The Use of Early Continuous Cerebral NIRS Monitoring to Predict Hemodynamically Significant Patent Ductus Arteriosus in Extremely Premature Infants

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Background and Aim

- **Incidence**: Patent Ductus Arteriosus (PDA) is common in extremely premature infants, affecting approximately 70% of 23-24-week gestational age (GA) infants, and 59% of 25-28-week GA infants.
- **Hemodynamically significant PDA (hsPDA) is associated with** increased mortality, pulmonary morbidities, prolonged need for mechanical ventilation, bronchopulmonary dysplasia, necrotizing enterocolitis, and intraventricular hemorrhage (IVH).
- **Our aim was to illustrate whether the clinical use of continuous cerebral NIRS monitoring in the first few days of life can delineate between infants with hsPDA and infants without hsPDA.**

Methods

Institutional protocol: At BWH, beginning January 1st, 2018, all infants born before 28 weeks GA were monitored clinically with a commercially available NIRS monitor (INVOS) for at least the first 3 days of life.

- This **retrospective study** was conducted at Brigham and Women's Hospital (BWH) between January 2018 – August 2020.
- **HsPDA was classified based on the presence of PDA by echocardiogram that required medical or surgical treatment.** The control group (Non-hsPDA) included infants without PDA or with PDA that did not require medical intervention.
- Data were binned into 12-hour segments with the exclusion of data that did not include at least 6 hours of data within each 12-hour segment.
- Within each 12-hour bin, the mean, median, interquartile range (IQR), standard deviation (SD), and the coefficient of variation (CV) of the rSO_2 values were calculated every hour.
- NIRS data obtained after an infant surpassed 108 hours of life (HoL) were excluded from the analysis.
- The cerebral oxygen saturation (rSO_2) mean, median, IQR, SD, and CV were compared across the two groups (hsPDA, non-hsPDA).
- JMP Pro version 15.2.0 was used for statistical analyses.



A picture of a 24-week and 3-day old male infant with the INVOS (NIRS) monitor on the left side of his forehead.

Results

Table 1. Characteristics of the study population

Characteristic	HsPDA (n = 57)	Non-hsPDA (n = 39)	p-value
Gestational age, weeks	25.6 (24.8 - 26.6)	26.4 (24.9 - 27.3)	**0.0427**
Birth weight, g	780 (652.5 - 925)	850 (690 - 940)	0.4054
Multiple Births, n	22 (38.6)	10 (25.6)	0.1860
Male, n	35 (59.3)	17 (43.6)	0.0854
Chorioamnionitis, n	9 (15.8)	7 (17.9)	0.7804
Cesarean section, n	42 (73.7)	28 (71.8)	0.8379
Apgar 1 min	4 (2.0 – 5.0)	4 (2.0 – 6.0)	0.9189
Apgar 5 min	7 (6.0 – 8.0)	6 (5.0 – 8.0)	0.6812
Cardiac Compressions in DR, n	4 (7)	2 (5.1)	0.7072
[a] Intubated in DR, n	51/54 (94.4)	33/36 (91.6)	0.6048
PDA, n	57 (100)	12 (30.8)	**< 0.001**
Sepsis before day 3, n	0 (0)	2 (5.1)	0.0840
Sepsis after day 3, n	6 (10.5)	5 (12.8)	0.7289
[a] ROP, n	40/50 (80)	24/38 (63.2)	0.0789
Death, n	6 (10.5)	0 (0)	**0.0364**
HoL NIRS Start	7 (4 – 14.5)	8 (4 – 13)	0.7505
HoL NIRS End	75 (66.5 – 98)	77 (65 – 103)	0.5258
Median duration of NIRS Measurement	60 (45.5 – 79.5)	67 (49 – 83)	0.5208

96/117 infants born during the study period were included in this analysis. Infants were excluded if the NIRS monitoring was not available (n = 8), if the measurement was less than 6 hours (n = 2), if the NIRS monitoring occurred after 108 HoL (n = 3), or if the infant passed away before being evaluated/treated for PDA (n = 11).

The clinical characteristics and demographic information of the study population are presented in **Table 1.** Data were obtained from the VON database. Data are reported as a percentage or median (IQR). DR = delivery room, PDA = Patent Ductus Arteriosus, ROP = Retinopathy of Prematurity, HoL = hour of life. [a]Ratios are given when the total sample size of the PDA group was not available. Bolded values Indicate $p < 0.05$. Differences among categories were assessed using chi-square (exact for tests of small sample size, $n < 5$), and Wilcoxon rank sum.[1]

Trajectories of mean cerebral rSO_2 in infants with and without hsPDA

Looking at the overall trends in the mean cerebral rSO_2 values between the two groups in the Least Squares Means (LS Means) plot, rSO_2 values trended towards significance between the 84th – 96th HoL 12hr classification and became statistically significant between the 96th – 108th HoL 12hr classification ($p = 0.09$, $p = 0.03$, respectively, **Figure 1**).

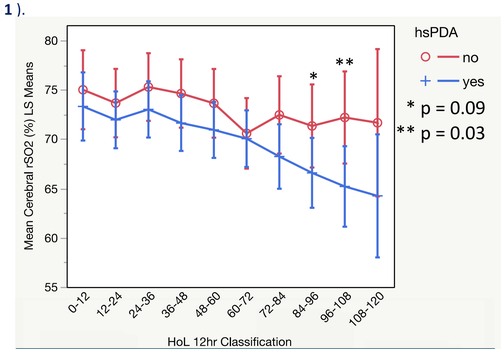


Table 2. Number of Subjects per HoL 12hr Classification by PDA Group

PDA Group	0 - 12	12 - 24	24 - 36	36 - 48	48 - 60	60 – 72	72 - 84	84 - 96	96 - 108	108 - 120
Non-hsPDA	17	32	34	32	31	27	18	14	10	3
HsPDA	21	43	46	48	47	44	25	19	12	4
Total	38	75	80	80	78	71	43	33	22	7

Figure 1. The mean cerebral rSO_2 (%) Least Squares Means plot (with 95% CIs) for the hsPDA and non-hsPDA subjects per HoL 12hr Classification.

Results and Discussion

- No statistical significance was found between the IQR, SD, and CV when stratified by hsPDA and non-hsPDA groups.

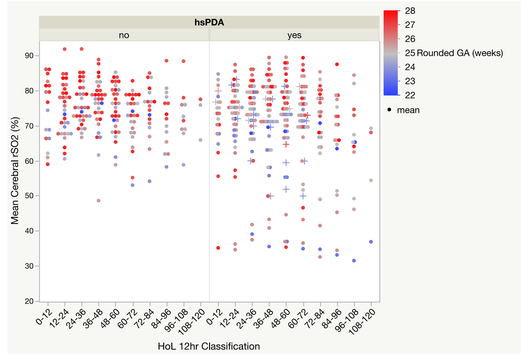


Figure 2. The mean cerebral rSO_2 (%) for the hsPDA and non-hsPDA subjects per HoL 12hr Classification. The color of each point indicates the subject's gestational age. Markers with a '+' indicate a deceased subject.

- One potential limitation of this analysis is that our LS Means plot hsPDA trajectory may be driven by a few cases of low rSO_2 values (**Table 2**). In addition, the LS Means plot does not account for the effect of multiple comparisons.

Conclusions

- There is a trend towards lower Least Squares Means of cerebral rSO_2 in extremely premature infants who developed hsPDA when compared to those without hsPDA, which reached statistical significance between the 96th – 108th HoL.
- No significance was found between the IQR, SD, and CV of the cerebral rSO_2 values stratified by PDA group.
- These results suggest that early NIRS monitoring for premature infants <28 weeks GA may provide useful information regarding the hemodynamic significance of the PDA if the infant's cerebral NIRS rSO_2 values trend downward between the 96th – 108th HoL.
- Future work will include looking for additional confounding variables (IVH, hematocrit), and implementing a stricter definition of hsPDA based on echocardiographic data.

References

- [1]*El-Dib M, et al. 2022 Association of early cerebral oxygen saturation and brain injury in extremely preterm infants. J Perinatol. 42:1385–1391.*