RISK FACTORS FOR ELECTROENCEPHALOGRAPHIC SEIZURES IN NEONATES FOLLOWING SURGERY WITH CARDIOPULMONARY BYPASS

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CARDIOLOGY 2023

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DISCLOSURES

None

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BACKGROUND

The New England
Journal of Medicine

Volume 329 OCTOBER 7, 1993 Number 15

Clinical seizure incidence 11%
Electroencephalographic (EEG) seizure incidence 26%

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BACKGROUND

The New England
Journal of Medicine

Volume 329 OCTOBER 7, 1993 Number 15

EEG analysis was not performed in real time
Only clinical seizures were treated

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BACKGROUND

Pediatric Cardiology

Seizures most important predictor of adverse neurodevelopmental outcomes including math scores, general memory, executive function score

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BACKGROUND – DOES TREATMENT MATTER?

Circulation

Developmental and Neurological Status of Children at 4 Years of Age After Heart Surgery With Hypothermic Circulatory Arrest or Low-Flow Cardiopulmonary Bypass

David C. Bellinger, PhD, MSc; David Wypij, PhD; Karl C. K. Kuban, MD, MSc; Leonard A. Rappaport, MD; Paul R. Hickey, MD; Gil Wernovsky, MD; Richard A. Jonas, MD; Jane W. Newburger, MD, MPH

BACKGROUND

TABLE 5. Associations Between Seizure Status and Developmental, Neurological, and Speech Outcomes

	Clinical Seizures			EEG Seizures		
Continuous Outcomes	Mean Deficit*	95% Confidence Interval	*P*	Mean Deficit	95% Confidence Interval	*P*
Full-Scale IQ	12.6	(3.8,21.4)	0.005	7.7	(1.8,13.7)	0.01
Verbal IQ	13.4	(4.1,22.6)	0.005	7.4	(1.0,13.8)	0.02
Performance IQ	7.8	(−0.9,16.5)	0.08	6.6	(0.7,12.5)	0.03
Gross motor scale	8.6	(−5.4,22.7)	0.22	6.9	(−1.5,15.4)	0.11
Fine motor scale	2.1	(−6.1,10.3)	0.62	4.8	(−0.1,9.6)	0.052
Dichotomous Outcomes	Odds Ratio†	95% Confidence Interval	*P*	Odds Ratio	95% Confidence Interval	*P*
Possible or definite neurological abnormalities	8.4	(1.0,71.5)	0.05	5.6	(1.7,18.8)	0.005
Apraxia of speech	5.0	(0.7,35.0)	0.10	3.3	(0.9,12.2)	0.07

*Mean deficits, 95% confidence intervals, and *P* values are for effects of seizures, with adjustment for treatment group, diagnosis, and social class. Adjustment was also made for child's age at testing in analysis of Peabody Developmental Motor Scales.

†Odds ratios, 95% confidence intervals, and *P* values are for effects of seizures, with adjustment for treatment group and diagnosis.

BACKGROUND

Postoperative electroencephalographic seizures are associated with deficits in executive function and social behaviors at 4 years of age following cardiac surgery in infancy

J. William Gaynor, MD,[a] Gail P. Jarvik, MD, PhD,[b] Marsha Gerdes, PhD,[c] Daniel S. Kim, BS,[b] Ramakrishnan Rajagopalan, MS,[b] Judy Bernbaum, MD,[d] Gil Wernovsky, MD,[e] Susan C. Nicolson, MD,[f] Thomas L. Spray, MD,[a] and Robert R. Clancy, MD[g]

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TABLE 3. Linear regression

Outcome	All (N = 130)*		HLHS (N = 39)	
	β	*P* value	β	*P* value
Math skills	−2.960	.597	−17.430	.226
Impulsivity	1.095	.555	2.51	.699
Attention	0.812	.622	4.256	.364
Restricted/repetitive behaviors	1.984	.057	**6.980**	**.050**
Social skills	−1.814	.632	−17.844	.084

Treatment of seizures may have resulted in improved neurodevelopmental outcomes

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BACKGROUND

Treating EEG Seizures in Hypoxic Ischemic Encephalopathy: A Randomized Controlled Trial

Preethi Srinivasakumar, MD[a], John Zempel, MD, PhD[b], Shamik Trivedi, MD[a], Michael Wallendorf, PhD[c], Rakesh Rao, MD[a], Barbara Smith, R.EEG T[d], Terrie Inder, MD[e], Amit M. Mathur, MD[a]

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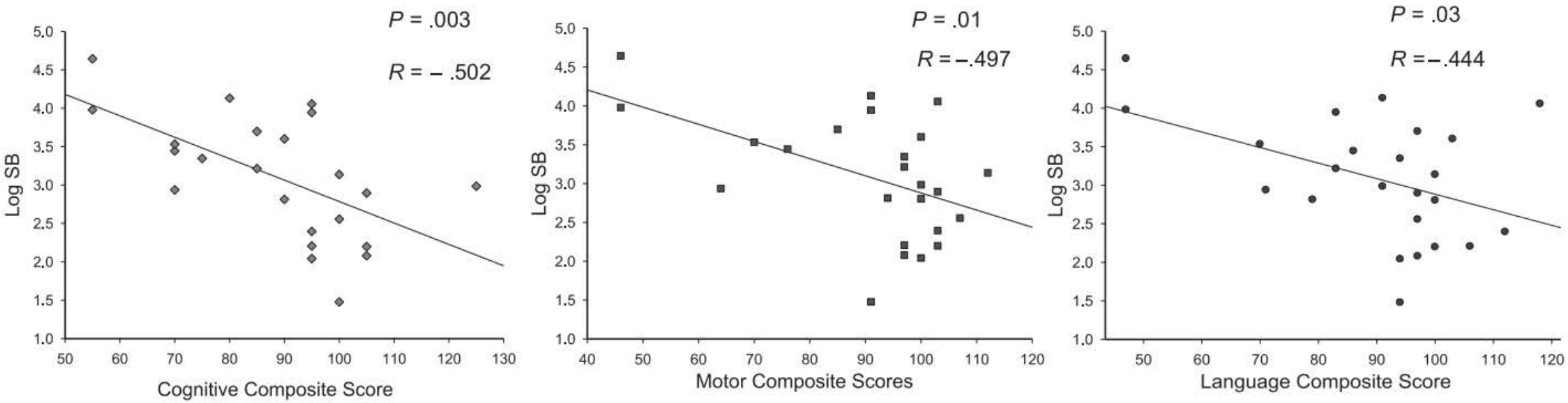

FIGURE 3

Correlation between electrographic SB and performance scores on BSID III. X-axis: Cognitive, motor, and language composite scores (BSID III); Y-axis: Log units of electrographic SB.

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BACKGROUND

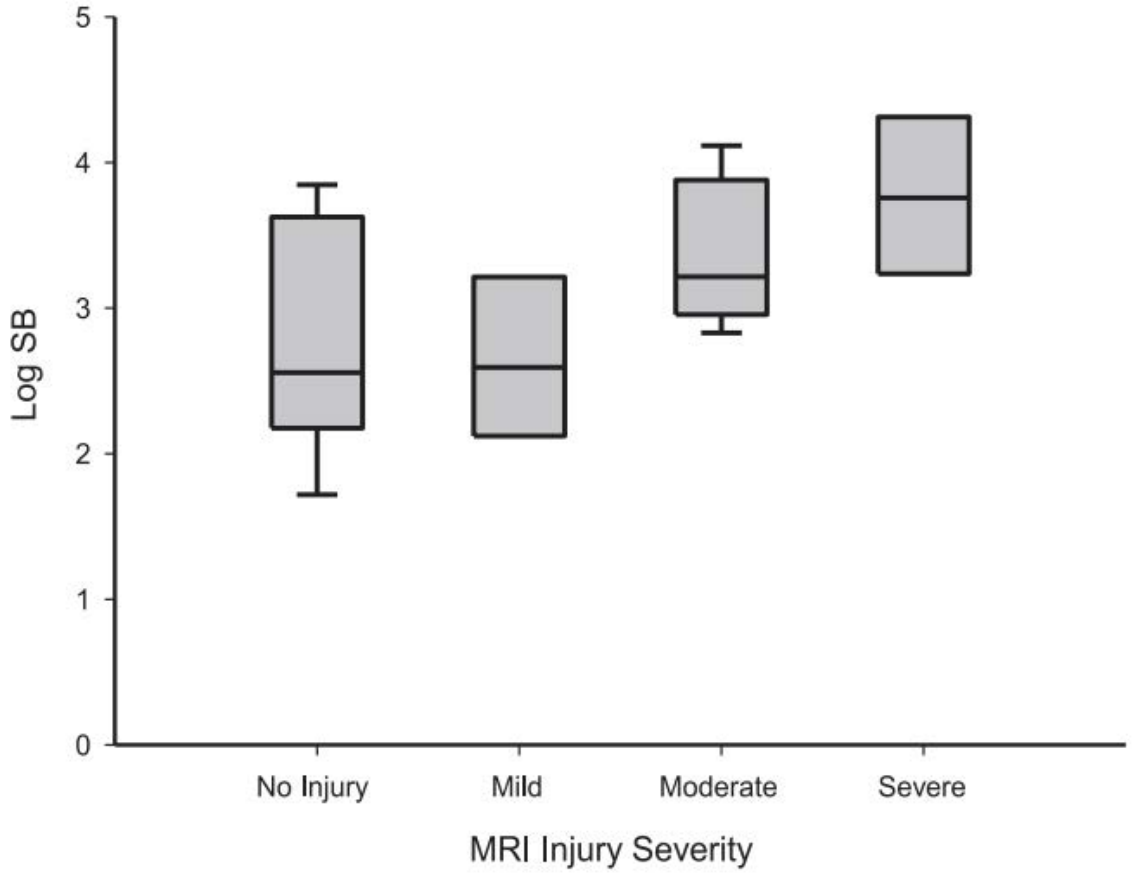

FIGURE 4
Overall trend of electrographic SB and severity of brain injury on MRI in the cohort. X-axis: Severity of brain injury on MRI; Y-axis: Log units of electrographic SB, $P < .03$ (no injury/mild versus moderate–severe).

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BACKGROUND

RISK FACTORS FOR SEIZURES

Preoperative ***Operative*** ***Postoperative***

Genetic syndrome
Lower APGAR
Gestational Age

DHCA
RCP
CPB duration
Open sternum

Cardiac arrest
ECMO

Seizures

DHCA, deep hypothermic circulatory arrest; RCP, regional cerebral perfusion; ECMO, extracorporeal membrane oxygenation

Helmes 1997, Clancy 2003, Gaynor 2005, Naim 2015, Topjian 2016, Lin 2017

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BACKGROUND

The American Clinical Neurophysiology Society recommends EEG monitoring in neonates undergoing cardiac surgery requiring CPB

At CHOP, we have been routinely monitoring patients on EEG post operatively since June 2012

Shellhaas 2011

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OBJECTIVE AND HYPOTHESIS

Objective: Determine seizure incidence and identify pre-operative and operative risk factors for seizures in neonates following CPB undergoing EEG monitoring

Hypothesis: There will be non-modifiable and modifiable risk factors associated with post-operative seizure risk

METHODS

Retrospective, single center cohort study of neonates (corrected gestational age < 44 weeks) undergoing surgery with CPB from June 2012 to May 2022

Exclusion criteria:

- Cardiac surgery done off bypass
- EEG monitoring not performed in the post operative period
- Underwent surgery not categorized by STAT classification

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METHODS

Patients monitored on EEG for 48 hours post-operatively

Neonatal EEG seizure defined as a sudden, abnormal EEG event defined by a repetitive and evolving pattern with an amplitude of at least 2 μV and duration of at least ten seconds

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METHODS

Univariable and multivariable analysis performed

Variables with significant P value on univariable analysis included in initial multivariable model

Multicollinearity assessed with variance inflation factor. Backward selection used to select variables in final model.

P value < 0.05 considered significant

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PATIENT DEMOGRAPHICS

N = 1080 neonates:

- 59% male
- 58% white,12% black, 30% other
- Median birth weight 3.2 kg (IQR 2.8, 3.5)
- Median gestational age 39 weeks (IQR 38.0,39.3)
- 82% prenatal diagnosis
- 17% preterm neonates <37 weeks gestational age
- 18% with identified genetic defects

RESULTS

Overall seizure incidence 9.4%

86% of patients with seizures had subclinical seizures

23% of patients with seizures had status epilepticus

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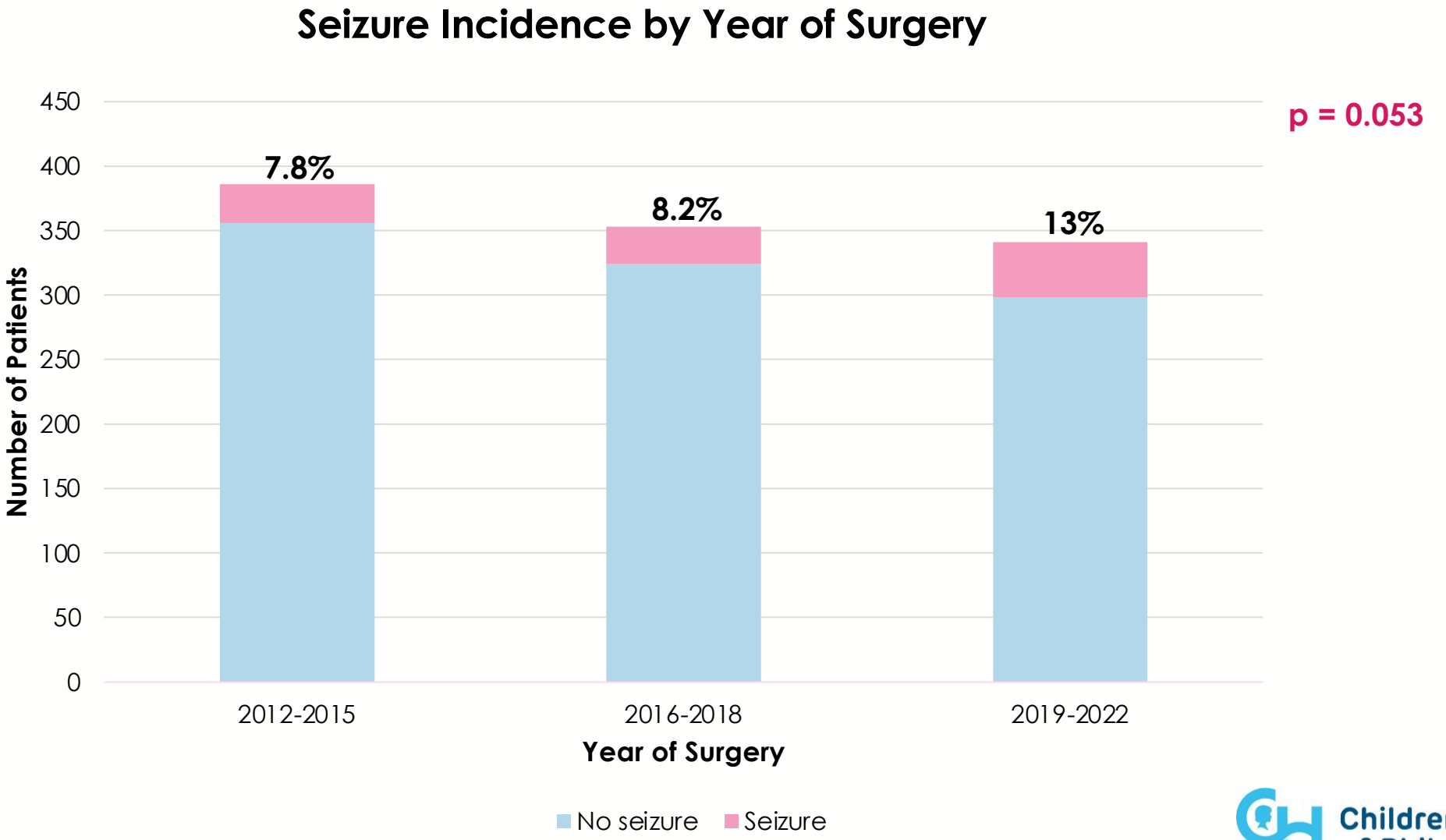
RESULTS – UNIVARIATE ANALYSIS

Pre-operative risk factors for seizures ($p < 0.05$):

- Decreasing gestational age
- Decreased head circumference
- Volume expansion at birth
- Need for urgent cardiac intervention at birth
- Single ventricle physiology
- Pre-operative seizures

RESULTS – UNIVARIATE ANALYSIS



p = 0.053

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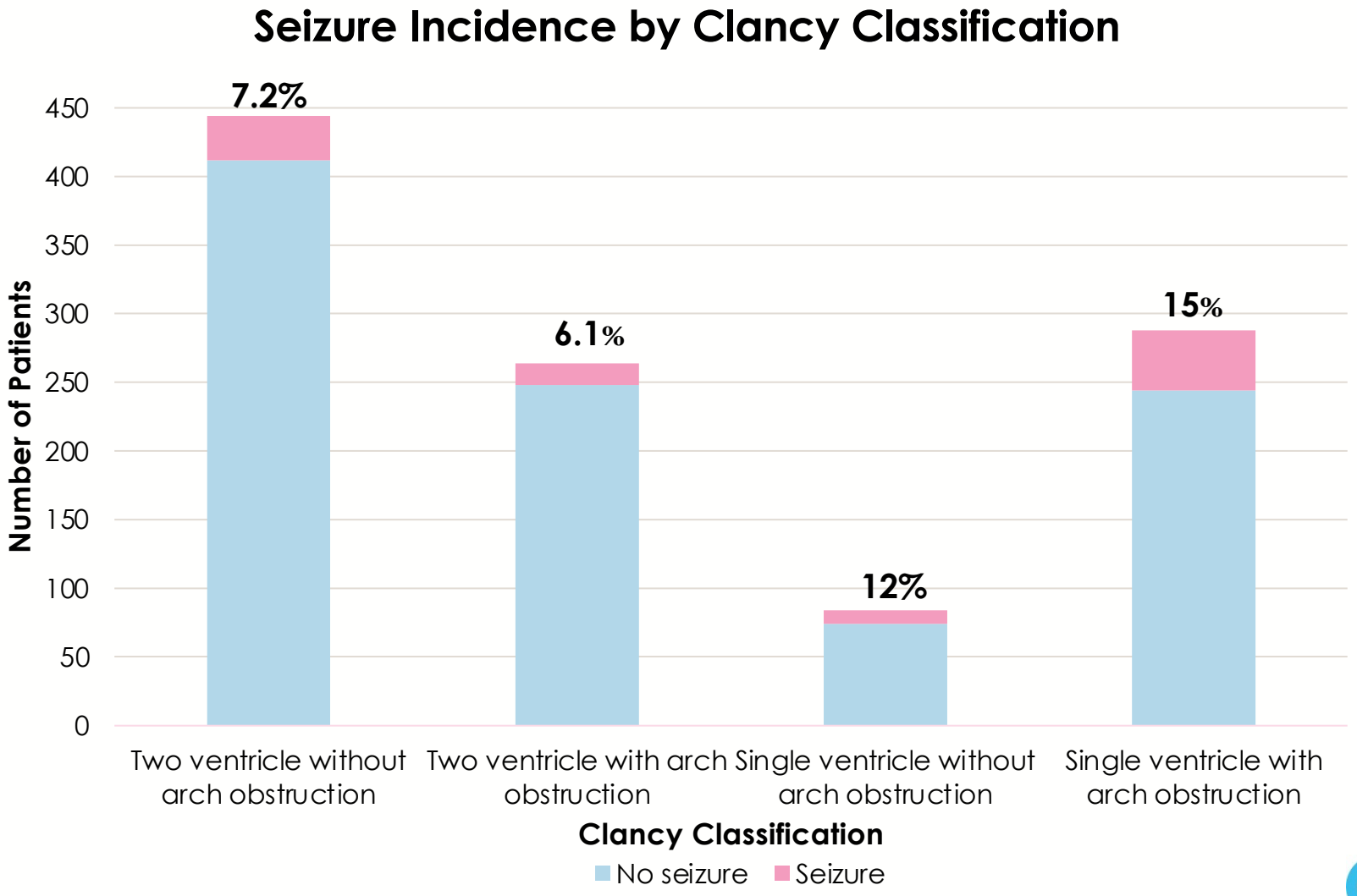
RESULTS – UNIVARIATE ANALYSIS



$p < 0.001$

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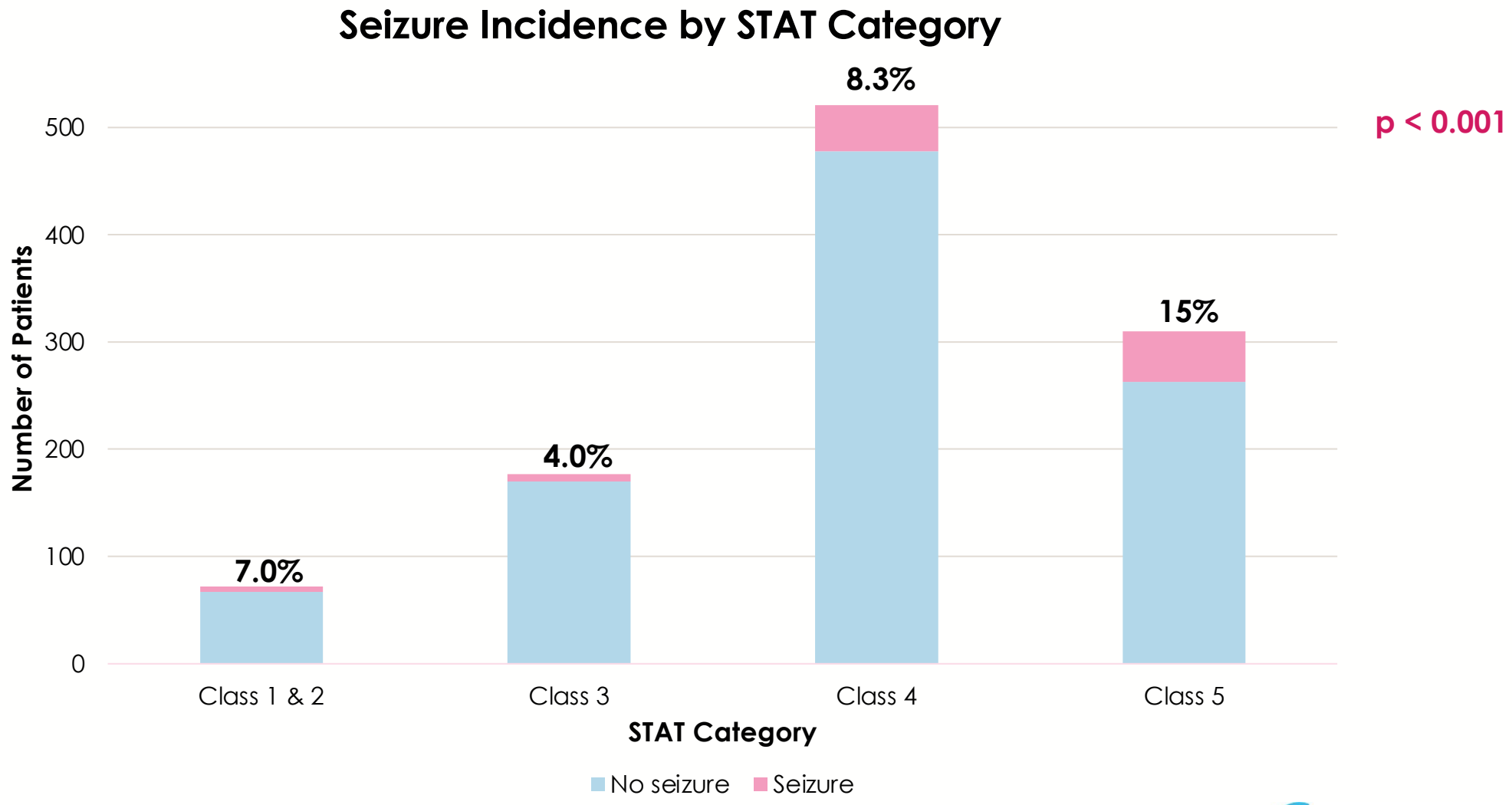
RESULTS – UNIVARIATE ANALYSIS



$p < 0.001$

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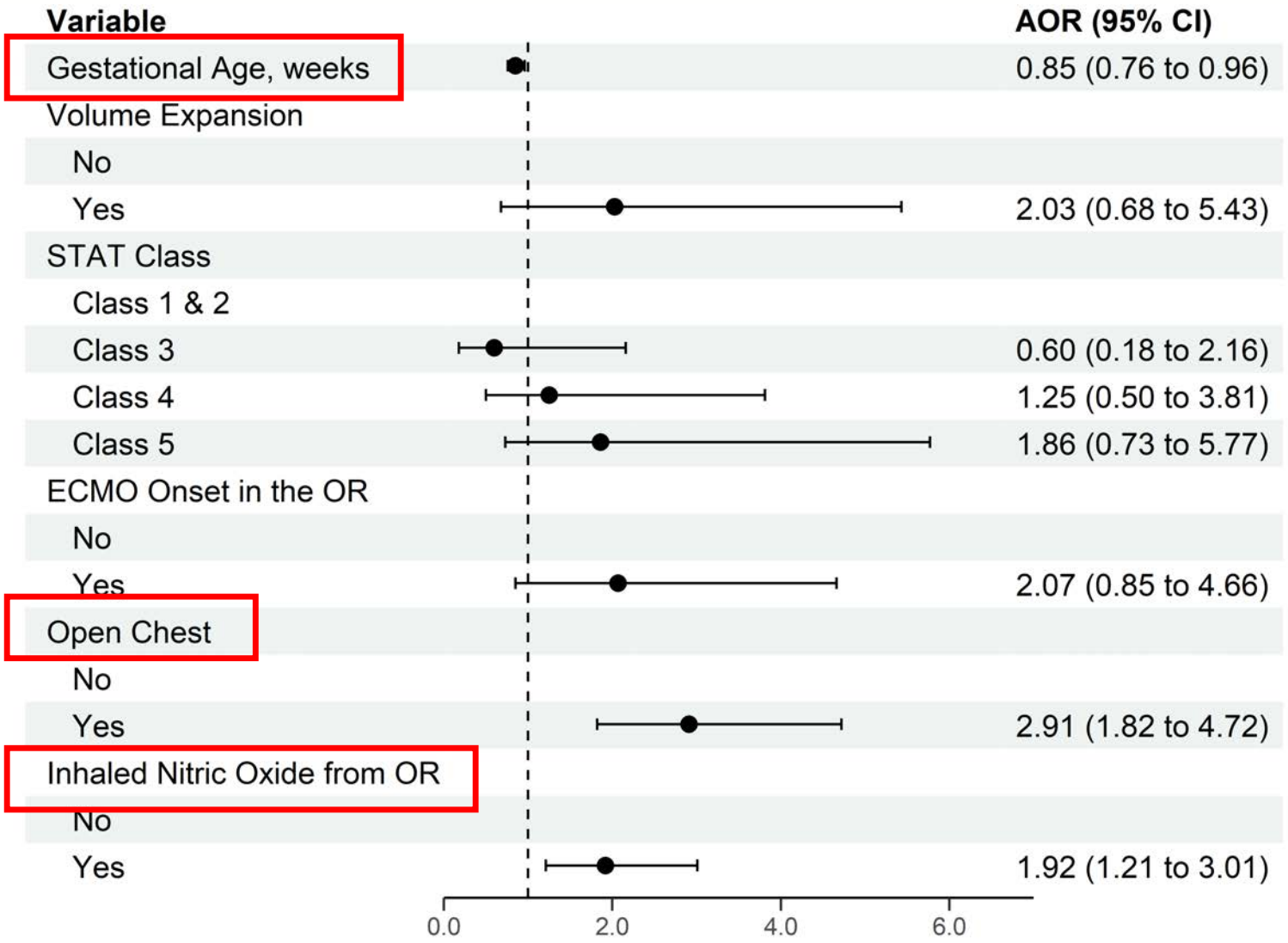
RESULTS – UNIVARIATE ANALYSIS

Operative risk factors for seizures ($p < 0.05$):

- Lower temperature on bypass
- Deep hypothermic circulatory arrest (DHCA) duration
- Use of regional cerebral perfusion (RCP)
- CPB duration
- Total support time
- Open sternum
- Inhaled nitric oxide (iNO) initiated in operating room (OR)
- ECMO in OR

RESULTS – MULTIVARIATE ANALYSIS



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RESULTS – OUTCOMES

Median length of cardiac intensive care unit (CICU) stay longer in patients with seizures (22 days versus 12 days, $p < 0.001$)

Total hospital length of stay longer in patients with seizures (35 days versus 20 days, $p < 0.001$)

Mortality higher in patients with seizures (27% versus 4%, $p < 0.001$)

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CONCLUSIONS

Over the past 10 years, post operative EEG seizure incidence is 9.4%

Risk factors for postoperative EEG seizures include decreasing gestational age, open sternum, use of nitric oxide in the OR

Seizures associated with longer duration of cardiac intensive care unit length of stay and higher mortality

The majority of seizures were subclinical and would not have been identified without routine post-operative EEG monitoring

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FUTURE DIRECTIONS

Focused comparison of patients undergoing DHCA compared to RCP

Impact of status epilepticus, seizure duration, and time to treatment on patient outcomes

Correlation of seizures with abnormalities in neuroimaging

Long term neurodevelopmental follow up

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ACKNOWLEDGEMENTS

CHOP Cardiac Center