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Supplemental material

Association of germinal matrix hemorrhage volume with neurodevelopment and hydrocephalus
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Supplementary Table 1. Clinical and radiologic factors and their association with global performance

	Needs assistance with ADLs		Walks freely		Symmetrical gait		Toe-walking		Cerebral palsy diagnosis	
Univariate Analysis	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Estimated GA, mean (SD), weeks	25 (1.48)	24.9 (2.13)	24.9 (2.02)	25.2 (1.54)	25.3 (2.21)	24.4 (1.12)	25.7 (1.23)	25.5	24.8 (1.24)	25.4 (2.93)
Male sex, no. (%)	9 (81.8)	17 (60.7)	22 (68.8)	7 (63.6)	17 (65.4)	12 (70.6)	14 (70)	14 (73.7)	22 (73.3)	7 (53.8)
Birth weight (g)	858.2 (202.9)	813.4 (176.8)	837.3 (171.6)	829.1 (207.5)	878.3 (196.6)	769.4 (126.4)	800 (131.8)	895 (219.1)	826.7 (152.5)	855 (234.8)
Medical risk index, median (IQR)	3 (2-5)	3 (1.25-5)	3 (2-5)	3 (2-5)	3 (1-4)	4 (2-5)	4 (2.24-5)	3 (1-4)	3 (2-5)	3 (1-4.5)
Sociodemographic Stressor Index, median (IQR)	2 (0-3)	2 (0-3)	2 (0-3)	2 (0-2)	2 (0-3)	2 (0-2.5)	2 (0-2.75)	2 (0-3)	2 (0-2.25)	2 (0.5-3.5)
Number of general anesthesia events, median (IQR)	4 (3-6)	2.5 (1-6)	2 (1-5.75)	4 (3-8)	2 (0.75-6)	4 (3-7)	3.5 (1.5-6)	2 (0-6)	3.5 (1-6)	2 (0.5-4.5)
Left GMH volume (cm^3)	0.230 (0.192)	0.112 (0.104)	0.115 (0.107)	0.234 (0.188)	0.080 (0.064)	0.240 (1.68)	0.195 (0.168)	0.082 (0.065)	0.177 (0.153)	0.0643 (0.0416)
Right GMH volume (cm^3)	0.544 (0.687)	0.239 (0.243)	0.225 (0.273)	0.533 (0.654)	0.270 (0.439)	0.368 (0.416)	0.323 (0.340)	0.344 (0.537)	0.359 (0.491)	0.193 (0.183)
Total GMH volume (cm^3)	0.774 (0.731)	0.326 (0.274)	0.311 (0.275)	0.767 (0.721)	0.324 (0.437)	0.587 (0.484)	0.476 (0.440)	0.403 (0.539)	0.512 (0.530)	0.232 (0.178)
Left PVHI volume (cm^3)	1.09 (1.17)	0.802 (0.992)	0.721 (0.961)	1.51 (1.17)	0.494 (0.941)	1.30 (1.07)	1.13 (1.06)	0.604 (1.12)	1.23 (1.10)	0.129 (0.194)
Right PVHI volume (cm^3)	2.19 (3.15)	1.51 (1.58)	0.706 (0.665)	4.41 (2.86)	1.29 (1.29)	2.22 (3.13)	2.60 (3.05)	1.15 (1.20)	2.31 (2.59)	0.595 (0.635)
Unadjusted logistic regression model	**OR (95% CI)**	*P* value	**OR (95% CI)**	*P* value	**OR (95% CI)**	*P* value	**OR (95% CI)**	*P* value	**OR (95% CI)**	*P* value
Estimated GA, mean (SD), weeks	1.03 (0.723-1.46)[a]	.876	0.930 (0.659-1.31)[a]	.677	1.50 (0.896-2.52)[a]	.123	.767 (.502-1.17)[a]	.219	0.856 (0.609-1.203)[a]	0.370
Male sex, no. (%)	2.91 (0.527-16.1)[a]	.220	1.26 (0.298-5.30)[a]	.755	0.787 (0.210-2.95)[a]	.722	.833 (.206-3.39)[a]	.798	1.33 (0.606-9.16)[a]	0.216
Birth weight (g)	1.01 (0.980-1.05)[b]	.490	1.00 (0.961-1.04)[b]	.894	1.04 (1-1.09)[b]	.061	.970 (.932-1.01)[b]	.119	0.999 (0.996-1.003)[b]	0.631
Medical risk index, median (IQR)	1.08 (0.751-1.55)[a]	.685	1.02 (0.709-1.47)[a]	.914	0.74 (0.523-1.05)[a]	.094	1.44 (.983-2.11)[a]	.061	1.18 (0.825-1.70)[a]	0.362
Sociodemographic Stressor Index, median (IQR)	0.997 (0.641-1.55)[a]	.991	1.16 (0.727-1.84)[a]	.540	1.08 (0.721-1.62)a	.703	1.01 (.665-1.52)[a]	.970	0.714 (0.457-1.12)[a]	0.139
Number of general anesthesia events, median (IQR)	1.13 (0.936-1.36)[a]	.207	0.830 (0.682-1.01)[a]	.061	**0.803 (0.652-0.989)[a]**	**.039**	1.07 (.892-1.27)[a]	.484	1.27 (0.965-1.68)[a]	0.087
Left GMH volume (cm^3)	**1.78 (1.03-3.34)[c]**	**.040**	**0.554 (0-0.943)[c]**	**.030**	**0.272 (0.000-0.833)[c]**	**.004**	**2.53 (1.09-5.87)[c]**	**.030**	**3.80 (1.01-14.3)[c]**	**0.049**
Right GMH volume (cm^3)	1.18 (0.974-1.43)[c]	.090	0.845 (0.699-1.02)[c]	.079	0.947 (0.814-1.10)[c]	.481	.989 (.852-1.15)[c]	.888	1.15 (0.895-1.15)[c]	0.278
Total GMH volume (cm^3)	**1.22 (1.02-1.47)[c]**	**.031**	**0.809 (0.673-0.972)[c]**	**.023**	0.875 (0.747-1.03)[c]	.099	1.03 (.903-1.18)[c]	.637	1.32 (0.949-1.83)[c]	0.100
Left PVHI volume (cm^3)	1.03 (0.929-1.14)[c]	.585	0.930 (0.842-1.03)[c]	.148	0.911 (0.804-1.03)[c]	.144	1.06 (.935-1.20)[c]	.370	1.49 (0.806-2.77)[c]	0.202
Right PVHI volume (cm^3)	1.01 (0.971-1.06)[c]	.531	**0.833 (0.702-0.989)[c]**	**.037**	0.980 (0.936-1.03)[c]	.381	1.04 (.977-1.10)[c]	.235	1.10 (0.961-1.27)[c]	0.162
Multivariable model										
Left GMH volume (cm^3)$^\%$	1.66 (0.897-3.07)[c]	.106	0.600 (.000-1.09)[c]	.095	**0.246 (.000-0.733)[c]**	**.012**	**2.48 (1.04-5.92)[c]**	**.041**	2.87 (0.774-10.6)[c]	0.115
Right GMH volume (cm^3)$^\%$	1.16 (0.947-1.43)[c]	.149	0.906 (0.747-1.10)[c]	.312	0.958 (0.793-1.16)[c]	.660	1.01 (0.829-1.23)[c]	.919	1.28 (0.800-2.04)[c]	0.303
Total GMH volume (cm^3)$^@$	**1.24 (1.01-1.51)[c]**	**.038**	0.843 (0.697-1.02)[c]	.079	0.869 (0.732-1.03)[c]	.110	1.10 (0.948-1.28)[c]	.248	1.37 (0.933-2.02)[c]	0.108
Left PVHI volume (cm^3)$^\#$	1.02 (0.924-1.13)[c]	.650	0.934 (0.846-1.03)[c]	.181	0.911 (0.713-1.32)[c]	.149	1.06 (0.931-1.20)[c]	.392	1.52 (0.864-2.67)[c]	0.146
Right PVHI volume (cm^3)$^\#$	1.10 (0.969-1.06)[c]	.585	**0.831 (0.694-0.994)[c]**	**.042**	0.981 (0.936-1.03)[c]	.416	1.04 (0.978-1.10)[c]	.231	1.39 (0.929-2.09)[c]	0.109
Left PVHI volume (cm^3)$^\&$	1.29 (0.941-1.77)[c]	.113	0.909 (0.806-1.02)[c]	.118	0.887 (0.772-1.02)[c]	.090	1.11 (0.961-1.29)[c]	.154	1.59 (0.829-3.05)[c]	0.162
Right PVHI volume (cm^3)$^\&$	1.01 (0.968-1.06)[c]	.603	0.833 (0.702-0.989)[c]	.037	0.983 (0.933-1.03)[c]	.507	1.04 (0.956-1.12)[c]	.390	1.14 (0.957-1.35)[c]	0.147

*The odds ratios of continuous variables have different units: a) per 1-unit increase, b) per 10-unit increase, c) per 0.1-unit increase, d) per 0.01-unit increase. The odds ratios of categorical variables are male vs. female (reference group), or yes vs. no (reference group)

%: controlling for medical risk index, number of general anesthesia events, and contralateral GMH volume
@: controlling for medical risk index and number of general anesthesia events
#: controlling for presence of contralateral GMH volume
&: controlling for presence of contralateral PVHI volume

Bolded values indicate P <.05
GA: gestational age
OR: odds ratio
SD: standard deviation
g: grams
GMH: germinal matrix hemorrhage
IQR: interquartile range
FTHR: fronto-temporal horn ratio

Supplementary Table 2. Correlation between hemorrhage volumes and ventricular size as measured by FTHR

Relationship	Correlation coefficient, P value
Left GMH volume (cm^3) and FTHR	**+0.3113, .04**
Right GMH volume (cm^3) and FTHR	+0.0841, .59
Left PVHI volume (cm^3) and FTHR	+0.0501, .84
Right PVHI volume (cm^3) and FTHR	-0.0305, .90

     P value calculated using Pearson's correlation analysis
     Bolded values indicate P <.05
     GMH: germinal matrix hemorrhage
     FTHR: fronto-temporal horn ratio
     PVHI: periventricular hemorrhagic infarction

Supplementary Table 3. Comparison between high-grade GMH-IVH and grade II GMH-IVH without contralateral higher-grade hemorrhage

Radiologic characteristics	Grade II (n=12)	Grade III/IV (n=38)	P value*
Right GMH volume (cm^3), mean (SD)	0.07 (0.05)	0.32 (0.43)	**<.001**
FTHR, mean (SD)	0.41 (0.04)	0.52 (0.08)	**<.001**
	(n=12)	(n=39)	
Left GMH volume (cm^3), mean (SD)	0.06 (0.03)	0.15 (0.14)	**.001**
FTHR, mean (SD)	0.41 (0.04)	0.52 (0.09)	**<.001**

    *P value calculated using Student's t-test
    Bolded values indicate P <.05
    GMH-IVH: germinal matrix hemorrhage-intraventricular hemorrhage
    GMH: germinal matrix hemorrhage
    FTHR: fronto-temporal horn ratio
    Total grade II patients = 15 and total grade III/IV patients = 43. Table delineated by laterality of GMH.

Supplementary Table 4. Shunt complications and neurodevelopmental outcomes by 2 years corrected age

Shunt revision^	Bayley-III composite score, mean (SD)					
	Cognition	P value	Language	P value	Motor	P value
No shunt revisions (n=9)	71.7 (13.7)		77.7 (16.4)		69.3 (16.3)	
One revision (n=6)	73.3 (11.3)	.85	76.8 (10.9)	.96	61.0 (9.3)	.46
Two or more revisions (n=4)	68.8 (9.5)		74.7 (16.9)		63.2 (7.5)	
Shunt infection*						
Yes (n=2)	72.5 (3.5)	.81	89 (0)	.799	67.0 (0)	.61
No (n=17)	71.5 (12.3)		76.2 (14.1)		65.2 (13.7)	

^*P* values calculated using one-way ANOVA
**P* values calculated using Student's t-test

Supplementary Table 5. Hemorrhage lengths and their association with neurodevelopmental outcomes

	Estimated change in Bayley-III composite score*, SE (*P* value)		
Unadjusted linear regression model	Cognition	Language	Motor
Left GMH length (cm)	-11.0, 6.40 (.093)	-7.06, 8.62 (.418)	-12.3, 6.65 (.073)
Right GMH length (cm)	-6.18, 4.00 (.130)	-8.71, 5.34 (.112)	-3.50, 4.19 (.410)
Total GMH length (cm)	-4.10, 2.36 (.090)	-5.66, 2.98 (.065)	**-5.67, 2.40 (.023)**
Left PVHI length (cm)	-4.57, 4.01 (.271)	-9.59, 5.73 (.116)	**-7.46, 3.50 (.049)**
Right PVHI length (cm)	-4.81, 3.13 (.144)	-6.26, 4.12 (.150)	**-7.92, 3.39 (.033)**
Multivariable model			
Left GMH length (cm)^%	-12.4, 6.27 (.057)	-10.3, 8.73 (.247)	**-14.1, 6.14 (.028)**
Right GMH length (cm)^%	**-9.03, 3.81 (.024)**	**-12.3, 5.43 (.031)**	-7.34, 4.69 (.128)
Total GMH length (cm)^@	-4.35, 2.31 (.067)	**-6.64, 2.94 (.030)**	**-5.88, 2.25 (.013)**
Left PVHI length (cm)^#	-4.63, 4.13 (.280)	-9.41, 5.92 (.136)	-7.42, 3.61 (.058)
Right PVHI length (cm)^#	-5.25, 3.06 (.107)	-6.56, 4.16 (.137)	**-8.34, 3.36 (.026)**
Left PVHI length (cm)^&	-7.20, 4.09 (.099)	-14.2, 10.1 (.185)	**-14.2, 5.34 (.018)**
Right PVHI length (cm)^&	-4.46, 3.09 (.168)	-6.23, 4.26 (.166)	**-7.51, 3.30 (.038)**
Left PVHI length (cm)^$	-11.7, 6.14 (.064)	-7.65, 8.30 (.363)	**-13.1, 6.26 (.043)**
Right PVHI length (cm)^$	-5.76, 2.70 (.050)	-6.83, 4.13 (.120)	**-9.06, 2.76 (.005)**
Left PVHI length (cm)^Δ	-2.37, 4.10 (.571)	-1.45, 1.83 (.444)	-5.78, 3.64 (.134)
Right PVHI length (cm)^Δ	-2.84, 3.16 (.384)	-5.77, 4.54 (.225)	-6.09, 3.52 (.104)

*estimated change of composite score with one unit increasing in the continuous factors or estimated score difference between two groups (yes minus no) for categorical factors
%: controlling for medical risk index, number of general anesthesia events, and contralateral GMH length
@: controlling for medical risk index and number of general anesthesia events
#: controlling for presence of contralateral GMH length
&: controlling for presence of contralateral PVHI length
$: controlling for medical risk index
Δ: controlling for number of general anesthesia events
Bolded values indicate *P* <.05
SE: standard error
GMH: germinal matrix hemorrhage
PVHI: periventricular hemorrhagic infarction

Supplementary Table 6. Hemorrhage lengths and their association with hydrocephalus outcomes

Unadjusted logistic regression model	Shunt (n=19)	No shunt (n=24)	Odds ratio* (95% CI)	P value
Left GMH length (cm), mean (SD)	1.09 (0.352)	0.851 (0.232)	1.33 (1.04-1.70)	**.022**
Right GMH length (cm), mean (SD)	1.23 (0.546)	1.04 (0.484)	1.08 (0.949-1.22)	.248
Total GMH length (cm), mean (SD)	2.08 (0.900)	1.65 (0.701)	1.07 (0.987-1.17)	.095
Left PVHI length (cm), mean (SD)	1.58 (0.737)	1.38 (0.885)	1.03 (0.916-1.17)	.587
Right PVHI length (cm), mean (SD)	2.13 (1.11)	1.57 (0.661)	1.08 (0.959-1.21)	.212
Multivariable model				
Left GMH length (cm), mean (SD)[%]	1.09 (0.352)	0.851 (0.232)	1.31 (0.991-1.74)	.058
Right GMH length (cm), mean (SD)[%]	1.23 (0.546)	1.04 (0.484)	1.13 (0.960-1.34)	.139
Total GMH length (cm), mean (SD)[^]	2.08 (0.900)	1.65 (0.701)	1.08 (0.983-1.19)	.107
Left PVHI length (cm), mean (SD)[#]	1.58 (0.737)	1.38 (0.885)	1.03 (0.909-1.17)	.619
Right PVHI length (cm), mean (SD)[#]	2.13 (1.11)	1.57 (0.661)	1.08 (0.958-1.21)	.211
Left PVHI length (cm), mean (SD)[&]	1.58 (0.737)	1.38 (0.885)	1.10 (0.938-1.28)	.250
Right PVHI length (cm), mean (SD)[&]	2.13 (1.11)	1.57 (0.661)	1.08 (0.955-1.22)	.224

*The odds ratios of continuous variables are presented per 0.1-unit increase. The odds ratios of categorical variables are male vs. female (reference group), or yes vs. no (reference group)

[^]: controlling for FTHR, GA, and sex

[%]: controlling for FTHR, GA, sex, and contralateral GMH length

[#]: controlling for presence of contralateral grade GMH length

[&]: controlling for presence of contralateral grade PVHI length

Bolded values indicate P <.05

SD: standard deviation