**Table S1a**. Cerebrovascular autoregulation and its relation to presence of IVH on cUS one week after birth.

| Day | Measurement variable | No IVH on cUS (*n* = 7) | IVH on cUS (*n* = 25) | *p*-value |
|---|---|---|---|---|
| 1 | | (*n* = 7) | (*n* = 25) | |
| | Mean COx | 0.09 ± 0.08 | 0.07 ± 0.12 | 0.574 |
| | Mean TOHRx | -0.01 ± 0.09 | -0.04 ± 0.12 | 0.453 |
| | %TimeCAR with MABP (%) | 28.1 ± 10.9 | 25.6 ± 13.9 | 0.623 |
| | %TimeCAR with HR (%) | | | |
| | TOHRx cc cut-off 0.3 | 14.8 ± 7.0 | 12.2 ± 8.7 | 0.437 |
| | TOHRx cc cut-off -0.3 | 16.1 ± 11.2 | 18.2 ± 13.8 | 0.690 |
| 2 | | (*n* = 5) | (*n* = 19) | |
| | Mean COx | 0.04 ± 0.16 | 0.06 ± 0.12 | 0.853 |
| | Mean TOHRx | 0.02 ± -0.49 | -0.07 ± 0.11 | 0.016* |
| | %TimeCARi with MABP (%) | 23.0 ± 12.5 | 25.6 ± 12.3 | 0.690 |
| | %TimeCARi with HR (%) | | | |
| | TOHRx cc cut-off 0.3 | 17.4 ± 8.1 | 11.2 ± 8.1 | 0.178 |
| | TOHRx cc cut-off -0.3 | 11.4 ± 7.6 | 21.0 ± 12.3 | 0.055 |
| 3 | | (*n* = 5) | (*n* = 23) | |
| | Mean COx | -0.01 ± 0.18 | 0.03 ± 0.15 | 0.695 |
| | Mean TOHRx | 0.04 ± 0.08 | -0.03 ± 0.15 | 0.179 |
| | %TimeCARi with MABP (%) | 21.3 ± 15.4 | 23.8 ± 12.8 | 0.740 |
| | %TimeCARi with HR (%) | | | |
| | TOHRx cc cut-off 0.3 | 15.6 ± 11.1 | 14.5 ± 11.1 | 0.841 |
| | TOHRx cc cut-off -0.3 | 11.9 ± 5.4 | 18.0 ± 10.6 | 0.089 |

**Table S1b**. Cerebrovascular autoregulation and its relation to presence of PVL on cUS one week after birth.

| Day | | Measurement variable | No PVL on cUS (*n* = 20) | PVL on cUS (*n* = 10) | *p*-value |
|---|---|---|---|---|---|
| 1 | | | (*n* = 20) | (*n* = 10) | |
| | | Mean COx | 0.092 ± 0.097 | 0.044 ± 0.145 | 0.280 |
| | | Mean TOHRx | -0.030 ± 0.102 | -0.026 ± 0.136 | 0.919 |
| | | %TimeCARi with MABP (%) | 27.3 ± 12.5 | 23.6 ± 14.8 | 0.496 |
| | | %TimeCARi with HR (%) | | | |
| | | TOHRx cc cut-off 0.3 | 12.2 ± 8.3 | 14.1 ± 8.6 | 0.554 |

| | | | | | |
|---|---|---|---|---|---|
| | | TOHRx cc cut-off -0.3 | 17.3 ± 12.3 | 18.5 ± 15.3 | 0.812 |
| 2 | | | (*n* = 15) | (*n* = 9) | |
| | | Mean COx | 0.047 ± 0.104 | 0.065 ± 0.154 | 0.723 |
| | | Mean TOHRx | -0.044 ± 0.096 | -0.064 ± 0.126 | 0.655 |
| | | %TimeCARi with MABP (%) | 26.1 ± 12.1 | 23.5 ± 12.8 | 0.621 |
| | | %TimeCARi with HR (%) | | | |
| | | TOHRx cc cut-off 0.3 | 12.8 ± 8.3 | 11.8 ± 9.0 | 0.782 |
| | | TOHRx cc cut-off -0.3 | 17.1 ± 9.8 | 22.1 ± 15.0 | 0.327 |
| 3 | | | (*n* = 19) | (*n* = 9) | |
| | | Mean COx | 0.031 ± 0.155 | -0.003 ± 0.146 | 0.575 |
| | | Mean TOHRx | 0.004 ± 0.114 | -0.051 ± 0.095 | 0.198 |
| | | %TimeCARi with MABP (%) | 24.2 ± 13.5 | 21.6 ± 12.6 | 0.631 |
| | | %TimeCARi with HR (%) | | | |
| | | TOHRx cc cut-off 0.3 | 16.0 ± 12.1 | 11.9 ± 7.9 | 0.287 |
| | | TOHRx cc cut-off -0.3 | 15.3 ± 9.8 | 20.1 ± 10.3 | 0.650 |

Data are presented as mean ± standard deviation. IVH, germinal matrix-intraventricular hemorrhage according to Papile (modified) [22, 23]; PVL, periventricular leukomalacia according to de Vries et al [24]; cUS, cranial ultrasonography; COx, cerebral oximetry index; TOHRx, tissue oxygenation heart rate reactivity index; %timeCARi, percentage of time with impaired cerebrovascular autoregulation; MABP, mean arterial blood pressure; HR, heart rate; cc, correlation coefficient. Numbers vary per day since CAR measurements were not available for all neonates on all days in this study. * *P*-value < 0.05.

**Table S2**. The clinical determinants of cerebral injury on cUS, determined by univariable logistic regression analysis.

| | | | | | **Univariable analysis** | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Variable | B | OR (95% CI) | *p*-value | B | OR (95% CI) | *p*-value | B | OR (95% CI) | *p*-value |
| Gestational age (weeks + days) | | | | 0.0 | 1.0 (0.9-1.1) | 0.991 | | | |
| Apgar 5min | | | | 0.0 | 1.0 (0.7-1.6) | 0.891 | | | |
| SGA | | | | -0.6 | 0.6 (0.7-4.6) | 0.585 | | | |
| HsPDA | | | | 0.3 | 1.4 (0.3-5.9) | 0.648 | | | |
| NEC | | | | -0.3 | 0.8 (0.1-4.1) | 0.741 | | | |
| EONS | | | | 20.8 | 1.1 x $10^9$ (0.0) | 0.999 | | | |
| | Day 1 | | | Day 2 | | | Day 3 | | |
| Sedatives | -0.4 | 0.7 (0.1-3.2) | 0.613 | 0.7 | 1.1 (0.2-4.9) | 0.923 | -0.7 | 0.5 (0.1-2.5) | 0.403 |
| Inotropes | 20.7 | 1.0 x $10^9$ (0.0) | 1.00 | 0.7 | 1.9 (0.2-21.1) | 0.586 | 20.8 | 1.1 x $10^9$ (0.0) | 0.999 |
| Mean $PCO_2$ | -0.1 | 1.0 (0.5-1.8) | 0.880 | -0.3 | 0.8 (0.3-1.6) | 0.756 | 0.4 | 1.5 (0.6-3.5) | 0.399 |
| Mechanical ventilation | 0.3 | 1.3 (0.3-5.7) | 0.706 | 1.3 | 3.7 (0.8-16.8) | 0.089* | 2.2 | 9.3 (1.6-54.8) | 0.014* |
| COx | -1.8 | 0.2 (0.0-101.6) | 0.576 | 4.3 | 72.9 (0.0-255195.2) | 0.303 | -3.0 | 0.1 (0.0-12.9) | 0.287 |
| TOHRx | -0.4 | 0.7 (0.0-481.8) | 0.911 | -7.5 | 0.0 (0.0-12.1) | 0.141 | -1.2 | 0.3 (0.0-384.0) | 0.740 |
| %TimeCARi with MABP (%) | 0.0 | 1.0 (0.9-1.1) | 0.765 | 0.0 | 1.0 (1.0-1.1) | 0.350 | 0.0 | 1.0 (0.9-1.0) | 0.320 |
| %TimeCARi with HR, cc cut-off 0.3 (%) | 0.0 | 1.0 (0.9-1.1) | 0.618 | 0.0 | 1.0 (0.9-1.1) | 0.406 | 0.0 | 1.0 (0.9-1.1) | 0.721 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| %TimeCARi with HR, cc cut-off -0.3 (%) | 0.0 | 1.0 (0.9-1.1) | 0.879 | | 0.1 | 1.1 (1.0-1.2) | 0.141 | | 0.0 | 1.0 (0.9-1.1) | 0.924 |

CUS, cranial ultrasonography; B, unstandardized coefficient; OR; odds ratio, CI, confidence interval; SGA, small for gestational age; HsPDA; hemodynamically significant patent ductus arteriosus; NEC, necrotizing enterocolitis; EONS, early onset of neonatal sepsis confirmed with a positive blood cult; $PCO_2$, partial pressure of carbon dioxide; COx; cerebral oximetry index; TOHRx; tissue oxygenation hear rate reactivity index; %timeCARi, percentage of time with impaired cerebrovascular autoregulation; MABP, mean arterial blood pressure; HR, heart rate; cc, correlation coefficient. * *P*-value < 0.10.

**Table S3**. The clinical determinants of cerebral injury on cUS, determined by multivariable logistic regression analysis.

| **Multivariable analysis** | | | |
|---|---|---|---|
| Variable | B | OR (95% CI) | *p*-value |
| Mechanical ventilation day 2 | 0.1 | 1.1 (0.2-8.1) | 0.929 |
| Mechanical ventilation day 3 | 2.2 | 8.8 (1.0-76.6) | 0.050 |

CUS, cranial ultrasonography; B, unstandardized coefficient; OR; odds ratio, CI, confidence interval.