

Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1. Entire cohort patient characteristics

| Characteristics | Overall n=1693 n (%) | Excluded n=1312 n (%) | Study Population n=381 n (%) | P value |
|--|----------------------------|-----------------------------|------------------------------------|---------|
| GA, median [IQR] in weeks | 39 [38,40] | 39 [38,40] | 39 [38,40] | 0.22 |
| BW, median [IQR] in grams | 3295 [2930,3700] | 3290 [2920,3686] | 3314 [2950,3788] | 0.11 |
| Female | 712 (42.1) | 550 (41.9) | 162 (42.5) | 0.86 |
| Maternal Race | | | | |
| White | 1033 (61.0) | 796 (60.7) | 237 (62.2) | 0.63 |
| Black | 364 (21.5) | 285 (21.7) | 79 (20.7) | 0.72 |
| Other | 232 (13.7) | 174 (13.3) | 58 (15.2) | 0.35 |
| Unknown | 64 (3.8) | 57 (4.3) | 7 (1.8) | 0.022 |
| Hispanic | 269 (15.9) | 206 (15.7) | 63 (16.5) | 0.88 |
| Birth location | | | | |
| Birthing Center, not hospital | 8 (0.5) | 6 (0.5) | 2 (0.5) | 0.99 |
| Home | 35 (2.1) | 28 (2.1) | 7 (1.8) | 0.99 |
| Hospital | 1650 (97.5) | 1278 (97.4) | 372 (97.6) | 0.99 |
| Delivery type | | | | |
| Vaginal, non-operative | 461 (27.2) | 354 (27.0) | 107 (28.1) | 0.69 |
| Vaginal, operative | 170 (10.0) | 133 (10.1) | 37 (9.7) | 0.85 |
| Cesarean | 1059 (62.6) | 822 (62.7) | 237 (62.2) | 0.90 |
| APGAR @10 min ≤5 | 461 (27.2) | 354 (27.0) | 107 (28.1) | 0.69 |
| Presenting pH <7 | 235 (13.9) | 153 (11.7) | 82 (21.5) | <0.001 |
| Cord gas BD (or 1st hr gas), median [IQR] | 7 [6.8,7.2] | 7 [6.9,7.1] | 7 [6.8,7.2] | 0.45 |
| Perinatal sentinel event | | | | |
| Nuchal Cord | 312 (18.4) | 240 (18.3) | 72 (19.0) | 0.82 |
| Cord Prolapse | 59 (3.5) | 44 (3.4) | 15 (3.9) | 0.63 |
| Uterine Rupture | 82 (4.8) | 58 (4.4) | 24 (6.3) | 0.14 |
| Placental Abruption | 193 (11.4) | 145 (11.1) | 48 (12.6) | 0.14 |
| Fetal Distress | 473 (27.9) | 393 (29.9) | 80 (21.0) | 0.001 |
| Encephalopathy severity | | | | |
| Mild Moderate | 247 (14.6) | 0 (0) | 247 (64.8) | <0.001 |
| Severe | 1330 (78.6) | 1312 (100) | 18 (4.7) | 0.06 |
| Unknown | 116 (6.9) | 0 (0.0) | 116 (30.5) | <0.001 |
| Head cooling | 272 (16.1) | 213 (16.2) | 59 (15.5) | 0.75 |
| Whole body cooling | 1411 (83.3) | 1085 (82.7) | 326 (85.6) | 0.21 |
| Clinical seizures | 142 (8.4) | 91 (6.9) | 51 (13.4) | <0.001 |
| EEG/aEEG confirmed seizures | 369 (21.8) | 264 (20.1) | 105 (27.6) | 0.002 |
| No seizures | 1073 (63.4) | 871 (66.4) | 202 (53.0) | <0.001 |
| ECMO | 56 (3.3) | 44 (3.4) | 12 (3.2) | 0.99 |
| iNO | 163 (9.6) | 136 (10.4) | 27 (7.1) | 0.18 |
| Tracheostomy | 7 (0.4) | 5 (0.4) | 2 (0.5) | 0.66 |
| Gastrostomy tube | 81 (4.8) | 61 (4.7) | 20 (5.3) | 0.68 |
| Ventilator days, median [IQR] | 2 [0,6] | 2 [0,5] | 4 [0,7] | <0.001 |
| Length of stay, median [IQR] | 12 [8,19] | 11 [8,19] | 12 [8,20] | 0.15 |

aEEG amplitude integrated electroencephalogram, BD base deficit, BW birthweight, EEG electroencephalogram, ECMO extracorporeal membrane oxygenation, GA gestational age, iNO inhaled nitric oxide, IQR interquartile range, NDI neurodevelopmental impairment
p<0.05 considered statistically significant

eTable 2. Demographics and Outcomes of study population and excluded deaths ≤4 days

| Characteristics | Overall n=446 n (%) | Death ≤4 days n=65 n (%) | Death>4 days n=80 n (%) | Survivors with NDI n=64 n (%) | Survivors without NDI n=237 n (%) | P value |
|--|---------------------------|-----------------------------------|----------------------------------|--|--|---------|
| GA, median [IQR] in weeks | 39 [38,40] | 39 [38,49] | 39 [38,40] | 39 [38,40] | 39 [38,40] | 0.69 |
| BW, median [IQR] in grams | 3294 [2950,3750] | 3220 [2975, 3640] | 3337 [2915,3840] | 3378 [3000,3780.5] | 3280 [2960,3751] | 0.46 |
| Female | 194 (43.5) | 32 (49.2) | 31 (38.8) | 31 (48.4) | 100 (42.2) | 0.49 |
| Maternal Race | | | | | | |
| White | 277 (62.1) | 40 (61.5) | 43 (53.8) | 41 (64.1) | 153 (64.6) | 0.38 |
| Black | 90 (20.2) | 11 (16.9) | 21 (26.3) | 13 (20.3) | 45 (19.0) | 0.49 |
| Other | 58 (15.2) | 10 (15.4) | 14 (17.5) | 7 (10.9) | 37 (15.6) | 0.75 |
| Unknown | 11 (2.5) | 4 (6.2) | 2 (2.5) | 3 (4.7) | 2 (0.8) | 0.02 |
| Hispanic, n (%) | 67 (15) | 4 (6.2) | 14 (17.5) | 10 (15.6) | 39 (16.5) | 0.23 |
| Birth location | | | | | | |
| Birthing Center, not hospital | 2 (0.5) | 0 (0) | 1 (1.3) | 1 (1.6) | 0 (0.0) | 0.5 |
| Home | 9 (2.02) | 2 (3.08) | 2 (2.5) | 0 (0.0) | 5 (2.1) | 0.75 |
| Hospital | 435 (97.5) | 63 (96.9) | 77 (96.3) | 63 (98.4) | 232 (97.9) | 0.75 |
| Delivery type | | | | | | |
| Vaginal, non-operative | 121 (27.1) | 14 (21.5) | 16 (20.0) | 19 (29.7) | 72 (30.4) | 0.21 |
| Vaginal, operative | 45 (10.1) | 8 (12.3) | 9 (11.3) | 8 (12.5) | 20 (8.4) | 0.58 |
| Cesarean | 280 (62.8) | 43 (66.2) | 55 (68.7) | 37 (57.8) | 145 (61.2) | 0.49 |
| APGAR @10 min ≤5 | 234 (52.5) | 46 (70.8) | 55 (68.8) | 39 (60.9) | 94 (39.7) | <0.001 |
| Presenting pH <7 | 97 (21.7) | 15 (23.1) | 11 (13.8) | 21 (32.8) | 50 (21.1) | 0.05 |
| Cord gas BD (or 1st hr gas), median [IQR] | 17 [11,22] | 23 [13,27] | 18 [8,22] | 18.5 [15,24] | 15 [10,20] | 0.02 |
| Perinatal sentinel event | | | | | | |
| Nuchal Cord | 75 (16.8) | 3 (4.6) | 16 (20.0) | 13 (20.3) | 43 (18.1) | 0.02 |
| Cord Prolapse | 16 (3.6) | 1 (1.5) | 2 (2.5) | 4 (6.3) | 9 (3.8) | 0.53 |
| Uterine Rupture | 29 (6.5) | 5 (7.7) | 7 (8.8) | 7 (10.9) | 10 (4.2) | 0.14 |
| Placental Abruption | 55 (12.3) | 7 (10.8) | 7 (8.8) | 11 (17.2) | 30 (12.7) | 0.14 |
| Fetal Distress | 100 (22.4) | 20 (30.8) | 20 (25.0) | 19 (29.7) | 41 (17.3) | 0.034 |
| Encephalopathy severity | | | | | | |
| Mild Moderate | 253 (56.7) | 6 (9.2) | 5 (6.3) | 47 (73.4) | 195 (82.3) | <.0001 |
| Severe | 175 (39.2) | 59 (90.8) | 70 (87.5) | 1 (1.6) | 12 (5.1) | <0.001 |
| Unknown | 18 (4.1) | | 5 (6.3) | 16 (25.0) | 30 (12.7) | 0.131 |
| Head cooling | 62 (13.9) ⁺ | 3 (4.6) | 12 (15.0) | 11 (17.2) | 36 (15.2) | 0.09 |
| Whole body cooling | 397 (87.8) ⁺ | 61 (93.8) | 68 (85.0) | 57 (89.1) | 201 (84.8) | 0.24 |
| Clinical seizures | 58 (13) | 7 (10.8) | 15 (18.8) | 4 (6.3) | 32 (13.5) | 0.16 |
| EEG/aEEG confirmed seizures | 125 (28.0) | 20 (30.8) | 36 (45.0) | 21 (32.8) | 48 (20.3) | <0.001 |
| No seizures | 238 (53.4) | 36 (55.4) | 21 (26.3) | 36 (56.3) | 145 (61.2) | <0.001 |
| ECMO | 14 (3.1) | 2 (3.1) | 5 (6.3) | 1 (1.6) | 6 (2.5) | 0.37 |
| iNO | 94 (21.1) | 20 (30.8) | 26 (32.5) | 14 (21.9) | 34 (14.3) | 0.005 |
| Tracheostomy | 2 (0.5) | 0 (0) | 0 (0) | 0 (0) | 2 (0.8) | 0.99 |
| Gastrostomy tube | 20 (5.3) | 0 (0) | 0 (0) | 9 (14.1) | 11 (4.6) | <0.001 |
| Ventilator days, median [IQR] | 4 [0,7] | 2 [1,3] | 8 [6,11] | 4 [2,8] | 4 [1,7] | <0.001 |
| Length of stay, median [IQR] | 11 [6,18] | 1 [1,2] | 7 [5,11] | 17 [9, 29] | 13 [9,21] | <0.001 |

aEEG amplitude integrated electroencephalogram, BD base deficit, BW birthweight, EEG electroencephalogram, ECMO extracorporeal membrane oxygenation, GA gestational age, iNO inhaled nitric oxide, IQR interquartile range, NDI neurodevelopmental impairment
p<0.05 considered statistically significant

eTable 3. Demographics and Outcomes of Survivors with or without developmental data vs lost to follow-up

| Characteristics | Overall n=1513 n (%) | Survivors with or without developmental data n=301 n (%) | Lost to follow up n=1212 n (%) | P value |
|--|----------------------------|--|--------------------------------------|---------|
| GA, median [IQR] in weeks | 39 [38,40] | 39 [38,40] | 39 [38,40] | 0.38 |
| BW, median [IQR] in grams | 3300 [2925,3710] | 3300 [2913.5,3690] | 3310 [2970,3751] | 0.18 |
| Female | 634 (41.9) | 503 (41.5) | 131 (43.5) | 0.56 |
| Maternal Race | | | | |
| White | 923 (61) | 729 (60.1) | 194 (64.4) | 0.19 |
| Black | 330 (21.8) | 272 (22.4) | 58 (19.3) | 0.24 |
| Other | 205 (13.5) | 161 (13.3) | 44 (14.6) | 0.57 |
| Unknown | 55 (3.6) | 50 (4.1) | 5 (1.7) | 0.04 |
| Hispanic | 243 (16.1) | 194 (16.0) | 49 (16.3) | 0.93 |
| Birth location | | | | |
| Birthing Center, not hospital | 7 (0.5) | 6 (0.5) | 1 (0.3) | 0.99 |
| Home | 30 (1.9) | 25 (2.1) | 5 (1.7) | 0.99 |
| Hospital | 1476 (97.5) | 1181 (97.4) | 295 (98.0) | 0.99 |
| Delivery type | | | | |
| Vaginal, non-operative | 427 (28.2) | 336 (27.7) | 91 (30.2) | 0.39 |
| Vaginal, operative | 150 (9.9) | 122 (10.1) | 28 (9.3) | 0.75 |
| Cesarean | 933 (61.7) | 751 (61.9) | 182 (60.5) | 0.64 |
| APGAR @10 min ≤5 | 669 (44.2) | 536 (44.2) | 133 (44.2) | 0.99 |
| Presenting pH <7 | 203 (13.4) | 132 (10.9) | 71 (23.6) | <0.001 |
| Cord gas BD (or 1st hr gas), median [IQR] | 15.6 [11,19] | 15.1 [11,19] | 16 [12,21] | 0.37 |
| Perinatal sentinel event | | | | |
| Nuchal Cord | 289 (19.1) | 233 (19.2) | 56 (18.6) | 0.87 |
| Cord Prolapse | 55 (3.6) | 42 (3.5) | 13 (4.3) | 0.49 |
| Uterine Rupture | 67 (4.4) | 50 (4.1) | 17 (5.7) | 0.27 |
| Placental Abruptio | 169 (11.2) | 128 (10.6) | 41 (13.6) | 0.27 |
| Fetal Distress | 421 (27.8) | 361 (29.8) | 60 (19.9) | 0.001 |
| Encephalopathy severity | | | | |
| Mild Moderate | 1195 (78.9) | 953 (78.6) | 242 (80.4) | 0.53 |
| Severe | 207 (13.7) | 161 (13.3) | 46 (15.3) | 0.53 |
| Unknown | 111 (7.3) | 98 (8.1) | 13 (4.3) | 0.08 |
| Head cooling | 240 (15.9) | 193 (15.9) | 47 (15.6) | 0.93 |
| Whole body cooling | 1264 (83.5) | 1006 (83) | 258 (85.7) | 0.29 |
| Clinical seizures | 114 (7.5) | 78 (6.4) | 36 (11.9) | 0.002 |
| EEG/aEEG confirmed seizures | 297 (19.6) | 228 (18.8) | 69 (22.9) | 0.12 |
| No seizures | 1009 (66.7) | 828 (68.3) | 181 (60.1) | 0.008 |
| ECMO | 46 (3.0) | 39 (3.2) | 7 (2.3) | 0.57 |
| iNO | 247 (16.3) | 199 (16.4) | 48 (15.9) | 0.79 |
| Tracheostomy | 1513 (100) | 1212 (100) | 301 (100) | 0.50 |
| Gastrostomy tube | 1513 (100) | 1212 (100) | 301 (100) | 0.99 |
| Ventilator days, median [IQR] | 5 [2,8] | 5 [2,8] | 4 [2,7] | 0.29 |
| Length of stay, median [IQR] | 12 [9,20] | 12 [9,20] | 13 [9,22] | 0.01 |

aEEG amplitude integrated electroencephalogram, BD base deficit, BW birthweight, EEG electroencephalogram, ECMO extracorporeal membrane oxygenation, GA gestational age, iNO inhaled nitric oxide, IQR interquartile range, NDI neurodevelopmental impairment
p<0.05 considered statistically significant

eTable 4. NDI component rates in infants who survived with NDI

| Component | Frequency (%) n=64 |
|-------------------------------|-----------------------|
| Composite cognitive score <85 | 27 (42.2) |
| Composite motor score <70 | 15 (23.4) |
| Deafness | 1 (1.6) |
| Blindness | 0 (0) |
| GFMCS score ≥2 | 11 (17.2) |

eTable 5. Unadjusted Costs by death, survivors with NDI and without NDI

| Costs | Total Median \$ [IQR] n=381 | Death >4 days Median \$ [IQR] n=80 | Survivors with NDI Median \$ [IQR] n=64 | Survivors without NDI Median \$ [IQR] n=237 | P value |
|---------------------------------|-----------------------------------|--|---|---|---------|
| Total hospitalization | 26,420 [21,664, 36,610] | 33,033 [24,993, 41,144] | 24,777 [22,419, 35,694] | 25,285 [20,964, 34,030] | <0.001 |
| EEG | 2,417 [1,293, 4,567] | 2,303 [1,264, 4,715] | 1,615 [994, 3,004] | 2,454 [1,462, 4,644] | 0.09 |
| Laboratory | 3,695 [1,984, 5,425] | 5498 [4,224, 8,347] | 3,857 [2,504, 4,807] | 2,707 [1,570, 4,698] | <0.001 |
| Anti-seizure medications | 40 [17, 100] | 41 [15, 149] | 67 [32,121] | 34 [16, 81] | 0.05 |

eTable 6. Unadjusted costs by death<4 days, death >4 days, survivors with NDI and without NDI

| Costs | Total Median \$ [IQR] n=381 | Death ≤4 days Median \$ [IQR] n=65 | Death >4 days Median \$ [IQR] n=80 | Survivors with NDI Median \$ [IQR] n=64 | Survivors without NDI Median \$ [IQR] n=237 | P value |
|---------------------------------|-----------------------------------|--|--|--|--|---------|
| Total hospitalization | 26,420 [21,664, 36,610] | 15,766 [8,216, 23,204] | 33,033 [24,993, 41,144] | 24,777 [22,419, 35,694] | 25,285 [20,964, 34,030] | <0.001 |
| EEG | 2,417 [1,293, 4,567] | 677 [450, 1,023] | 2,303 [1,264, 4,715] | 1,615 [994, 3,004] | 2,454 [1,462, 4,644] | <0.001 |
| Laboratory | 3,695 [1,984, 5,425] | 2,980 [1,594, 4,529] | 5498 [4,224, 8,347] | 3,857 [2,504, 4,807] | 2,707 [1,570, 4,698] | <0.001 |
| Anti-seizure medications | 40 [17, 100] | 46 [12.3, 100] | 41 [15, 149] | 67 [32,121] | 34 [16, 81] | 0.09 |