Intact Survival in Extremely Low Birth Weight Infants After Delivery Room Resuscitation

Neil N. Finer, MD; Thomas Tarin, BS; Yvonne E. Vaucher, MD, MPH; Keith Barrington, MB, ChB, MRCP, FRCP; and Raul Bejar, MD

ABSTRACT. Objective. None of the 20 previously reported infants weighing <750 g at birth who received cardiopulmonary resuscitation (CPR) in the delivery room (DR) survived. To clarify whether such resuscitation is futile in our center, we evaluated our experience with DR-CPR over a 4-year period.

Study Design. We retrospectively reviewed the outcomes of all inborn infants with birth weights <1000 g at University of California, San Diego Medical Center from January 1993 to December 1996. Surviving infants and matched control infants were followed for ≤40 months' adjusted age using standardized neurodevelopmental assessments.

Results. Of the infants with birth weight <1000 g born during this period, 29% (51/177) died, including 44% of those <750 g and 16% of those ≥750 g. Overall, 19 infants received DR-CPR, of whom 12 were <750 g. Of the infants who received DR-CPR, 79% (15/19) survived, including 10 of 13 infants <750 g and 5 of 6 infants ≥750 g. Of the 15 survivors, 10 were followed beyond 10 months' adjusted age (median: 28 months). At last examination, 70% were both neurologically and developmentally normal. Two infants had cerebral palsy with mild cognitive and severe motor developmental delay. Of 7 infants with birth weight <750 g, 6 had normal neurodevelopmental outcomes. The mean composite mental and motor scores of DR-CPR survivors were 93 ± 10 and 89 ± 25, respectively. No differences were found in neurologic or developmental outcome between DR-CPR survivors and control infants matched for gestational age, sex, and year of birth.

Conclusions. Our results indicate that intact survival is possible for infants weighing <750 g at birth after DR-CPR. Pediatrics 1999;104(4). URL: http://www.pediatrics.org/cgi/content/full/104/4/e40; infant, premature, cardiopulmonary resuscitation, neurodevelopment, survival, extremely low birth weight.

ABBREVIATIONS. ELBW, extremely low birth weight; DR-CPR, delivery room cardiopulmonary resuscitation; DR, delivery room; IVH, intraventricular hemorrhage; UCSD, University of California, San Diego; AA, adjusted age; NS, not significant.

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According to American Academy of Pediatrics guidelines, cardiac compressions and intratracheal or intravenous epinephrine are indicated for neonatal resuscitation when severe bradycardia does not resolve with effective positive pressure ventilation and 100% oxygen or when the infant is born with no heart rate. However, there are no specific recommendations regarding the use of such resuscitative efforts for extremely low birth weight (ELBW) or extremely immature infants.

No intact survivors have been described in published literature to date for infants with birth weight <750 g or 28 weeks' gestation who received delivery room cardiopulmonary resuscitation (DR-CPR). Despite these observations, current clinical practice includes DR-CPR for ELBW infants. To determine whether ELBW infants survive DR-CPR without significant neurodevelopmental abnormality, we reviewed the neonatal and early childhood outcomes of ELBW infants born over a 4-year period in our institution who received CPR including epinephrine and/or chest compressions in the delivery room (DR).

METHODS

A retrospective chart review was conducted for all inborn infants with birth weight ≤1000 g from January 1993 through December 1996. Information was obtained regarding the DR-CPR, Apgar scores at 1 and 5 minutes, evidence of neonatal central nervous system injury, survival to discharge, and neurodevelopmental follow-up. Infants with lethal congenital malformations or <23 weeks' gestational age were excluded. Gestational age, recorded as completed weeks, was determined from menstrual dates confirmed by early obstetrical ultrasound. If obstetrical ultrasound confirmation was unavailable, gestational age was determined using the clinical estimate of the attending neonatologist that was recorded on admission.

Infants were considered to have received CPR if chest compressions and/or intratracheal or intravenous epinephrine were used in the DR for resuscitation.

Neonatal central nervous system abnormalities, identified by echoencephalography, included intraventricular hemorrhage (IVH) (grades 0–4), ventricular dilatation (mild: 10–11.9 mm, moderate: 12.0–14.9 mm, and large: ≥15 mm), and echolucencies (small/large). White matter injury was defined as the presence of grade 4 hemorrhage, echolucencies, or ventricular dilatation unrelated to hemorrhage.

DR-CPR survivors were enrolled at discharge in the University of California, San Diego (UCSD) Infant Special Care Follow-Up Program and were followed longitudinally from 4 to 40 months' adjusted age (AA). Each DR-CPR survivor followed for >10 months' AA was matched for gestational age, sex, and year of birth with a control infant who had not received CPR at any time before discharge from UCSD and also was enrolled in the Infant Special Care Follow-Up Program and followed for >10 months' AA. Neurodevelopmental assessments included the Amiel-Tison
Neurologic Screen in the first year, a standard neurologic examination thereafter, and the Knobloch-Gesell Developmental Inventory. Composite mental (adaptive, language, and personal/social) and motor (fine and gross motor) scores were calculated from scores for individual skill areas. Head growth was assessed using the National Center for Health Statistics growth centiles.

Neuromotor outcome was categorized as normal, questionable (hypotonia, hypertonia, and asymmetry), or abnormal (cerebral palsy). Developmental outcome was considered normal if both mental and motor composite scores were ≥86, questionable if either score was 76 to 85, and abnormal if either score was ≤75. Overall neurodevelopmental outcome was considered normal if both neuromotor and developmental evaluations were normal, questionable if either evaluation was questionable, and abnormal if either evaluation was abnormal.

Statistical analyses were performed using the SPSS (8.0). Univariate comparisons were performed using Student’s t test for parametric and the Mann-Whitney U test for nonparametric comparisons for continuous variables, and the likelihood ratio χ² or Fisher’s exact test for categoric variables. Results were considered significant if the P value was <.05. Results are presented as the mean ± standard deviation unless otherwise indicated. Each child is represented once by the most recent neurodevelopmental examination during the follow-up interval.

RESULTS

There were 177 infants with birth weight <1000 g born at the UCSD Medical Center during the 4-year review period. As shown in Table 1, 11% (19/177) of the infants weighing <1000 g at birth received DR-CPR, 13 of whom had birth weight <750 g. A total of 126 infants survived to discharge, including 56% of those ≤750 g (44/79) and 84% of those ≥750 g (82/98) at birth.

DR-CPR Survivors

Of the 19 ELBW infants with birth weight <1000 g who received DR-CPR, 15 (79%) survived to discharge. The mean birth weight and gestational age of survivors were 720 ± 119 g (range: 450–935 g) and 26.3 ± 1.4 weeks (range: 24–28 weeks). Of the survivors, 9 (60%) were female, and 4 (27%) were small for gestational age. The mean Apgar scores were 2 (range: 0–5) and 5 (range: 3–9) at 1 and 5 minutes, respectively. Forty-seven percent (7/15) had normal neonatal echocardiography. Six infants had one or more of the following: grades 1 to 2 IVH, small echolucency, or mild ventricular dilatation. Only 2 survivors had evidence of severe neonatal brain injury (ie, grade 3 IVH, large echolucencies, and/or moderate/large ventricular dilatation) identified by echocardiography.

Of the 13 infants with birth weight <750 g who received DR-CPR, 10 (77%) survived as did 5 of the 6 (83%) infants weighing ≥750 g. The mean birth weight of the 10 survivors <750 g was 648 ± 86 g and the mean gestational age was 25.8 ± 1.4 weeks. Of these infants, 4 were small for gestational age, and 8 were female. One infant received chest compressions alone, 2 received both chest compressions and epinephrine, and 7 received only epinephrine. For the 5 survivors with birth weight >750 g, the mean birth weight was 875 ± 71 g, the mean gestational age was 27.2 ± 0.8 weeks; none was small for gestational age; and 1 was female. Of these infants, 2 received epinephrine alone, 1 received chest compressions alone, and 2 infants received both epinephrine and compressions.

DR-CPR Nonsurvivors

All 4 nonsurvivors were born at 24 weeks’ gestation. The mean birth weight was 700 g (range 500–950). Of the nonsurvivors, 2 received epinephrine alone, and 2 received both epinephrine and chest compressions. Apgar scores of nonsurvivors ranged from 0 to 2 at 1 minute and ranged from 0 to 4 at 5 minutes. Resuscitative efforts were discontinued in 2 infants at 10 minutes and 1 hour, respectively. In the other two cases, ventilatory support was withdrawn after discussion with the families, because of intractable respiratory failure and hypoxemia at 8 and 13 hours of age. One nonsurvivor had a grade 3 IVH by echoencephalography, another had intraventricular (grade 1), subarachnoid, and subgaleal hemorrhages on autopsy. No autopsy or echoencephalography was available for the other 2 nonsurvivors.

Neurodevelopmental Outcome

Of the 15 DR-CPR survivors, 10 (4 male and 6 female) infants were seen in follow-up beyond 10 months’ AA. Five infants were lost to follow-up, 1 of whom died shortly after discharge, before the first scheduled assessment. The median birth weight and gestational age of DR-CPR survivors followed for >10 months’ AA were 663 g (range: 440–968) and 25 weeks (range: 24–28), respectively. DR-CPR survivors and matched control infants had similar mean birth weights and length of follow-up. Seven of the 10 DR-CPR survivors and 6 of the 10 control infants weighed <750 g at birth.

As expected, median Apgar scores were lower in the DR-CPR group compared with control infants at 1 minute (2 vs 4; not significant [NS]) and at 5 minutes (5 vs 8; P = .01). DR-CPR infants were more likely to have an IVH (70% vs 10%; P = .015) and large echolucencies (20% vs 0%; NS). Ventricular dilatation occurred in 30% of DR-CPR survivors and 20% of control infants (NS). White matter injury occurred in 40% of DR-CPR survivors and in 20% of control infants (NS).

The length of follow-up was similar in DR-CPR cases and control infants, with the median AA of the last neurodevelopmental examination being 28 months (range: 11–40 months). As shown in Table 2, the neurologic, developmental, and overall outcome of DR-CPR survivors was similar to that of the matched control infants. At the most recent examination, 70% of the DR-CPR survivors were neurodevelopmentally normal, 10% had questionable neurologic or developmental outcomes, and 20% were abnormal. The 2 neurologically abnormal infants with cerebral palsy had mild cognitive and severe motor delays. Neurodevelopmental outcome was similar in DR-CPR survivors with birth weight <750 and ≥751 g. Mean head circumference centiles at last

<table>
<thead>
<tr>
<th>TABLE 1.</th>
<th>Neonatal Survival and DR-CPR in ELBW Infants</th>
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<tr>
<td>Survivors/DR-CPR</td>
<td>Survivors/No DR-CPR</td>
</tr>
<tr>
<td>All</td>
<td>15/19 (79%)</td>
</tr>
<tr>
<td>&lt;750 g</td>
<td>10/13 (77%)</td>
</tr>
<tr>
<td>≥750 g</td>
<td>5/6 (83%)</td>
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</table>
recently, Sims et al. noted that all 5 of their infants survived. However, this study lacked the power to received compressions and/or epinephrine in the DR area.

Outcome was described by Davis, who reported that these infants died in the neonatal period. A similar outcome was described by Jain et al. who reviewed the experiences of infants weighing <750 or ≥751 g at birth.

**DISCUSSION**

There are no reports to date in the published literature describing intact survival of extremely small and immature infants after DR-CPR. Lantos et al. in 1988 reported that none of the 38 infants weighing <1500 g at birth, who received CPR in the first 3 days after birth, survived. This study did not include CPR in the delivery area, probably the most frequent setting for CPR in the very low birth weight infant. Sood and Giacoia noted that 11 of 41 infants with birth weight <1500 g did survive after CPR, including all 5 of the infants who had received CPR at delivery; however, no breakdown of infant survival by weight group was provided. Jain et al. reviewed neonatal outcome after CPR from a large perinatal network in Illinois that included 81 242 mother–infant pairs over a 5-year period (1982–1986). Although most of the 10 infants with birth weight ≤750 g seemed to respond to the initial resuscitation, all of these infants died in the neonatal period. A similar outcome was described by Davis, who reported that none of the 10 infants with birth weight <751 g who received compressions and/or epinephrine in the DR survived. However, this study lacked the power to conclude that CPR was futile for such infants. More recently, Sims et al. noted that all 5 of their infants born at ≤28 weeks’ gestation, who required adrenalin and atropine at delivery, either died (3 infants) or were severely handicapped (2 infants).

In contrast to the above reports, the results of our review indicate that intact survival in early childhood is possible for very immature, ELBW infants who receive CPR in the DR. At the time of last follow-up examination, 70% seemed neurologically and developmentally normal for AA. Only 2 of the 10 DR-CPR survivors seen in follow-up had cerebral palsy. Indeed, the survival and neurodevelopmental outcome of infants weighing 500 to 750 g at birth who required DR-CPR were comparable to those of gestational age-matched control infants.

Similar to previous reports, we were unable in this retrospective chart review to document either the specific indications for chest compressions or epinephrine administration in the DR or the time course of the resuscitative efforts. During the period reviewed, parents delivering at our institution could elect to forego aggressive resuscitative efforts if the gestational age was <24 weeks, the birth weight was <500 g, and/or survival was unlikely. Therefore, it is probable that selection bias accounted for the higher survival rate of <750 g infants who received DR-CPR compared with that of <750 g infants who did not receive DR-CPR.

Our observations represent the retrospective review of a single center’s experience, with small numbers of infants who received DR-CPR, the probable inconsistent application of DR-CPR and selection bias in the use of it, and incomplete, short-term follow-up, all of which are significant potential shortcomings and limit generalizability of our findings. Retrospective and prospective evaluation of larger datasets is required to confirm our observations and to develop recommendations for the use of CPR in the DR resuscitation of the <1000 g birth weight infant. Nevertheless, it does seem that intact early childhood outcome is possible after DR-CPR and that this intervention is not necessarily futile. Decisions regarding the application of DR-CPR for the ELBW infant should be based on individual unit experiences.

**REFERENCES**


**Table 2.** Neuromotor and Developmental Outcome

<table>
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<tr>
<th></th>
<th>Neuromotor Outcome</th>
<th>Developmental Outcome</th>
<th>Neurodevelopmental Outcome</th>
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<tbody>
<tr>
<td></td>
<td>Normal</td>
<td>Questionable</td>
<td>Abnormal</td>
</tr>
<tr>
<td>DR-CPR (n = 10)</td>
<td>7</td>
<td>1</td>
<td>2</td>
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<tr>
<td>Control (n = 10)</td>
<td>7</td>
<td>3</td>
<td>0</td>
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</table>

**Table 3.** Developmental Scores at Last Examination (Median AA 28 Months)

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<tr>
<th></th>
<th>Composite Mental</th>
<th>Composite Motor</th>
<th>Adaptive</th>
<th>Language</th>
<th>Personal/Social</th>
<th>Fine Motor</th>
<th>Gross Motor</th>
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<tbody>
<tr>
<td>DR-CPR</td>
<td>93 ± 10</td>
<td>89 ± 25</td>
<td>90 ± 18</td>
<td>90 ± 16</td>
<td>93 ± 16</td>
<td>88 ± 21</td>
<td>90 ± 32</td>
</tr>
<tr>
<td>Control</td>
<td>88 ± 13</td>
<td>93 ± 15</td>
<td>90 ± 11</td>
<td>80 ± 18</td>
<td>93 ± 13</td>
<td>92 ± 15</td>
<td>94 ± 16</td>
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