

Supplementary Online Content

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

eTable 1. Postresuscitation Hospital Data Overall and by Favorable and Unfavorable Outcome Groups

Variables, n (%)	Overall N=120	Favorable N=70	Unfavorable N=50	p-value
Fever (> 38°C)	59 (49.2)	34 (48.6)	25 (50.0)	0.877
Seizure occurrence	33 (27.5)	12 (17.1)	21 (42.0)	0.003
Arterial blood gas values, median (interquartile range [IQR]), day 1				
Lowest PaO ₂ , mmHg	63.5 (48.0, 83.0) N=94	60.0 (46.5, 74.8) N=52	71.0 (55.0, 88.0) N=42	0.062
Highest PaO ₂ , mmHg	193.5 (105.0, 283.7) N=94	235.5 (119.0, 325.0) N=52	169.8 (100.0, 239.0) N=42	0.048
Lowest PaCO ₂ , mmHg	30.4 (27.0, 36.0) N=94	30.0 (27.7, 35.9) N=52	30.7 (26.0, 36.5) N=42	0.948
Highest PaCO ₂ , mmHg	50.2 (42.5, 63.7) N=94	53.5 (43.5, 67.5) N=52	44.0 (38.7, 52.0) N=50	0.003
Lowest systolic blood pressure, median (IQR), mmHg	67.0 (55.5, 79.5) N=120	67.5 (58.0, 80.0) N=70	65.5 (52.0, 78.0) N=50	0.377
Highest systolic blood pressure, median (IQR), mmHg	124.0 (111.0, 141.5) N=120	122.0 (109.0, 140.0) N=70	125.5 (114.0, 144.0) N=50	0.583
Invasive mechanical ventilation	117 (97.5)	67 (95.7)	50 (100.0)	0.138
Invasive mechanical ventilation, median (IQR), days	8.0 (4.0, 16.0) N=117	8.0 (4.0, 13.0) N=67	9.5 (4.0, 22.0) N=50	0.278
Vasoactive infusions, day 1				
Epinephrine	76 (63.33)	76 (63.33)	76 (63.33)	0.370
Milrinone	28 (23.33)	17 (24.29)	11 (22.00)	0.770
Norepinephrine	22 (18.33)	10 (14.29)	12 (24.00)	0.175
Dopamine	13 (10.83)	5 (7.14)	8 (16.00)	0.124
Vasopressin	12 (10.00)	5 (7.14)	7 (14.00)	0.217
Phenylephrine	6 (5.00)	4 (5.71)	2 (4.00)	0.671
Isoproterenol	1 (0.83)	1 (1.43)	0 (0)	0.396
Dobutamine	0	0	0	NA

First lactate, median (IQR), mmol/L	5.8 (2.9, 10.9) N=107	4.8 (2.3, 8.9) N=62	8.6 (3.8, 13.2) N=45	0.014
Pediatric Index of Mortality, median (IQR), %	16 (7-31)	14 (5-18)	29 (15-88)	<0.001
First Glasgow Coma Scale score in the ICU, median (IQR)	4 (3, 9) N=88	7 (3, 11) N=48	3 (3, 7) N=40	0.016
Extracorporeal membrane oxygenation	28 (23.3)	18 (25.7)	10 (20.0)	0.466
Extracorporeal CPR	22 (78.6)	15 (83.3)	7 (70.0)	0.410
Target temperature management, prevention of fever	31 (25.8)	12 (17.1)	18 (36.0)	0.032
Target temperature management, therapeutic hypothermia	15 (12.5)	12 (17.1)	3 (6.0)	0.069
Duration at target temperature, median (IQR), h	59 (40, 82)	59 (41, 82)	62 (19, 130)	0.942

ICU, intensive care unit; CPR, cardiopulmonary resuscitation. p-value are based on Chi-square test for categorical variables, Kruskal-Wallis test for continuous variables. Favorable outcome was Vineland Adaptive Behavioral Scale-III (VABS) score ≥ 70 and Unfavorable outcome was VABS < 70 or died.

eTable 2. Unadjusted Biomarker Concentrations on Days 1 to 3 Overall, by Outcome Group, and by Alive With Unfavorable Outcome and Death at 1 Year After Cardiac Arrest

A. Day 1

Median (interquartile range)	Overall N=120	Favorable N=70	Unfavorable N=50	Kruskal-Wallis p-value	VABS < 70 N=7	Dead N=43
NFL	n=118	n=70	n=48	<0.001	n=7	n=41
	27.95 (9.88, 70.75)	13.81 (6.29, 49.98)	50.54 (20.56, 169.00)		14.17 (9.88, 41.39)	62.40 (28.70, 199.00)
Tau	n=118	n=70	n=48	<0.001	n=7	n=41
	8.97 (2.85, 60.70)	5.59 (1.89, 18.85)	50.10 (6.53, 149.30)		6.58 (3.30, 14.95)	60.70 (8.87, 171.10)
GFAP	n=118	n=70	n=48	0.002	n=7	n=41
	212.51 (109.00, 816.76)	174.85 (79.63, 401.27)	469.88 (137.70, 2780.48)		311.21 (159.02, 445.62)	621.39 (136.06, 3009.46)
UCH-L1	n=118	n=70	n=48	<0.001	n=7	n=41
	138.95 (40.04, 518.77)	73.39 (25.36, 230.77)	310.40 (110.73, 848.36)		57.50 (19.73, 89.71)	399.78 (171.22, 915.71)

All biomarker concentrations are in pg/ml. GFAP, Glial fibrillary acidic protein; UCH-L1, ubiquitin carboxyl-terminal esterase- L1; NfL, neurofilament light

B. Day 2

Median (interquartile range)	Overall N=120	Favorable N=70	Unfavorable N=50	p-value	VABS < 70 N=7	Dead N=43
NFL	n=104	n=61	n=43	<0.001	n=6	n=37
	75.45 (20.08, 299.66)	31.17 (13.15, 88.67)	287.26 (78.23, 898.47)		147.04 (66.09, 1169.23)	303.00 (126.50, 786.34)
Tau	n=104	n=61	n=43	<0.001	n=6	n=37
	15.17 (2.40, 108.41)	5.04 (1.34, 20.23)	99.59 (10.09, 702.00)		24.46 (1.83, 102.81)	114.00 (10.15, 1296.00)
GFAP	n=104	n=61	n=43	<0.001	n=6	n=37
	342.01 (139.43, 1912.20)	162.39 (104.46, 361.89)	1515.27 (386.16, 16470.00)		407.60 (283.30, 8109.00)	1575.70 (584.00, 16470.00)
UCH-L1	n=104	n=61	n=43	<0.001	n=6	n=37
	94.18 (32.80, 285.75)	51.31 (22.85, 98.31)	319.10 (163.24, 2129.17)		194.52 (27.30, 292.52)	410.87 (172.72, 3163.00)

All biomarker concentrations are in pg/ml. GFAP, Glial fibrillary acidic protein; UCH-L1, ubiquitin carboxyl-terminal esterase- L1; NfL, neurofilament light

C. Day 3

Median (interquartile range)	Overall N=120	Favorable N=70	Unfavorable N=50	p-value	VABS < 70 N=7	Dead N=43
NFL	n=94	n=55	n=39	<0.001	n=6	n=33
	177.60 (35.33, 469.38)	60.63 (23.59, 217.99)	490.88 (136.52, 1512.99)		232.58 (95.99, 1359.43)	528.00 (199.87, 1512.99)
Tau	n=94	n=55	n=39	<0.001	n=6	n=33
	15.44 (2.63, 103.01)	6.92 (1.78, 29.16)	97.65 (4.33, 964.00)		103.07 (2.12, 178.22)	93.30 (8.32, 964.00)
GFAP	n=93	n=55	n=38	<0.001	n=6	n=32
	334.30 (150.55, 5205.00)	166.21 (98.36, 404.55)	2736.71 (368.75, 12812.05)		1599.75 (347.03, 7303.49)	3543.37 (382.99, 17253.52)
UCH-L1	n=93	n=55	n=38	<0.001	n=5	n=33
	117.72 (32.75, 344.54)	49.67 (21.43, 133.10)	357.36 (188.96, 1737.00)		341.60 (16.57, 358.88)	389.02 (192.96, 1737.00)

All biomarker concentrations are in pg/ml. GFAP, Glial fibrillary acidic protein; UCH-L1, ubiquitin carboxyl-terminal esterase- L1; NfL, neurofilament light

P-value, Kruskal-Wallis test, Favorable vs. Unfavorable Outcome

VABS, Vineland Adaptive Behavior Scales

eTable 3. Biomarker Area Under the Receiver Operating Characteristic Curves (AUROCs), Specificity, Threshold (pg/mL), and Sensitivity on Univariate Biomarker Models, With Set Specificity of 95% for Favorable vs Unfavorable Outcome

A. Day 1

Model	AUROC	Specificity (95%CI)	Threshold level		Sensitivity (95%CI)	Patients, N (%)				
			(pg/mL)	Base 10 logarithm		True Positive	False Negative	False Positive	True Negative	Total
NFL	0.731 (0.624, 0.820)	0.957 (0.880, 0.991)	184.00	2.26	0.250 (0.136, 0.396)	12 (10.17)	36 (30.51)	3 (2.54)	67 (56.78)	118
Tau	0.704 (0.646, 0.831)	0.957 (0.880, 0.991)	111.75	2.05	0.333 (0.204, 0.484)	16 (13.56)	32 (27.12)	3 (2.54)	67 (56.78)	118
GFAP	0.670 (0.571, 0.768)	0.957 (0.880, 0.991)	129544.00	5.11	0.043 (0.005, 0.143)	2 (1.69)	46 (38.98)	3 (2.54)	67 (56.78)	118
UCH-L1	0.708 (0.614, 0.803)	0.957 (0.878, 0.991)	2319.00	3.37	0.146 (0.061, 0.278)	7 (5.98)	41 (35.04)	3 (2.56)	66 (56.41)	117

Biomarkers on base-10 logarithm scale.

B. Day 2

Model	AUROC	Specificity (95%CI)	Threshold level		Sensitivity (95%CI)	Patients, N (%)				
			(pg/mL)	Base 10 logarithm		True Positive	False Negative	False Positive	True Negative	Total
NFL	0.857 (0.788, 0.926)	0.951 (0.863, 0.990)	389.01	2.59	0.442 (0.291, 0.601)	19 (18.27)	24 (23.08)	3 (2.88)	58 (55.77)	104
Tau	0.780 (0.687, 0.874)	0.951 (0.863, 0.990)	240.15	2.38	0.395 (0.259, 0.556)	17 (16.35)	26 (25.00)	3 (2.88)	58 (55.77)	104
GFAP	0.795 (0.707, 0.883)	0.951 (0.863, 0.990)	92690.00	4.97	0.12 (0.04, 0.25)	5 (4.81)	38 (36.54)	3 (2.88)	58 (55.77)	104
UCH-L1	0.860 (0.785, 0.935)	0.948 (0.856, 0.989)	276.15	2.44	0.581 (0.421, 0.730)	25 (24.75)	18 (17.82)	3 (2.97)	55 (54.46)	101

Biomarkers on base-10 logarithm scale.

C. Day 3

Model	AUROC	Specificity (95%CI)	Threshold level		Sensitivity (95%CI)	Patients, N (%)				
			(pg/mL)	Base 10 logarithm		True Positive	False Negative	False Positive	True Negative	Total
NFL	0.824 (0.742, 0.907)	0.946 (0.849, 0.989)	490.88	2.69	0.513 (0.348, 0.676)	20 (21.28)	19 (20.21)	3 (3.19)	52 (55.32)	94
Tau	0.752 (0.647, 0.857)	0.946 (0.849, 0.989)	108.48	2.04	0.487 (0.324, 0.652)	19 (20.21)	20 (21.28)	3 (3.19)	52 (55.32)	94
GFAP	0.807 (0.716, 0.897)	0.946 (0.849, 0.989)	40040.00	4.60	0.211 (0.096, 0.373)	8 (8.60)	30 (32.26)	3 (3.23)	52 (55.91)	93
UCH-L1	0.837 (0.747, 0.926)	0.962 (0.870, 0.995)	341.60	2.53	0.605 (0.434, 0.760)	23 (25.27)	15 (16.48)	2 (2.20)	51 (56.04)	91

Biomarkers on base-10 logarithm scale.

eTable 4. Univariate Logistic Regression Models for Favorable or Unfavorable Outcome at 1 Year by Blood-Based Brain Injury Biomarker on Post–Cardiac Arrest Days 1, 2, and 3

A. Neurofilament light

	Day 1		Day 2		Day 3	
	Odds Ratio	95% Wald CI	Odds Ratio	95% Wald CI	Odds Ratio	95% Wald CI
Neurofilament light, log pg/ml	4.23	2.12, 8.45	11.55	4.52, 29.54	7.76	3.22, 18.69
Age, years	0.98	0.92, 1.04	0.98	0.92, 1.04	0.98	0.92, 1.04
Male vs Female sex	0.92	0.44, 1.93	0.92	0.44, 1.93	0.92	0.44, 1.93
Non-White vs White Race	0.82	0.38, 1.79	0.82	0.38, 1.79	0.82	0.38, 1.79
Cardiac vs Asphyxia etiology	0.89	0.38, 2.07	0.89	0.38, 2.07	0.89	0.38, 2.07
In-hospital vs Out of hospital event	0.24	0.11, 0.52	0.24	0.11, 0.52	0.24	0.11, 0.52
Witnessed	0.09	0.03, 0.26	0.09	0.03, 0.26	0.09	0.03, 0.26
Bystander resuscitation	3.38	1.54, 7.41	3.38	1.54, 7.41	3.38	1.54, 7.41
Extracorporeal membrane oxygenation	0.72	0.30, 1.73	0.72	0.30, 1.73	0.72	0.30, 1.73
Pediatric Index of Mortality score	2.10	1.53, 2.89	2.10	1.53, 2.89	2.10	1.53, 2.89
TTM used for prevention of fever	2.47	1.07, 5.68	2.47	1.07, 5.68	2.47	1.07, 5.68
TTM used for therapeutic hypothermia	0.31	0.08, 1.16	0.31	0.08, 1.16	0.31	0.08, 1.16

TTM, targeted temperature management; CI, confidence interval; NA, not applicable

B. Ubiquitin carboxyl-terminal esterase- L1

	Day 1		Day 2		Day 3	
	Odds Ratio	95% Wald CI	Odds Ratio	95% Wald CI	Odds Ratio	95% Wald CI
Ubiquitin carboxyl-terminal esterase- L1, log pg/ml	2.85	1.61, 5.05	16.32	5.13, 51.92	7.14	2.90, 17.60
Age, years	0.98	0.92, 1.04	0.98	0.92, 1.04	0.98	0.92, 1.04
Male vs Female sex	0.92	0.44, 1.93	0.92	0.44, 1.93	0.92	0.44, 1.93
Non-White vs White Race	0.82	0.38, 1.79	0.82	0.38, 1.79	0.82	0.38, 1.79
Cardiac vs Asphyxia etiology	0.89	0.38, 2.07	0.89	0.38, 2.07	0.89	0.38, 2.07
In-hospital vs Out of hospital event	0.24	0.11, 0.52	0.24	0.11, 0.52	0.24	0.11, 0.52
Witnessed	0.09	0.03, 0.26	0.09	0.03, 0.26	0.09	0.03, 0.26
Bystander resuscitation	3.38	1.54, 7.41	3.38	1.54, 7.41	3.38	1.54, 7.41
Extracorporeal membrane oxygenation	0.72	0.30, 1.73	0.72	0.30, 1.73	0.72	0.30, 1.73
Pediatric Index of Mortality score	2.10	1.53, 2.89	2.10	1.53, 2.89	2.10	1.53, 2.89
TTM used for prevention of fever	2.47	1.07, 5.68	2.47	1.07, 5.68	2.47	1.07, 5.68
TTM used for therapeutic hypothermia	0.31	0.08, 1.16	0.31	0.08, 1.16	0.31	0.08, 1.16

TTM, targeted temperature management; CI, confidence interval; NA, not applicable

C. Glial fibrillary acidic protein

	Day 1		Day 2		Day 3	
	Odds Ratio	95% Wald CI	Odds Ratio	95% Wald CI	Odds Ratio	95% Wald CI
Glial fibrillary acidic protein, log pg/ml	1.69	1.11, 2.57	2.57	1.60, 4.14	2.74	1.66, 4.50
Age, years	0.98	0.92, 1.04	0.98	0.92, 1.04	0.98	0.92, 1.04
Male vs Female sex	0.92	0.44, 1.93	0.92	0.44, 1.93	0.92	0.44, 1.93
Non-White vs White Race	0.82	0.38, 1.79	0.82	0.38, 1.79	0.82	0.38, 1.79
Cardiac vs Asphyxia etiology	0.89	0.38, 2.07	0.89	0.38, 2.07	0.89	0.38, 2.07
In-hospital vs Out of hospital event	0.24	0.11, 0.52	0.24	0.11, 0.52	0.24	0.11, 0.52
Witnessed	0.09	0.03, 0.26	0.09	0.03, 0.26	0.09	0.03, 0.26
Bystander resuscitation	3.38	1.54, 7.41	3.38	1.54, 7.41	3.38	1.54, 7.41
Extracorporeal membrane oxygenation	0.72	0.30, 1.73	0.72	0.30, 1.73	0.72	0.30, 1.73
Pediatric Index of Mortality score	2.10	1.53, 2.89	2.10	1.53, 2.89	2.10	1.53, 2.89
TTM used for prevention of fever	2.47	1.07, 5.68	2.47	1.07, 5.68	2.47	1.07, 5.68
TTM used for therapeutic hypothermia	0.31	0.08, 1.16	0.31	0.08, 1.16	0.31	0.08, 1.16

TTM, targeted temperature management; CI, confidence interval; NA, not applicable

D. Tau

	Day 1		Day 2		Day 3	
	Odds Ratio	95% Wald CI	Odds Ratio	95% Wald CI	Odds Ratio	95% Wald CI
Tau, log pg/ml	2.97	1.78, 4.96	3.03	1.88, 4.90	2.59	1.63, 4.12
Age, years	0.98	0.92, 1.04	0.98	0.92, 1.04	0.98	0.92, 1.04
Male vs Female sex	0.92	0.44, 1.93	0.92	0.44, 1.93	0.92	0.44, 1.93
Non-White vs White Race	0.82	0.38, 1.79	0.82	0.38, 1.79	0.82	0.38, 1.79
Cardiac vs Asphyxia etiology	0.89	0.38, 2.0)	0.89	0.38, 2.07	0.89	0.38, 2.07
In-hospital vs Out of hospital event	0.24	0.11, 0.52	0.24	0.11, 0.52	0.24	0.11, 0.52
Witnessed	0.09	0.03, 0.26	0.09	0.03, 0.26	0.09	0.03, 0.26
Bystander resuscitation	3.38	1.54, 7.41	3.38	1.54, 7.41	3.38	1.54, 7.41
Extracorporeal membrane oxygenation	0.72	0.30, 1.73	0.72	0.30, 1.73	0.72	0.30, 1.73
Pediatric Index of Mortality score	2.10	1.53, 2.89	2.10	1.53, 2.89	2.10	1.53, 2.89
TTM used for prevention of fever	2.47	1.07, 5.68	2.47	1.07, 5.68	2.47	1.07, 5.68
TTM used for therapeutic hypothermia	0.31	0.08, 1.16	0.31	0.08, 1.16	0.31	0.08, 1.16

TTM, targeted temperature management; CI, confidence interval; NA, not applicable

eTable 5. Multivariate Area Under the Receiver Operating Characteristic Curves (AUROCs) With and Without Individual Biomarkers on Days 1, 2, and 3

Day post-cardiac arrest, biomarker	AUROC with biomarker ^a	AUROC without biomarker ^a	p-value ^b
Day 1, NfL	0.912	0.886	0.162
Day 1, UCH-L1	0.894	0.886	0.496
Day 1, GFAP	0.893	0.886	0.338
Day 1, Tau	0.895	0.886	0.579
Day 2, NfL	0.932	0.871	0.017
Day 2, UCH-L1	0.918	0.875	0.055
Day 2, GFAP	0.890	0.871	0.250
Day 2, Tau	0.895	0.871	0.248
Day 3, NfL	0.921	0.870	0.034
Day 3, UCH-L1	0.904	0.867	0.165
Day 3, GFAP	0.899	0.865	0.069
Day 3, Tau	0.881	0.870	0.534

NfL, Neurofilament light; UCH-L1, Ubiquitin carboxyl-terminal esterase- L1; GFAP, Glial fibrillary acidic protein

^a p<.2, after adjusting for age, sex, race, etiology, location, witnessed, bystander status, ECMO, severity of illness (PIM3), TTM for fever or hypothermia

^b Chi-square analysis of AUROC between models with and without biomarker

eTable 6. Comparison of Patient and Cardiac Arrest Characteristics Among Children With and Without Data Available on 1 Year Outcomes

N (%) or Median (interquartile range)	One year outcome obtained N=120	One year outcome not obtained N=43	p-value
Age, y	1.0 (0.0, 8.5)	3.0 (1.0, 10.0)	0.039
Sex			0.590
Female	49 (40.8)	20 (46.5)	
Male	71 (59.2)	33 (53.5)	
Race	n=120	n=43	<.001
Asian	5 (4.2)	0 (0)	
Black	19 (15.8)	17 (39.5)	
White	81 (67.5)	23 (53.5)	
Unknown	15 (12.5)	3 (7.0)	
Hispanic Ethnicity	11 (10.0), n=110	3 (7.1), n=42	0.759
Pre-existing conditions ¹	77 (68.1), n=113	26 (60.5), n=43	0.450
Cardiovascular	45 (37.8), n=119	6 (14.0), n=43	0.004
Pulmonary disease	25 (20.8), n=120	10 (23.3), n=43	0.829
Premature birth	24 (21.8), n=110	6 (15.4), n=39	0.489
Congenital syndrome	14 (11.8), n=119	4 (9.3), n=43	0.783
Neurologic	11 (9.2), n=120	4 (9.3), n=43	1.000
Oncologic syndrome	3 (2.5), n=120	1 (2.3), n=43	1.000
Organ or cellular transplant	3 (2.5), n=119	1 (2.3), n=43	1.000
Primary etiology	n=107	n=41	0.091
Asphyxia	74 (69.2)	34 (82.9)	
Cardiac	33 (30.8)	7 (17.1)	
Location, out of hospital	60 (50.0)	30 (69.8)	0.032
Duration of cardiopulmonary resuscitation, minutes	7.00 (3.00, 20.00), n=99	7.00 (2.00, 17.00), n=33	0.596
Total number of epinephrine doses	1.0 (0.0, 3.0), n=100	0.0 (0.0, 2.0), n=37	0.031
Defibrillated	18 (17.8), n=101	7 (18.4), n=38	1.000
First monitored rhythm	n=96	n=28	0.030
Sinus bradycardia	33 (34.4)	11 (39.3)	
Pulseless electrical activity	23 (24.0)	6 (21.4)	

Asystole	19 (19.8)	1 (3.6)	
Ventricular tachycardia or fibrillation	15 (15.6)	3 (10.7)	
Sinus tachycardia/Junctional ectopic tachycardia	4 (4.2)	3 (10.7)	
Normal sinus rhythm	2 (2.1)	4 (14.3)	
Witnessed	92 (76.7)	29 (67.4)	0.309
Bystander resuscitation	42 (35.0)	23 (53.5)	0.045
Hospital length of stay, d	18.0 (6.5, 35.5), n=120	10.0 (6.0, 20.0), n=42	0.033
Intensive care unit length of stay, d	12.0 (5.0, 25.0), n=117	8.0 (2.5, 11.0), n=40	0.002
Disposition at hospital discharge	n=120	n=42	<.001
Home	55 (45.8)	33 (78.6)	
Died	41 (34.2)	0 (0)	
Inpatient rehabilitation	17 (14.2)	6 (14.3)	
Transfer to other hospital	2 (1.7)	3 (7.1)	
Long-term care facility	5 (4.2)	0 (0)	
Days from cardiac arrest event to death	10 (3, 25), n=43	NA	
Cause of death	n=43	n=0	
Multiple Organ Failure	13 (30.2)	NA	
Brain death	11 (25.6)	NA	
Neurologic injury	11 (25.6)	NA	
Cardiovascular	8 (18.6)	NA	

¹Children may have more than one pre-existing condition

p-value are based on Chi-square test for categorical variables, Kruskal-Wallis test for median