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Apgar Scores at 10 Minutes and Outcomes in Term and Late Preterm Neonates with Hypoxic-Ischemic Encephalopathy in the Cooling Era

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Abstract

Objective—To determine the short-term outcomes (abnormal brain magnetic resonance imaging [MRI]/death) in infants born with a 10-minute Apgar score of 0 who received therapeutic hypothermia and compare them with infants with higher scores.

Study Design—This is a retrospective review of 293 neonates (gestational age ≥ 35 weeks) born between November 2006 and October 2015 admitted with hypoxic-ischemic encephalopathy who received therapeutic hypothermia. Results of brain MRIs were assessed by the basal ganglia/watershed scoring system. Short-term outcomes were compared between infants with Apgar scores of 0, 1 to 4, and ≥5 at 10 minutes.

Results—Eight of 17 infants (47%) with an Apgar of 0 at 10 minutes survived, having 4 (24%) without abnormalities on the brain MRI and 7 (41%) without severe abnormalities. There was no significant difference in the combined outcomes of “death/abnormal MRI” and “death/severe abnormalities on the MRI” between infants with Apgar scores of 0 and 1 to 4. Follow-up data were available for six of eight surviving infants, and none had moderate or severe neurodevelopmental impairment.

Conclusion—In the cooling era, 47% of infants with no audible heart rate at 10 minutes and who were admitted to the neonatal intensive care unit survived; 24% without abnormalities on the brain MRI and 41% without severe abnormalities.

Keywords

Apgar 0; neonatal encephalopathy; hypothermia; outcomes

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Conflict of Interest

None.

Apgar score is a widely utilized tool in neonates to describe an infant's condition immediately after birth. Moreover, it helps physicians to drive the resuscitation process in the delivery room. Apgar score was first introduced in 1952 by an American anesthesiologist named Virginia Apgar. Her intent was to establish a rapid "grading" system that would provide an objective assessment of the neonatal resuscitation process.[1] Her initial work focused on a 1-minute score and was later extended to 5 minutes of life.[2] Standard practice today includes assigning Apgar scores at 1 minute and 5 minutes after birth for all infants and at 5-minute intervals thereafter until 20 minutes for infants with a score of less than 7.[3]

The current guidelines from the International Liaison Committee on Resuscitation (ILCOR), the American Heart Association (AHA), and the Neonatal Resuscitation Program (NRP) suggest that in infants with an Apgar score of 0 after 10 minutes of resuscitation, if the heart rate remains undetectable, it may be reasonable to stop resuscitative efforts.[4–6] However, the decision to continue or discontinue should be individualized.[4–7] This recommendation is based on small observational studies that included both preterm and term infants born in the 1980s and 1990s.[8–10] Since that time, therapeutic hypothermia has helped improve the survival and neurodevelopmental outcomes of infants with hypoxic-ischemic encephalopathy (HIE).[11] The resuscitation techniques and the supportive measures in neonates with HIE have also improved over time.[4,12] There are conflicting data on the survival and outcomes of neonates with an Apgar score of 0 at 10 minutes in the cooling era.[13–15] The neurodevelopmental outcomes in neonates with HIE correlate with abnormalities on brain magnetic resonance imaging (MRI) performed during the neonatal period.[16–18] The primary objective of this study was to determine survival without abnormalities on brain MRI in late preterm and term neonates (≥35 weeks of gestation) with no signs of life at 10 minutes of age (Apgar 0 at 10 minutes) who received therapeutic hypothermia. We also sought to compare the number of infants who survived with abnormalities on brain MRI between the groups with Apgar scores of 0, 1 to 4, and ≥ 5 at 10 minutes of life.

Materials and Methods

This is a retrospective observational study of term and late preterm neonates (≥ 35 weeks of gestation at birth) born between November 2006 and October 2015 who were admitted to the level III neonatal intensive care unit (NICU) at Thomas Jefferson University Hospital in Philadelphia, PA and received therapeutic hypothermia for HIE. The Institutional Review Committee at Thomas Jefferson University Hospital approved this study. The infants were identified from a neonatal database (Neodata, Isoprime Corporation, Lisle, IL). The clinical details of infants admitted to our NICUs are routinely entered into this database by trained staff members including: neonatologists, residents, pediatric hospitalists, neonatal fellows, and neonatal nurse practitioners. Relevant demographic, clinical, laboratory, and radiological data were collected from the database and medical records. Diagnosis of HIE was established by the presence of a peripartum event(s), a significant metabolic acidosis of the umbilical cord and/or neonatal blood gas, and clinical signs of neonatal encephalopathy as outlined by the modified Sarnat scoring system.[19] All included infants were started on therapeutic hypothermia within 6 hours after birth. Infants received therapeutic hypothermia via selective head cooling or whole body cooling for a duration of 72 hours unless they died before that time. Our medical team adopted and utilized protocols derived from the neonatal

hypothermia trials.[20,21] All team members were adherent to established therapeutic hypothermia guidelines. The rest of the care provided was considered standard at the time and was based on medical team discretion. A brain MRI was performed in surviving infants after 7 days of life. A blinded neuroradiologist (K.T.) reviewed all MRIs and scored them by the basal ganglia/watershed (BG/W)scoring system.[22] The scores in the BG/W scoring system ranges between 0 and 4 (0–normal; 1–abnormal signal in basal ganglia or thalamus; 2–abnormal signal in cortex; 3–abnormal signal in cortex and basal ganglia or thalamus; and 4–abnormal signal in entire cortex and basal nuclei). In a study by Twomey et al, the mean BG/W score for infants with favorable neurodevelopmental outcome at 2 years was 0.60 (range, 0–2) and infants with unfavorable outcome was 2.27 (range, 1–4).[23] Severe abnormality in the MRI was defined as a BG/W score of 3 or 4. An electroencephalogram (EEG) was performed before discharge or before making a decision to withdraw support and was defined as abnormal based on the neurologist's report.

In a secondary analysis of infants enrolled in the National Institute of Child Health and Human Development hypothermia trial, survival without moderate-to-severe disability was higher in infants with 10-minute Apgar score of 5 or higher.[24] Based on this study, infants were divided into three groups based on their Apgar scores at 10 minutes: Apgar scores of 0 (Apgar 0), between 1 and 4 (Apgar 1–4), and 5 or more (Apgar ≥ 5). We defined two composite primary outcomes as: death or abnormal MRI and death or severe abnormalities on MRI. In addition, predetermined secondary outcomes included: hypotension requiring pressors, need for mechanical ventilation (MV), duration of MV, days to room air, abnormal EEG, and length of hospital stay. The diagnosis of hypotension was made by the medical team taking care of the infant based on the mean arterial blood pressure in mm Hg (<gestational age in weeks), perfusion, urine output, and laboratory values (worsening metabolic acidosis and serum lactate). Dopamine and dobutamine were used as pressors.

The long-term follow-up data on infants with an Apgar score of 0 at 10 minutes were collected if they had seen a pediatric neurologist or developmental psychologist. The pediatric neurologist evaluated infants using the Denver Developmental Screening Test and the developmental psychologist used the Bayley Scale of Infant Development (III) or Wechsler Preschool Primary Scale of Intelligence, third and fourth editions.

Demographic data, clinical characteristics, and primary and secondary outcomes were compared among the three groups. Statistical analysis was performed using the Sigma Stat 3.1 for Windows statistical package (Systat Software, Inc., Point Richmond, CA). The three groups were compared using analysis of variance for continuous variables with a post hoc pairwise comparison of groups using a Tukey/Dunn's test. For categorical data, analysis was performed by chi-square and an extended Fisher's exact test using 3 × 2 contingency tables with a pairwise comparison of groups by 2 × 2 contingency tables. Statistical significance was attributed to a p-value less than 0.05. Sample size calculation was not performed as this is a retrospective observational study. Therapeutic hypothermia was started at our institution in late 2006. Every term and late preterm infants (≥35 weeks of gestation) with HIE admitted to the NICU who received therapeutic hypothermia at our institution was included in the analysis.

Results

A total of 293 infants met the inclusion criteria. Seventeen infants (5.8%) had an Apgar score of 0 at 10 minutes, 109 infants (37.2%) had a score of 1 to 4, and 167 infants (57%) had a score of ≥5. Baseline characteristics comparing the three assigned groups are shown in ►Table 1. There was no significant difference in birth weight, gestational age, and other baseline demographics between the groups except that more infants were born by cesarean section in the Apgar 0 group (►Table 1). More than 80% of infants in each assigned group were outborn and transferred for therapeutic hypothermia. Cord blood pH was lower and base deficit was higher in infants in the Apgar 0 group (►Table 2). Similarly, more infants in the Apgar 0 group received chest compressions, epinephrine, and fluid bolus compared with the Apgar 1 to 4 and Apgar ≥ 5 groups. The number of infants with Sarnat stage 3 HIE was also higher in the Apgar 0 group. The median age of performing MRI was 9 days (interquartile range: 7–12 days).

Eight out of 17 infants (47%) with an Apgar score of 0 at 10 minutes survived. All eight infants who survived had an MRI, and four out of nine infants who died had an MRI. Of the infants who died, MRI was performed on day 1 in one infant, day 6 on two infants, and day 7 on one infant. The infants died between days 3 and 32. Five out of nine infants who died had sentinel events (abruption of placenta). Autopsy was performed in three out of the nine infants who died, and all showed global anoxic ischemic neuronal injury. Seven out of 17 (41%) infants with an Apgar score of 0 at 10 minutes survived without severe abnormalities on MRI and 4 infants (24%) survived with normal brain MRI (►Table 3). There was no significant difference in the primary outcomes of death or abnormal MRI and death with severe abnormalities on MRI between the Apgar 0 and Apgar 1 to 4 groups. Survival without abnormalities on an MRI was significantly higher in infants with an Apgar score of ≥5 at 10 minutes.

A higher proportion of infants with asystole at 10 minutes received inotropes compared with the other two groups (►Table 4). However, there was no significant difference in the number of infants who required MV, the duration of MV, days to room air, and the length of hospitalization for infants in the Apgar 0 group compared with the Apgar 1 to 4 group. Moreover, the number of infants with abnormal EEG at discharge was similar in those two groups. All secondary outcomes were better in infants with Apgar scores of ≥ 5 at 10 minutes. A total of 274 infants (93.5%) were monitored on amplitude-integrated EEG (aEEG), and 246 infants (89.8%) had an abnormal aEEG. All infants with a 10-minute Apgar score of 0 had an abnormal aEEG.

►Table 5 depicts 17 infants with an Apgar score of 0 at 10 minutes in our cohort. The median time of first HR detection was 18 minutes (range, 11–27 minutes). In four neonates (23%), the first HR was detected at >20 minutes. Two of those infants survived and had normal neurodevelopmental outcomes at 24 months. Additionally, we were able to obtain results of long-term follow-up for six out of eight surviving infants. One infant was lost to follow-up and another died at 11 months of age. The infant who died at 11 months of age was diagnosed with biliary atresia. The cause of death was liver failure following the Kasai procedure. Age of follow-up for surviving infants ranged between 4 months and 5 years.

Each patient was evaluated by a developmental psychologist, pediatric neurologist, or both. For all six patients, assessments of cognitive, language, fine motor, and gross motor development ranged from normal to mild delay. None of six surviving infants had a moderate or severe delay in any area assessed. Seven surviving infants had an abnormal EEG at discharge. No follow-up data are available on two infants, and the remaining five infants had a normal (four infants) or mildly abnormal (one infant) neurodevelopmental outcome at follow-up.

Discussion

The current guidelines suggest that it may be reasonable to stop resuscitative efforts in infants with an Apgar score of 0 after 10 minutes of resuscitation.[4–6] Our study demonstrates that ~41% of infants with an Apgar score of 0 after 10 minutes of resuscitation efforts who received therapeutic hypothermia survived without severe abnormalities on brain MRI. Moreover, there was no difference in survival without abnormal brain MRI between neonates with an Apgar score of 0 and an Apgar score of 1 to 4 at 10 minutes. None of the six infants who survived and were followed up had moderate or severe abnormalities on neurological or neurodevelopmental assessment between 4 and 24 months.

The decision to discontinue resuscitation in neonates at birth represents a challenging problem for clinicians. The recommendation to discontinue resuscitation in neonates at birth has changed on several occasions. Earlier NRP guidelines suggested that discontinuation of resuscitative efforts was permissible after 15 minutes of asystole if spontaneous circulation had not been restored.[25] The most recent ILCOR, AHA, and NRP guidelines suggest that in infants with an Apgar score of 0 after 10 minutes of resuscitation, if the heart rate remains undetectable, it may be reasonable to stop resuscitation; however, the decision to continue or discontinue resuscitative efforts should be individualized.[4–6] Variables to be considered may include whether the resuscitation was considered to be optimal, availability of advance neonatal care, such as therapeutic hypothermia, specific circumstances before delivery (e.g., known timing of insult), and wishes expressed by the family.[5,6] The rationale for current resuscitation guidelines was derived from several small case series of preterm and term neonates born between 1982 and 1999. Jain et al reported death of 57 out of 58 term and preterm infants (gestational age at birth ≥ 26 weeks) with an Apgar score of 0 at ≥ 10 minutes of life.[9] The only surviving infant in the series was diagnosed with cerebral palsy. Two other small case series reported similar rates of death and abnormal neurodevelopmental outcomes in late preterm and term infants (36–42 weeks of gestation) and preterm and term infants (mean gestational age at birth, 32 weeks).[8,10] Of note, these case series took place at a time when therapeutic hypothermia was not available. Moreover, the resuscitation techniques and supportive measures in neonates with HIE have also improved over time, including a change in the technique of chest compressions, the use of intravenous epinephrine, limiting oxygen use during and after resuscitation, inhaled nitric oxide for pulmonary hypertension, and avoidance of hypocarbia.[4,26] In recent case series, only Sarkar et al have reported uniformly poor outcomes in their cohort of 12 infants with Apgar score of 0 at 10 minutes who received therapeutic hypothermia.[13] Others have reported better outcomes of late preterm and term neonates with an Apgar score of 0 at 10 minutes. Natarajan et al reported 20.8% survivors without moderate-to-severe disability at 6

to 7 years of age in infants with asystole at 10 minutes of life.[14] However, only 13 out of 24 infants in their study received therapeutic hypothermia. A review of four randomized controlled trials and an observational study done by Kasdorf et al found 27% survival at 18 to 24 months without moderate-to-severe neurodevelopmental outcomes with optimal resuscitation followed by therapeutic hypothermia; 21% of infants in their cohort without therapeutic hypothermia also survived without moderate-to-severe neurodevelopment impairment.[15] Shah et al reported that 30.7% (4/13) of infants with a 10-minute Apgar score of 0 who survived to reach the NICU had normal scores on developmental assessment at 1 to 2 years.[27] Two of the 13 infants in their series did not receive therapeutic hypothermia and both died. Most recently, Sproat et al reported survival and long-term outcomes of all infants born with no heart rate at 10 minutes for whom resuscitation was attempted in a tertiary referral center.[28] In their cohort, 7 out of 13 term and late preterm (≥ 35 weeks) neonates survived, and 5 out of 6 infants who had follow-up at 2 years had normal neurodevelopmental outcome (1 lost to follow-up). Ours is a larger case series of infants with an Apgar score of 0 at 10 minutes who received therapeutic hypothermia. Our report adds to the existing evidence that the short- and long-term outcomes of infants with an Apgar score of 0 at 10 minutes who survived to reach the NICU are not universally poor. Support was withdrawn in 7 out of 9 infants who died in the Apgar 0 group and 7 out of 10 infants who died in the Apgar 1 to 4 group. The decision to withdraw support on each infant in both groups was based on the clinical examination, EEG findings, MRI results, and parent's wishes. Our data indicate that an Apgar score of 0 at 10 minutes did not influence the withdrawal of the care.

In our review, we found that 41% of infants with Apgar score of 0 at 10 minutes survived without severe abnormalities on the brain MRIs. The combined rates of death and abnormal MRI were similar in infants with an Apgar score of 0 and an Apgar score of 1 to 4 at 10 minutes. It is possible that the lack of difference in the primary outcome could be due to the small sample size in the Apgar score 0 group. Laptook et al also reported the primary outcomes of death or moderate/severe disability at 18 to 24 months in neonates with Apgar scores of 0 was similar to the infants with Apgar scores of 1 or 2.[24] Our findings and the recent reports of improved survival in neonates with no HR at 10 minutes of life support the current AHA and NRP guidelines which state that the availability of therapeutic hypothermia and consideration of completeness and efficacy of resuscitation may be used to guide the duration of resuscitation. However, as therapeutic hypothermia is a standard of care for neonates with moderate-to-severe HIE in the United States, the AHA and NRP may consider revising the guidelines to extend the resuscitation efforts beyond 10 minutes for every late preterm and term neonates. If the neonates are successfully resuscitated, optimal care including therapeutic hypothermia can be provided. A later consideration of withdrawing life-sustaining support can be offered if an infant meets the criteria for brain death or has severe abnormalities on brain MRI. There is no ethical difference between withholding and withdrawing life-sustaining treatment.[29]

Our study adds to the current literature on survival and outcomes in term and late preterm neonates with an Apgar score of 0 at 10 minutes who received therapeutic hypothermia. However, we recognize several limitations of this report. This is a retrospective observational study from a single center. The primary objective was to determine the short-

term outcome of death and abnormal MRI. However, an abnormal MRI correlates with long-term outcomes in infants with HIE. Moreover, we reported limited data on long-term outcomes in neonates with Apgar score of 0 at 10 minutes. The age of follow-up of surviving infants was wide and the tests used to evaluate neurodevelopmental outcome were not always the same. The improved outcomes in neonates with an Apgar score of 0 could be overestimated as we do not have data on infants who had an Apgar score of 0 at 10 minutes and died in the delivery room. However, Sproat et al recently reported similar improved outcomes in term and late preterm infants on all neonates born with no heart rate at 10 minutes of age where resuscitation was attempted in a tertiary referral center.[28] As most infants in our cohort were outborn, it is difficult to determine if every neonate received effective resuscitation for 10 minutes. However, all referring hospitals are staffed by trained resuscitators. There is also a concern about the reliability of heart rate readings in the delivery room. A majority of the hospitals utilized auscultation alone to detect heart rate. There is a potential that neonates with asystole at 10 minutes had a low heart rate that was not appreciated by the auscultator. The number of infants with a 10-minute Apgar score of 0 is small, and it is possible that the difference in outcomes of infants with Apgar of 1 to 4 would have been significant if more infants were included in the Apgar 0 group. There are also several strengths to this study. Our cohort included only late preterm and term infants (≥ 35 weeks of gestation), and every neonate received therapeutic hypothermia with standardized care and infants were born in a more recent time frame (between 2006 and 2015). We were also able to limit the variability in MRI scoring by using a single neuroradiologist who was blinded to the infants' Apgar scores and clinical outcomes.

In conclusion, our data indicate that in the cooling era, a significant number of infants with no audible HR at 10 minutes, who were admitted to the NICU, survived without severe abnormalities on brain MRI. None of the six surviving infants who had follow-up data developed moderate or severe neurodevelopmental impairment. Our data also suggest that the survival without an abnormal MRI may be similar in infants with an Apgar score of 0 or 1 to 4 at 10 minutes. This study adds to the growing literature on improved disability-free survival of term and late preterm infants who had no signs of life at 10 minutes of age. Our study and the pooled data can potentially help the AHA and NRP in determining future recommendations for the duration of resuscitation in term and late preterm neonates with no signs of life after 10 minutes of effective resuscitation.

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Table 1

The demographics and baseline clinical characteristics in three groups (n = 293) (mean ± SD)

	Apgar 0 (n = 17)	**Apgar1–4 (n = 109)**	**Apgar ≥ 5 (n = 167)**
Birth weight (kg)	3.2 ± 0.70	3.24 ± 0.65	3.2 ± 0.54
Gestational age (wk)	38 ± 2	39 ± 1.8	39 ± 1.8
Male gender, n (%)	8(47)	48 (44)	89 (53.3)
Caucasian race, n (%)	10 (59)	43 (39)	59 (35)
Maternal age (y)	29.6 ± 6	27.4 ± 7	28.1 ± 5
Multiple gestations, n (%)	0(0)	1 (0.9)	6 (3.6)
Outborn, n (%)	15 (88)	101 (93)	136 (81)
Chorioamnionitis, n (%)	1 (5.9)	12(11)	11 (6.6)
Meconium stained amniotic fluid, n (%)	6(35.3)	28 (25.7)	51 (30.5)
C-section, n (%)	16 (94.1)	84 (77.1)	98 (58.7)[a]

Abbreviation: SD, standard deviation.

[a] $p < 0.05$ between Apgar 0 and Apgar ≥5.

Table 2

Resuscitation efforts, cord blood gases, and immediate outcomes

	Apgar 0 (*n* = 17)	**Apgar1–4 (*n* = 109)**	**Apgar ≥ 5 (*n* = 167)**
5-min Apgar (med, range)	0(0)	2 (1 –2)[a]	5 (4–6)[b,c]
10-min Apgar (med, range)	0(0)	3 (2–4)[a]	6 (6–7)[b,c]
Cord blood pH (mean ± SD)	6.78 ± 0.16	6.91 ± 0.22[a]	6.99 ± 0.18[b,c]
Base deficit (med, IQR)	25 (20.7–29.5)	15 (10.3–21.5)	11 (7.5– 17)[b]
Positive pressure ventilation *n* (%)	17 (100)	109 (100)	152 (91)[c]
Intubation, *n* (%)	17 (100)	107 (98)	107 (64.1)[b,c]
Chest compressions, *n* (%)	17 (100)	62 (56.9)[a]	27 (16.2)[b,c]
Epinephrine given, *n* (%)	17 (100)	46 (42.2)[a]	11 (6.6)[b,c]
Fluid bolus, *n* (%)	14 (82.4)	45 (41.2)[a]	36 (21.6)[b,c]
Sarnat stage 3, *n* (%)	11 (58.8)	31 (28.4)[a]	14 (8.4)[b,c]
Seizures before cooling, *n* (%)	8(47)	53 (49)	43 (26)[c]

Abbreviations: IQR, interquartile range; SD, standard deviations.

[a] $p < 0.05$ between Apgar 0 and Apgar 1 to 4.

[b] $p < 0.05$ between Apgar 0 and Apgar ≥5.

[c] $p < 0.05$ between Apgar 1 to 4 and Apgar ≥5.

Table 3

Primary outcomes (death or abnormal MRI)

	Apgar 0 (*n* = 17)	**Apgar1–4 (*n* = 109)**	**Apgar ≥ 5 (*n* = 167)**
Death or abnormal MRI, *n* (%)	13 (76.5)	61 (56.0)	58 (34.7)[a,b]
Death or severe abnormalities on MRI, *n* (%)	10 (59)	36 (33)	26 (16)[a,b]
Death, *n* (%)	9 (52.9)	10 (9.2)[c]	8 (4.8)[a]
Abnormal MRI, *n* (%)	8/12 (67)	43/107 (40)	52/161 (32)[a]
Severely abnormal MRI, *n* (%)	5/12(42)	30/107 (28)	20/161 (12)[a,b]
Survived with normal MRI, *n* (%)	4(24)	48 (40)	109 (65)[a,b]

Abbreviation: MRI, magnetic resonance imaging.

[a] $p < 0.05$ between Apgar 0 and Apgar ≥5.

[b] $p < 0.05$ between Apgar 1 to 4 and Apgar ≥5.

[c] $p < 0.05$ between Apgar 0 and Apgar 1 to 4.

Table 4

Secondary outcomes in three groups

	Apgar 0 (*n* = 17)	**Apgar1–4 (*n* = 109)**	**Apgar ≥ 5 (*n* = 167)**
Hypotension requiring pressors, *n* (%)	12 (70.6)	37 (33.9)[a]	44 (26.3)[b]
Required MV, *n* (%)	17 (100)	95 (87.2)	109 (65.3)[b,c]
Days on MV, *n* (med, IQR)	7(5–13)	8.4 (2–9)	2 (0–5)[b,c]
Days to room air, *n* (med, IQR)	9 (6–19)	10 (5–18)	5 (1 –11)[c]
Abnormal EEG, *n* (%)	14 (82.4)	69 (63.3)	103 (61.7)[b]
Length of hospitalization (med, IQR)	17 (7–26)	19.5 (11–37.5)	13 (11–21)

Abbreviations: EEG, electroencephalogram; IQR, interquartile range; MV, mechanical ventilation.

[a] $p < 0.05$ between Apgar 0 and Apgar 1 to 4.

[b] $p < 0.05$ between Apgar 0 and Apgar ≥5.

[c] $p < 0.05$ between Apgar 1 to 4 and Apgar ≥5.

Table 5

Initial characteristics and long-term outcomes of patients with 0 Apgar score at 10 minutes

Pt. no.	GA (wk)	HR detected (min)	Cord gas pH	Sarnat	EEC	MRI BC/W scoring	Outcome	Neurodevelopmental outcome age, assessment (cognitive/ language/motor)
1	37	18	Not recorded	3	Excessively low amplitude and discontinuous consistent with diffuse cerebral dysfunction	4	Withdrawal of care	NA
2	40	19	6.7	2	Excessively discontinuous, extended periods of burst suppression > 30 s—consistent with severe dysmaturity, no seizures	4	Survived to discharge	Lost to follow-up
3	41	27	Not recorded	3	Excessively low amplitude, no definitive cerebral activity	4	Withdrawal of care	NA
4	37	15	6.78	3	No brain activity	3	Withdrawal of care	NA
5	36	14	6.2	3	No cerebral activity, low amplitude attenuation	2	Withdrawal of care	NA
6	36	25	7.15	3	Focal sharp waves/spikes right greater than left parietooccipital	2	Survived to discharge	*13 months assessed with BSID (III) by developmental psychologist* Cognitive: 100 (50%) Language: 97 (42%) Motor: 103 (58%) *32 months assessed with BSID (III) by developmental psychologist* Cognitive: 90 (25%) Language: 83 (13%) Motor: 88 (21%)
7	37	15	6.63	2	Normal	2	Survived to discharge	*3 years assessed with Bayley Scales of Infant Development, third edition by developmental psychologist* Cognitive: low average Language: delayed Motor: average *5 years assessed with Wechsler Preschool Primary Scale of Intelligence, fourth edition by developmental psychologist* Verbal comprehension index: 81 (10%) Visual spatial index: 78 (7%) Fluid reasoning index: 111 (77%) Working memory index: 67 (1%) Processing speed index: 97 (42%) Full scale IQ: 80 (9%) *On the Bracken Basic Concept Scale, third edition (receptive measure of children's comprehension of basic educational concepts)* Standard score = 104 (61%)
8	41	12	Not recorded	2	Burst suppression, breakthrough seizures	1	Survived to discharge	Deceased at 11 months of age due to hepatic failure
9	36	12	6.77	2–3	Nonspecific focal abnormality left temporal region	0	Survived to discharge	*13 months assessed with BSID (III) by developmental psychologist* Cognitive composite score = 105 (63%) Language composite score = 100 (50%) Motor composite score = 88 (21%) *5 years assessed with the Wechsler Preschool and Primary Scale of Intelligence, third edition by developmental psychologist* Verbal score = 83 (13%) Performance score = 93 (31%) Processing speed score = 85 (16%) Full scale score = 86 (18%) *On the Bracken Basic Concept Scale, third edition (receptive*

Pt. no.	GA (wk)	HR detected (min)	Cord gas pH	Sarnat	EEC	MRI BC/W scoring	Outcome	Neurodevelopmental outcome age, assessment (cognitive/ language/motor)
								measure of children's comprehension of basic educational concepts) Composite score = 90 (25%) average
10	38	20	6.5	2–3	Discontinuous, excessive T3 sharp waves	0	Survived to discharge	*4 months assessed with Denver by pediatric neurologist* Cognitive: average Language: average Motor: mild delayed, spasticity noted
11	41	26	6.8	3	Excessively discontinuous; low amplitude	0	Survived to discharge	*12 months assessed with BSID (III) by developmental psychologist* Cognitive score: 95 (37%) Language score: 94 (34%) Motor score: 94 (34%) *3 years assessed with the Bayley Scales of Infant Development, third edition by developmental psychologist* Cognitive: average Language: average Motor: average Behavioral: normal
12	41	13	7	2	Excessively discontinuous, sharp wave focus T3 and T4, positive temporal sharp waves; may represent diffuse cerebral dysfunction	0	Survived to discharge	*6.5 months assessed with Denver by pediatric neurologist* Cognitive: normal Language: average Motor: average
13	40	20	6.87	2	Excessively low amplitude, excessively discontinuous, multiple electrographic seizures onset from left and right hemispheres. Diffuse cerebral dysfunction	Not done	Withdrawal of care	NA
14	36	11	7.08	2	No brain activity	Not done	Withdrawal of care	NA
15	37	22	6.8	3	Not done	Not done	Withdrawal of care	NA
16	38	20	6.8	3	Not done	Not done	Deceased	NA
17	40	20	6.77	3	Severe diffuse suppression with periods of absent or near absent activity—severe diffuse cortical dysfunction	Not done	Deceased	NA

Abbreviations: BG/W, basal ganglia/watershed; BSID, Bayley Scale of Infant Development; EEG, electroencephalogram; GA, gestational age; HR, heart rate; IQR, interquartile range; MRI, magnetic resonance imaging; NA, not available; Pt., patient.