475) [n = 131]	913 (374) [n = 190]	642 (264) [n = 119]	<0.001
Male	254/438 (58%)	61 (59%)	75 (53%)	107 (52%)	68 (52%)	0.07
Multiple gestation	11 (3%)	9 (9%)	7 (5%)	31 (15%)	14 (11%)	<0.001
Race						
White	283 (64%)	67 (65%)	73 (51%)	105 (51%)	62 (47%)	<0.001
Black	75 (17%)	24 (23%)	48 (34%)	64 (31%)	44 (34%)	<0.001
Asian	18 (4%)	3 (3%)	2 (1%)	10 (5%)	6 (5%)	0.78
Other	63 (14%)	9 (9%)	19 (13%)	28 (14%)	19 (15%)	0.99
Hispanic ethnicity	70 (16%)	18 (17%)	17 (12%)	41 (20%)	27 (21%)	0.19
Nighttime delivery	137 (31%)	24 (23%)	48 (34%)	63 (30%)	38 (29%)	0.87
Weekend delivery	121 (28%)	28 (27%)	50 (35%)	82 (40%)	45 (34%)	0.004
Birth complication ^a	97 (22%)	27 (26%)	53 (37%)	46 (22%)	27 (21%)	0.84
Fetal monitoring	377/401 (94%)	81/91 (89%)	118/132 (89%)	166/182 (91%)	111/118 (94%)	0.49
Cesarean section	262/436 (60%)	74/99 (75%)	115/138 (83%)	148/207 (71%)	66/127 (52%)	0.41
1-minute Apgar score = 0	142/425 (33%)	38/100 (38%)	43/131 (33%)	42/195 (22%)	15/124 (12%)	<0.001
5-minute Apgar score; median (IQR)	3 (1, 6) [n = 425]	3 (1, 5) [n = 100]	2 (1, 5) [n = 130]	2 (1, 5) [n = 195]	1 (1, 4) [n = 122]	<0.001
10-minute Apgar score; median (IQR)	5 (2, 7) [n = 120]	4 (1, 6) [n = 29]	4 (1, 7) [n = 33]	4 (1, 6) [n = 56]	3 (1, 6) [n = 28]	0.02
Adrenaline administration	175/436 (40%)	61/102 (60%)	90/141 (64%)	119/207 (57%)	84/130 (65%)	<0.001
Duration CPR, minutes; median (IQR)	6 (2, 15) [n = 384]	9 (4, 20) [n = 99]	9 (4, 20) [n = 131]	8 (3, 16) [n = 192]	10 (5, 20) [n = 113]	0.1

CPR: cardiopulmonary resuscitation; IQR: interquartile range.

Denominator given for any cell with incomplete data.

^a birth complications are placenta previa, placental abruption, cord prolapse, or shoulder dystocia.

Table 2 – Characteristics of infants who received delivery room cardiopulmonary resuscitation according to survival to hospital discharge.

Characteristic	Survived to discharge (n = 659)	Did not Survive to discharge (n = 363)	p Value
Gestational age, weeks; median (IQR)	37 (30, 39)	27 (24, 34)	<0.001
Birth weight, g; median (IQR)	2761 (1453, 3450) [n = 628]	1045 (640, 2305) [n = 331]	<0.001
Male	368/658 (56%)	197 (54%)	0.61
Multiple gestation	35 (5%)	37 (10%)	0.004
Race			0.87
White	384 (58%)	206 (57%)	
Black	160 (24%)	95 (26%)	
Asian	24 (4%)	15 (4%)	
Other	91 (14%)	47 (13%)	
Hispanic ethnicity	96 (15%)	77 (21%)	0.007
Nighttime delivery	208 (32%)	102 (28%)	0.25
Weekend delivery	192 (29%)	134 (37%)	0.01
Birth complication ^a	159 (24%)	91 (25%)	0.74
Fetal monitoring	558/604 (92%)	295/320 (92%)	0.92
Cesarean section	416/653 (64%)	249/354 (70%)	0.03
1-minute Apgar score = 0	155/643 (24%)	125/332 (38%)	<0.001
5-minute Apgar; median (IQR)	3 (1, 6) [n = 643]	1 (0, 2) [n = 329]	<0.001
10-minute Apgar; median (IQR)	6 (3, 7) [n = 172]	1 (0, 3) [n = 94]	<0.001
Adrenaline administration	235/655 (36%)	294/361 (81%)	<0.001
Duration CPR, minutes; median (IQR)	5 (2,10) [n = 584]	15 (8, 24) [n = 335]	<0.001

CPR: cardiopulmonary resuscitation; IQR: interquartile range.

Denominator is given for any cell with incomplete data.

^a Birth complication includes placenta previa, placental abruption, cord prolapse, or shoulder dystocia.

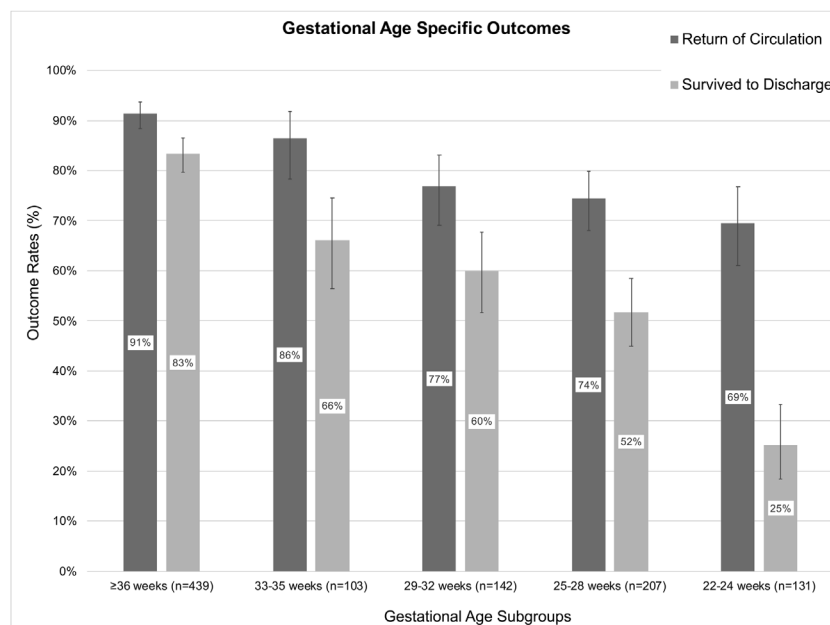


Fig. 1 – Survival outcomes with 95% confidence intervals, stratified by gestational age. Significant trend with gestational age for both outcomes, $p < 0.001$ for trend.

Discussion

DR-CPR is a high acuity, low occurrence event. In this large report of over 1000 infants who received DR-CPR in the GWTR registry, 64% of infants survived to hospital discharge following DR-CPR. Lower GA, cesarean delivery, 1-minute Apgar score of 0, adrenaline

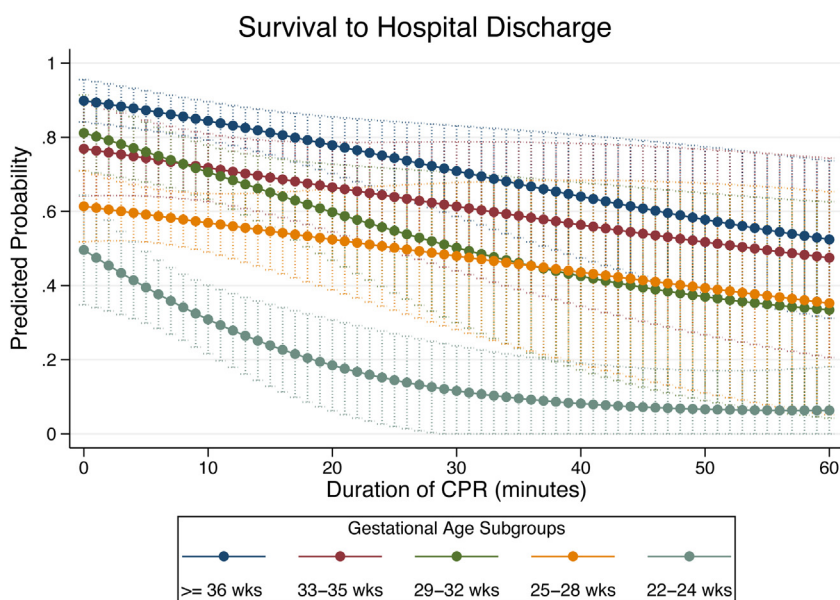
administration during CPR, and duration of CPR were associated with decreased odds of survival to hospital discharge.

To our knowledge, this is the first multi-site study to report survival outcomes following DR-CPR among infants at or greater than 36 weeks gestation. Estimates of the incidence of DR-CPR range from 1.2 to 2.4 among 1000 of live births,^{1,12} with a disproportionately higher incidence among preterm infants. Thus, even at high-volume

Table 3 – Multivariable analysis of factors associated with survival to hospital discharge following delivery room cardiopulmonary resuscitation.

Characteristic	Adjusted odds ratio	95% confidence interval	p Value
Gestational age subgroup			
≥36 weeks	Ref		
33–35 ^{6/7} weeks	0.46	0.26, 0.81	0.008
9–32 ^{6/7} weeks	0.40	0.23, 0.69	0.001
25–28 ^{6/7} weeks	0.21	0.11, 0.41	<0.001
22–24 ^{6/7} weeks	0.06	0.03, 0.10	<0.001
Hispanic ethnicity	0.60	0.29, 1.23	0.16
Multiple gestation	0.61	0.29, 1.27	0.19
Cesarean section	0.69	0.49, 0.97	0.03
Weekend delivery	0.82	0.57, 1.19	0.30
1-minute Apgar score = 0	0.51	0.35, 0.76	0.001
Adrenaline administration	0.19	0.12, 0.29	<0.001
Duration of CPR	0.97	0.95, 0.98	<0.001

GEE model adjusted for clustering by site.
CPR: cardiopulmonary resuscitation.

**Fig. 2 – Predicted probability of survival to discharge based on duration of CPR event, stratified by gestational age. Point estimate and 95% confidence intervals of the predicted probability of survival to hospital discharge for the first 60 min of resuscitation. Model adjusted for adrenaline administration, 1-minute Apgar score = 0, Cesarean section, and site. Model limited to events lasting 60 min or less, to exclude undue influence from events with CPR durations in the top 2.5% of the sample distribution.****CPR: cardiopulmonary resuscitation**

centers, DR-CPR is rarely performed in mature infants. Published single center studies of DR-CPR in populations that included late preterm and term newborns consisted of small samples ranging from 39 to 50 infants.^{1,2,11} By leveraging data collected from 129 hospitals contributing to the GWTG-R registry, we were able to define the characteristics and outcomes of DR-CPR among 439 infants at or greater than 36 weeks gestation.

Similar to other studies, we observed decreasing survival rates at lower gestational ages. In an analysis of 10 studies examining DR-CPR in very low birth weight infants, the pooled in-hospital mortality rate was 38%.²² At the lower extremes of gestation, Goel et al. reported a 43% in-hospital mortality rate among infants at 23-

25 weeks gestation who received DR-CPR.²³ In contrast to these data, 75% of infants born between 22–24 weeks gestation in the present study died before hospital discharge. There are several potential explanations for the differences in reported mortality rates among infants born at or near the limits of viability. The categorical definitions of GA subgroups differed between the studies, and the inclusion of infants born at 22 weeks gestation may contribute to the lower survival rates observed in this study. In addition, censoring brief episodes of CPR can increase observed mortality rates.²³ We excluded infants who received <1 min of CPR, as these brief episodes may be more likely to represent only transient cardiovascular compromise or CPR that was not indicated. This is consistent with

the pediatric CPR literature^{24–27} but is not uniform across neonatal reports.

Longer duration of CPR was associated with increased mortality. However, it is noteworthy that 25% of infants who survived to hospital discharge received 10 min or more of CPR. The duration of CPR after which ongoing resuscitation no longer improves the probability of intact survival has not been defined, and favorable neurologic outcomes have been reported following durations of CPR that were previously considered futile.^{12,28} In the delivery room setting, the impact of duration of CPR on neurologically intact survival is likely influenced by multiple factors such as the duration of asphyxia before birth, the presenting condition of the infant, the quality of resuscitative efforts, and post-resuscitative care.²⁹ Unfortunately, neurologic outcomes of infants in the present study are not known, as this information is not captured in the GWTG-R registry.

Additional characteristics associated with increased mortality prior to discharge included an Apgar score of 0 at 1 min and adrenaline administration. Kumar et al. also found that infants born without a detectable heart rate were less likely to survive than infants with bradycardia at birth.³⁰ Thus, it may be reasonable to account for the presence of detectable heart rate versus asystole in future studies of CPR in the delivery room setting. The association between adrenaline administration and mortality should be interpreted with caution, as there may be residual confounding by indication. In addition, because it can take 5 min or more to administer the first dose of adrenaline during a CPR event,¹¹ adrenaline administration may be an additional indicator of the duration of resuscitation.

We found significant differences in baseline and resuscitation characteristics based on GA. Racial characteristics varied across gestation, likely due to disparities in preterm birth rates that have been previously described.³¹ In addition, infants at lower GA were less likely to have a 1-minute Apgar score of 0, indicating that more mature infants who received DR-CPR may have been more severely asphyxiated at birth compared to extremely preterm infants. The American Academy of Pediatrics and American Heart Association Guidelines for Neonatal Resuscitation emphasize the importance of establishing ventilation to reverse underlying asphyxia prior to initiating chest compressions during resuscitation after birth.³² It is possible that extremely preterm infants who had a detectable heart rate after birth received CPR due to the difficulty establishing effective ventilation in this population.³³ Alternatively, it is possible that resuscitation was not initiated among extremely preterm infants with a 1-minute Apgar score of 0, due to a perception of futility in this population.^{20,34} If CPR was not performed, those events would not be captured in the GWTG-R registry. In addition, it is possible that some infants who received CPR but never demonstrated any signs of life were registered as stillbirths and not included in the registry.

This study had several limitations. GWTG-R is a voluntary QI registry and therefore represents a cohort of hospitals that choose to enter data. Only infants who received DR-CPR are included in this dataset. Thus, the incidence of DR-CPR across participating hospitals cannot be calculated. The infant and resuscitation characteristics examined were limited to variables that were consistently captured throughout the study period. Incomplete variables that would be of interest include cord pH, adrenaline dosing, and method of performing chest compressions. Factors that may influence the quality of resuscitation, such as training level of providers who performed CPR, are not available. In addition, vital

sign monitors were used prior to CPR in only a fraction of infants; we cannot distinguish whether infants required CPR or received CPR. Last, neurodevelopmental outcomes following DR-CPR are unknown, as the GWTG-R registry does not capture post-discharge information for surviving infants.

Study strengths include a multi-site dataset using prospectively gathered data. Because entry to the registry occurred at the time of CPR (as opposed to neonatal intensive care unit admission), we were able to report ROC following CPR and survival to hospital discharge for all infants who received DR-CPR. Finally, this is one of the largest datasets of infants receiving DR-CPR inclusive of all gestational ages, which made it possible to characterize survival outcomes among GA groups that are infrequently studied, to identify differences in resuscitation characteristics based on GA, and to determine the independent effect of GA on survival following DR-CPR.

Conclusions

In this report of more than 1000 newly born infants who received delivery room cardiopulmonary resuscitation in the American Heart Association GWTG-R Registry, 83% experienced return of circulation and 64% survived to hospital discharge. This study contributes to defining gestational-age specific survival outcomes following cardiopulmonary resuscitation in the delivery room setting.

Conflicts of interest

None.

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In addition to the authors Elizabeth E. Foglia MD MSCE and Taylor Sawyer DO MEd, members of the American Heart Association Get With the Guidelines- Resuscitation Pediatric Taskforce include Anne-Marie Guerguerian MD PhD FRCPC; Dianne Atkins MD; Ericka Fink MD; Javier J. Lasa MD FAAP; Joan Roberts MD; Jordan Duval-Arnould MPH DrPH; Melania M. Bembea MD MPH PhD; Michael Gaies MD MPH MSc; Monica Kleinman MD; Punkaj Gupta MBBS; Robert M. Sutton MD MSCE FAAP FCCM.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.resuscitation.2020.01.010>.

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